National Registry of Myotonic Dystrophy and Facioscapulohumeral Muscular Dystrophy Patients and Family Members

The National Registry continues to grow and offer new opportunities to participate in research. We appreciate your continued support and are eager to share updates on our current projects as well as plans for future studies.

The energy that you provide to report your symptoms and to participate in research has been very important to help investigators learn more about the biology and progression of DM and FSHD. Over the past year, the Registry staff has had the opportunity to present several of our projects to scientists, healthcare professionals and patient advocacy groups at international research conferences. Many of the projects were inspired by data collected directly from members of the Registry and include:

- A description of gastrointestinal symptoms in adults with DM1
- The clinical characteristics of infantile FSHD
- Description of tumors in DM patients

In the coming months, the Registry will work to expand the studies described on pages 2-6 and hopes to offer additional opportunities to participate in research. The new Fields Center for FSHD research (see page 5), will also partner with the Registry to recruit participants for their new studies. On page 6 we describe an important opportunity for members of the Registry to partner with NIH in developing new ways to measure the effectiveness of treatments to relieve symptoms.

We remain enthusiastic about the potential for expanding the resources of the Registry and offering additional opportunities for investigators and patients. With your continued support, we believe the greatest contributions of the Registry lie ahead.

We send our best wishes to you and your families for a happy and healthy New Year.

Warm regards,

Richard T. Moxley, III, MD
Principal Investigator

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Research Updates

Chronic pain in persons with DM and FSHD
Presented by University of California, Davis researchers at the October 2007 meeting of the FSHD International Research Consortium in San Diego, California.
Published in the February 2008 issue of Archives of Physical Medicine and Rehabilitation.

Dr. Abresch and colleagues at the University of California, Davis along with researchers at the University of Washington completed one of the largest studies of pain in DM and FSHD patients. Your participation was vital for the success of this research study. The researchers mailed 296 questionnaires to interested Registry members and 235 questionnaires were returned.

The results indicated that 60% of DM and 82% of FSHD patients reported pain, with 23% of respondents reporting that their pain was severe. Most patients reported having pain symptoms for over 10 years. The most common sites of pain for FSHD patients were located in the lower back (74% of patients) and legs (72% of patients).

These results and other information presented by Dr. Abresch and colleagues indicate that pain is a very important symptom of DM and FSHD. More research and clinical guidelines are needed to identify treatments for pain. The Registry will work closely with colleagues at UC-Davis and other investigators to develop studies to further analyze pain and to develop potential prevention strategies.

Clinical description of infantile FSHD
Presented by Registry staff at the April 2007 Annual Meeting of the American Academy of Neurology, in Chicago, Illinois.

Approximately 5% of individuals diagnosed with FSHD have a more severe sub-type of the disease which begins in early childhood, referred to as infantile/childhood FSHD. Only a few published reports describe the symptoms and characteristics of infantile FSHD patients. We presented information obtained from Registry participants. The Registry maintains one of the largest samples of patients with a history of infantile FSHD symptoms. Infantile FSHD was defined by two symptoms: facial weakness before the age of five and shoulder weakness before the age of ten.

Our report helps confirm a more consistent and severe pattern of symptoms compared to adult FSHD. Our results differed in some aspects from previous studies, because Registry members reported a larger amount of muscle weakness and respiratory problems. However, a smaller percentage of patients were dependent on wheelchairs. More research is needed to determine how age, biology of FSHD, and other factors influence disease progression and severity of FSHD.

Study of tumors in patients with DM1
Presented by Registry staff at the April 2007 Annual Meeting of the American Academy of Neurology, in Chicago, Illinois.

Through a partnership with investigators at the National Cancer Institute, we analyzed tumors that have been reported by DM1 patients enrolled in the Registry. We also summarized information published by other researchers in medical journals that describe certain types of tumors found in DM1 patients.

The most common type of growths in DM1 are non-cancerous skin lumps. These small, hard lumps are called pilomatricomas and are commonly found on the neck and forehead. Other benign and malignant (cancerous) tumors have been reported in DM1 but there is limited information on the overall prevalence of cancer in DM1. Previous reports in medical journals have involved only 1 or 2 patients .

Additional research is needed to clarify if the biology of DM or other factors may lead to non-cancerous skin tumors or other types of tumors. The Registry is developing a study to investigate if patients with DM1 and their family are diagnosed with more tumors compared to the general population of the United States. This project is in its early planning stages and more information will be sent to eligible members when it becomes available.

Gastrointestinal symptoms in DM1 patients
Presented by Registry staff at the 6th International Myotonic Dystrophy Consortium meeting (IDