A Publication of the Facioscapulohumeral Muscular Dystrophy Society

FSH Watch INCLUDING DONORS 2009

CONNECTING THE COMMUNITY OF PATIENTS, FAMILIES, CLINICIANS AND INVESTIGATORS

CLINICAL MANAGEMENT

Breathing and respiration in neuromuscular disease

by JOSHUA BENDITT, M.D.
Professor of Medicine, and Director, Respiratory Care Services, University of Washington Medical Center, Seattle

Breathing disorders are now recognized as the leading cause of mortality in neuromuscular disease. A wide variety of neuromuscular disorders result in weakness of the respiratory muscles that in turn can lead to respiratory failure, pneumonia and even death – this includes FSHD. Fortunately, a number of noninvasive (no tracheostomy) methods of breathing support are available to individuals with neuromuscular disease. This is largely due to rapid and progressive advances in pulmonary medicine and medical device technology. Thankfully, appropriate intervention prevents complications and today can prolong the lives of individuals with neuromuscular disease affecting the respiratory system.

FSH muscular dystrophy is an autosomal dominant genetic disease that causes muscle weakness of the facial, shoulder and arm as well as the pelvic girdle and leg muscles. Weakness can affect the breathing muscle and in one of the best studies of 53 patients with FSHD over 10 years, published in 1995, 50% of the patients had evidence of muscle weakness on pulmonary function testing (office breathing measurements), 13% had severe involvement and about 22% had a history of some breathing system

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Participants at the 2009 International Research Consortium. Daniel Paul Perez, FSH Society, Inc., front left and Charles P. Emerson, Jr., Ph.D., BBRI front right.

RESEARCH

FSH Society and Boston Biomedical Research Institute host international conference on most prevalent form of muscular dystrophy

Daniel Paul Perez, President & CEO, FSH Society, Inc., organized the two-day event

by PATTI JACOBS

Scientists, clinicians, patients, advocates, and biotech and pharmaceutical companies, as well as clinicians from throughout the world gathered at Boston Biomedical Research Institute (BBRI) in Watertown, Massachusetts in November to attend the FSH Society 2009 International Research Consortium and Research Planning Meetings for FSHD. Daniel Paul Perez, President and CEO of the FSH Society, Kathryn Wagner, M.D., Ph.D., Kennedy Krieger Institute and The Johns Hopkins University School of Medicine, and Silvère van der Maarel, Ph.D., Leiden University Medical Center, the Netherlands, and Co-Director of the Fields Center at the University of Rochester, organized the meetings which focused on collaborating to find new treatments and a cure for FSHD, which is the most common adult form of muscular dystrophy and affects one in 14,000 individuals.

According to Perez, "These were two very productive days. I believe we have set an important common agenda for future work together to find a solution for this illness. I was pleased to see the significant progress in national funding and in the research domain for FSHD.

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WHAT'S INSIDE

FSH Watch
WINTER 2010

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LETTER FROM THE EXECUTIVE DIRECTOR

Dear Friends,

By now, you have received the program and registration for the FSH Society 2010 **International Patient and Researcher Network Meeting,** Friday-Sunday, July 30-August 1, 2010.

Sponsored by the FSH Society, the meeting is a partnership among patients, families, clinicians and scientists. It will include lectures by and question and answer sessions with leaders in the field of FSHD, reports from major clinical centers and research centers, and educational sessions on the genetics of FSHD, breathing and respiration, and exercise and physical therapy. Popular breakout sessions include topics that participants have requested as well as the interests of teenagers and young adults.

Overnight accommodations are available at Paris and Bally's Las Vegas. The FSH Society has a special conference rate of at $89.00 (Bally's) per night (single or double occupancy) and $120.00 (Paris) per night (single or double occupancy), plus taxes. These facilities have many wheelchair accessible guestrooms, including a total of 100 rooms with roll-in showers. There is no charge for parking. The group code for our conference rate for Bally's is SBIPR0 (last digit zero) and for Paris, SPIPR0 (last digit zero). For the best selection of accessible rooms and showers, please make your reservations early. The closing date for the Society's block of rooms is July 9th. For reservations, call 1-877-603-4389, or reserve online at *http://www.harrahs.com/CheckGroupAvailability.do?propCode=BLV&groupCode=SBIPR0* for Bally's, and *http://www.harrahs.com/CheckGroupAvailability.do?propCode=PLV&groupCode=SPIPR0* for Paris.

Registration for the meeting, including lunches Friday-Sunday, is $180 per adult (with current FSH Society membership), $200 for non members, $105 per young adult age 12 – 18, and no charge for children under 12.

The full program and registration are available at www.fshsociety.org, or email 2010Meeting@fshsociety.org.

We hope to see you there!

Sincerely,

Nancy Van Zant

Nancy Van Zant
Executive Director

BREATHING AND RESPIRATION IN NEUROMUSCULAR DISEASE

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complications [1]. A 2004 study of adult patients suggests that respiratory problems are less common as the need for breathing support of some type was found in only 1% of all adult patients with FSHD studied in the Netherlands [2]. The difference between the two studies is likely that the first study included younger patients who may have had a more severe form of the disease. A more recent study published in October 2009, on sleep-disordered breathing conducted research on 51 genetically confirmed FSHD patients between the ages of 26-72 [23 women and 28 men] who underwent medical and neurological evaluations, subjective evaluation of sleep and full-night laboratory-based polysomnography showed that 20 patients had SDB [3]. "Thirteen presented obstructive apneas, four presented REM related oxygen desaturations and three showed a mixed pattern. Three patients needed positive airways pressure. SDB was not related to the severity of the disease." This shows that respiratory issues and SDB might be more frequent than previously thought.

Sleep-disturbed breathing

When breathing problems do occur, they most often affect the patients during sleep first. This is because during sleep muscles other than the diaphragm (the major muscle of breathing) become atonic (relaxed) and are no longer able to help with taking a breath. The diaphragm has to take on the breathing load itself; if the diaphragm is weak, it may not be able to do so and the patient will breathe less (hypoventilation). In addition, during sleep the muscles of the upper airway often relax and, if they are weak to begin with, can obstruct the airway (obstructive sleep apnea). Both obstructive sleep apnea and hypoventilation, referred to as sleep-disturbed breathing (SDB), can lead to increases in the blood level of carbon dioxide and decreases in oxygen levels. These changes have serious effects on the body and can cause hypertension, heart problems such as abnormal rhythms, and disruption in sleep that leads to daytime tiredness, decreased concentration and even depression.

In our clinic, we screen for the presence of sleep-disturbed breathing in two ways. First at each annual visit we ask the patients about symptoms of sleep-disordered breathing. These include repetitive morning headaches, sleepiness during the daytime, unexplained nighttime awakenings (including increases in visits to the bathroom), unexplained hypertension, lack of concentration during the day (feeling of "fogginess"), and depression. In addition at each visit, we measure breathing function which involves measuring a forced vital capacity (FVC) and a maximal inspiratory pressure (MIP) measurement. If the FVC is less than 50% of the predicted value and/

"These changes have serious effects on the body and can cause hypertension, heart problems such as abnormal rhythms, and disruption in sleep that leads to daytime tiredness, decreased concentration and even depression."

or the MIP measurement is a more positive value than -60 centimeters water pressure as measured or if the patient has symptoms, then we will often consider sending the patient for a polysomnogram (overnight sleep study) where hypoventilation and obstructive sleep apnea can be evaluated in the most accurate way possible. This involves spending a night in a sleep laboratory while brainwaves, breathing and other sleep indicators are carefully measured. We will often also measure the exhaled carbon dioxide level, a noninvasive method of measuring blood carbon dioxide level. If elevated above 45 millimeters of mercury (mmHg), this test suggests that a sleep study should be performed. In centers where this test is not available, an arterial blood gas sample may be necessary.

Treatment

If sleep-disturbed breathing is found, treatment with noninvasive methods is the most common treatment in use. This involves the use of either continuous positive airway pressure (CPAP) that relieves obstructive sleep apnea or bi-level positive airway pressure (BiPAP™) that treats hypoventilation or a combination of the two. CPAP and BiPAP™ are small machines about the size of a shoebox that have a long flexible hose with a mask on the end of the hose. Both methods of breathing support are delivered via masks that fit over the nose, or the nose and mouth or that fit into the nostrils (nasal pillows). CPAP delivers a constant pressure through the mask that keeps the airway open and prevents obstructive apnea. BiPAP™ delivers two pressures, an upper pressure that provides a boost during inhalation and lower pressure that keeps the airway open. FSHD patients who use BiPAPs™ should be sure that their machine is equipped with a backup rate function that will breathe for them in case they stop breathing. As the BiPAP™ follows the patients' breathing, and if the patient is not inhaling or exhaling, it will not give the pressure boost and lower pressure. It is really a form of active breathing support. The masks are generally well tolerated after a period of adaptation. Monitoring of treatment efficacy is best performed by asking the patient about symptom resolution. However, if symptoms are not a major issue then either a follow-up sleep study or measuring oxygen levels during sleep in the home (nocturnal pulse oximetry) can be helpful. Because muscle weakness can progress, follow-up questions on a regular basis concerning sleep quality are important as is repeat pulmonary function testing and measurement of exhaled or arterial carbon dioxide levels.

Fortunately, if picked up early and treated, nocturnal breathing problems rarely progress to daytime breathing failure in patients with FSHD. However, on occasion, daytime breathing support will be needed. In this case the most common treatment would be with a tracheostomy and a mechanical ventilator. These can be adapted for wheelchair use quite easily.

In summary, breathing disorders in patients with FSHD can occur. They most commonly occur at night and a high index of suspicion needs to be maintained to pick up what can be subtle symptoms and findings. The patient history, breathing measurements and perhaps a polysomnogram may be required to diagnose the problem. Progression to daytime breathing problems, is fortunately, very rare.

[1] Kilmer D, Abresch RT, McCrory MA, et al. Profiles of neuromuscular diseases: facioscapulohumeral muscular dystrophy. Am J Phys Med Rehabil 1995;74(Suppl); 131-139.

[2] Wolgemuth M, van der Kooi EL, Van Kesteren RG, et al. Ventilatory support in facioscapulohumeral muscular dystrophy. Neurology 2004;63:176-178.

[3] Della Marca G, Frusciante R, Dittoni S, Vollono C, Buccarella C, Iannaccone E, Rossi M, Scarano E, Pirronti T, Cianfoni A, Mazza S, Tonali PA, Ricci E. Sleep disordered breathing in facioscapulohumeral muscular dystrophy. J Neurol Sci. 2009 Oct 15;285(1-2):54-8. Epub 2009 Jun 5.

FSH Society Research Fund will help advance research on infantile form of FSH dystrophy (IFSHD) at the University of Iowa

Researchers at the University of Iowa will lead an investigation on the infantile form of FSH muscular dystrophy, thanks to a one-year, $39,998 grant from the FSH Society.

Led by Yi Xing, Ph.D., UI assistant professor of internal medicine, biomedical engineering, and biostatistics, the team will use cutting-edge genomic technologies, including exon array chips and ultra-deep mRNA-sequencing, to identify RNA splicing differences among healthy people and people with FSHD or the infantile form of FSHD. RNA splicing differences affect how the genetic code is assembled and translated, and these differences can end up creating defective messenger RNAs or proteins. Dr. Xing and colleagues will compare the severe clinical phenotype of iFSHD and the "less severe" adult onset forms of FSHD to see if there are differences in transcriptome dysregulation at the level of splicing. They believe this project will provide significant insight into the role of aberrant splicing in the pathogenesis of FSHD/iFSHD, revealing novel disease markers and therapeutic targets.

This research opportunity comes, in part, as a result of the IFSHD clinic that Dr. Katherine Mathews ran in conjunction with the FSH Society patient meeting at the University of Iowa in July 2008 and the data collected at that time from IFSHD patients. Xing is collaborating with Katherine Mathews, M.D., UI professor of pediatrics and neurology, who has collected skin fibroblast cells from FSHD patients, iFSHD patients and healthy controls made available through the efforts of the University of Iowa NIH-Funded Senator Paul D. Wellstone Muscular Dystrophy Cooperative Research Center cell core run by Steven Moore, M.D., Ph.D., and the efforts of the FSH Society in recruiting donors.

Dr. Xing will test to see if there is much more extensive alternative splicing occurring in FSHD than has been already reported by others. The idea is that the FRG1-gene over expressing mouse model of FSHD shows alternative splice form usage of two genes involved in muscle development. The plan is to acquire from Dr. Mathews fibroblast cell lines from normal, FSHD and iFSHD patients. Dr. Xing will use a myoD construct to convert these cells into myogenic cells and then, following differentiation into mature muscle cultures, do expression profiling on the newest Affymetrix exon array HJAY chips, which are supposed to be highly accurate in detection of alternative exon usage. The transcripts detected as alternatively spliced on the chip experiments will be confirmed using RT-PCR technology. They also plan to move any results that they might find into RNA prepared from mature muscle biopsies taken from FSHD patients.

According to FSH Society President & CEO, Daniel Paul Perez, "Excellent, high quality research made possible by seed funds set an important course for future work together to find a solution for this most devastating illness of children. I am pleased to see the significant progress in research coming out of seminal work between the University of Iowa Wellstone, FSH Society and UI pediatrics and neurology. This progress is largely due to the efforts of FSH Society funding of postdoctoral research across a wider group of scientific disciplines, our efforts in Washington, DC, and participation at the federal advisory committee level on the muscular dystrophy coordinating committee (U.S. DHHS MDCC). This work shows the power of partnerships between scientists, patients, advocates, government funding agencies and clinicians from throughout the world all focused at UI on solving infantile and adult FSHD."

The award to Dr. Xing is made possible by the Society's Aubrie Lee Family Research Fund for Infantile FSHD and the Fire Island Fellowship Fund.

Birmingham members meet on October 25, 2009

People came to Birmingham, Alabama, from Georgia, Tennessee, and Mississippi to gather at the home of George "Tommy" Kuykendall, lower right, for an afternoon of sharing experiences and making new friends.

▶ Have you made a gift to the Society in 2010?

The FSH Society is a world leader in combating muscular dystrophy. It has provided over $2 million in seed grants to pioneering research worldwide and has created an international collaborative network of patients and researchers.

If you are not already a member, won't you join in this effort? Please return your membership gift, or another gift, in the enclosed envelope. Or contribute online at *www.fshsociety.org*. Go to Contribute, and select the gift category you wish to make. Thank you.

▶ Volunteers are still needed for muscle biopsy study

Go to *www.fshsociety.org* for more information, or contact Jenny Lazzaro at the FSH Society, 617-658-7877 or *jennifer.lazzaro@fshsociety.org,* or Regina Brock-Simmons at Johns Hopkins, 410-502-7220

▶ Is your email address current at the Society?

If we do not have your current e-mail address, and if you want to be sure of receiving up-to-the-minute information from the Society as news breaks, please send your e-mail address to us at *jennifer.lazzaro@fshsociety.org*. Thank you.

ING New York City Marathon, November 1, 2009

Geoff Bello raises pledges in honor of Jeff Johnston, his colleague at Detwiler Fenton in New York. Geoff finished the Marathon in 4 hours, 9 minutes, and 44 seconds, and sent a tidy sum of over $5,000 to the FSH Society for FSHD research. Thank you, Geoff!

FSH SOCIETY AND BOSTON BIOMEDICAL RESEARCH INSTITUTE HOST INTERNATIONAL CONFERENCE ON MOST PREVALENT FORM OF MUSCULAR DYSTROPHY

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He continues, "I was also heartened to see the rapid progress brought by the BBRI Wellstone, by the scientific progress of the entire community, by the dedication of those who work on our disease, and by those who in turn volunteer their energy, time and money to this cause. Based on what was reported, we can expect major advances in our understanding of how the mechanism of FSHD works in the next year or two."

Dr. Charles Emerson, president of BBRI agrees. He added that BBRI was the natural venue for the meetings because it is home to the only research center in the world focused entirely on FSHD. This center, established with a Wellstone grant in 2008, is also the only Wellstone Center in New England. Senator Paul Wellstone, who worked closely with Perez to ensure federal funding for all types of muscular dystrophy, including FSHD, was a congressional champion for those afflicted with all forms of muscular dystrophy.

At the November meetings, scientists presented promising preliminary research results and joined corporate leaders and physicians to develop strategies and new collaborations to accelerate the rate at which discoveries become treatments and ultimately cures.

This year's meetings attracted 85 individuals from institutions across the US and around the world, including Johns Hopkins, University of Milan, University of Sydney (Australia), Children's National Medical Center (DC), Acceleron, University de Mons-Hainaut (Belgium), Leiden University Medical Center (Netherlands), University of Nottingham (UK), University of Rochester, Muscular Dystrophy Association (Tucson, AZ), University of California at Irvine, Genzyme, King's College London, Children's Hospital and Harvard Medical School.

Also joining the meetings were three program directors from the NIH: Ljubisa Vitkovic, Ph.D., program director for the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD); John Porter, Ph.D., program director for the National Institute of Neurodegenerative Disorders and Stroke (NINDS); and Glen Nuckolls, Ph.D., program director for the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS).

Sponsors for the event included Acceleron Pharma, Association Francaise Contre les Myopathies (AFM), Athena Diagnostics, The Fields Center at University of Rochester, FSH Society, FSHD Global Research Foundation, Genomic Vision, Genzyme, the NIH Eunice Kennedy Shriver NICHD, and Boston Biomedical Research Institute Senator Paul D. Wellstone Muscular Dystrophy Cooperative Research Center.

For a program and abstracts of the conference, see *www.fshsociety.org/assets/pdf/FSHSocietyIRC2009ProgramAbstracts.pdf*

Annual Donor Report

Gifts to Membership, Research and Education

Gifts received January 1, 2009 through December 31, 2009

FUNDRAISING

The 2009 Fundraising Challenge for FSHD reaches its goal!

FROM THE CHAIRMAN, BOARD OF DIRECTORS, FSH SOCIETY

Dear Friends,

In November, the Board of Directors and other major donors joined together to offer a challenge to the Society's members and friends to support promising new work. We asked you to make gifts to the 2009 Fundraising Challenge for FSHD, the most prevalent form of muscular dystrophy, and we agreed to match your gifts up to a total of $131,000, on a dollar-for-dollar basis, if you sent them by December 31, 2009.

I am delighted to report that 503 individuals, foundations and businesses in the FSHD community contributed $160,540 to our Challenge. Together, we have all contributed $291,540 at year's end.

Notwithstanding the extraordinary economic environment in which we find ourselves, the FSH Society has concluded the second most successful fundraising year ever, raising $767,208 from generous friends like you. Thank you for supporting advances in research, education, outreach and advocacy.

The list that follows includes donors to the FSH Society in 2009. We hope you will continue to support this work by joining the Society again in 2010. Thank you and all good wishes to you and your families for the New Year.

Sincerely,

William R. Lewis, Sr., M.D.

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FSH Watch Newsletter Annual Donor Report

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Family and friends of these individuals have made gifts in their memory in 2009

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FSH Watch Newsletter Annual Donor Report

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In Honor of

Family and friends of these individuals have made gifts in their honor in 2009

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Coco and Glenn Wing and Family
Carden D. Wyckoff
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Helen Younger on her 60th birthday
Helen and Marc Younger

FSHD Future Fund

Members of the FSHD Future Fund are individuals who have included the FSH Society in their estate planning

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Amy Bekier
Greg and Tanya Bernstein
Howard Chabner and Michele DeSha
Barbara and James A. Chin, Sr.
Barry M. Clayton
JoAnn P. Forance
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Jeffrey and Christine Jacobs
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Family Fundraising 2009

Chabner Family
Corradino-Kerr Family
Gillespie and Gibson Families
Hereford Family
Herzberg Family
Jacobs and Conners Families
Kelly Family (Lucero, Wing, Paladino, Cuoco, Gregorio, Owens, MacDonald)
Lee Family

Gifts received January 1, 2009 through December 31, 2009. We deeply regret any errors or omissions.

Gatherings of Members and Fundraising Events 2009

JANUARY
Los Angeles, CA, Luncheon

FEBRUARY
Hobe Sound, FL, Gathering
Hosted by Mimi Brown

MARCH
Festive Evening of Music and Song
New York, NY
Judy Seslowe, Chair

APRIL
Tango and Comedy Night
Washington, DC
Manuel Gomez, Chair

MAY
11th Annual After Tax Season Celebration
Quincy, MA
Ellen & Chris Stenmon, Chairs

JUNE
Spring Lake, NJ, Luncheon

Denver, CO, Reception
Hosted by Debby & Rick Levinson

JULY
Yard Sale
Fire Island, NY
Grace Corradino & Brian Kerr, Chairs

Alexander, MN, Picnic
Hosted by Helen & Brian Wagner

Twin Cities, MN, Picnic

AUGUST
Osceola, IN, Poker Tournament
Mark Dunderman, Chair

1st Annual Pig Roast
Selkirk, NY
Hosted by Mary Rieger & Jude Watkins

50th Anniversary Party
Hartford, CT
Barbara & Robert Birnbaum, Hosts

SEPTEMBER
Trunk Show Shopping for a Cure
New York, NY
Wendy Herzberg, Chair

OCTOBER
1st Annual Walk 'N' Roll
Cape Cod, MA
Rich Holmes, Chair

Frederick County, MD, Gathering
Hosted by Deb & Brad Calhoun

Birmingham, AL, Gathering
Hosted by Tommy Kuykendall

NOVEMBER
New York City Marathon
Geoff Bello, Runner
Jeff Johnston, Coach

Hamilton, NJ, Luncheon

Walk "N" Roll for FSH Muscular Dystrophy raises nearly $18,000 for FSHD research

Participants gather around the FSH Society banner before the walk begins. Bob Smith, member of the Society's board of directors, sits on the right.

Rich Holmes, right, organizer of the First Annual Walk "N" Roll for FSH Muscular Dystrophy, displays a memento of the walk, in conversation with Carol and Charlie Perez, October 10, 2009, Cape Cod, Massachusetts

Save the Date!

April 30
12th Annual End of Tax Season Fundraiser, Florian Hall, Dorchester, Massachusetts

May 12
A Festive Evening of Music and Song
New York Botanical Garden, Bronx, New York

June
Gathering in a private home on Gull Lake, Hickory Corners, Michigan (SW Michigan near Battle Creek) Details to follow

July 30—August 1
FSH Society 2010 International Patient and Researcher Network Meeting, Las Vegas, Nevada

October 9
Second Annual Walk 'N' Roll for FSH Muscular Dystrophy, Cape Cod, Massachusetts

October
Walk 'N' Roll, Southern California, details to follow

Interested in participating? Want more information?
Go to *www.fshsociety.org*, or e-mail *nancy.vanzant@fshsociety.org.*

A Festive Evening of Music and Song
New York Botanical Garden
Bronx, New York
May 12, 2010

∗Dinner by the Bite∗ Silent Auction
and a special piano concert performance
by Steven Blier, with a guest vocalist

To benefit the FSH Society, Inc.
FSH Muscular Dystrophy

Invitation to follow
For more information, visit www.FSHSociety.org

The Fsh Society is a 501(c)(3) organization
dedicated to solving facioscapulohumeral muscular dystrophy.

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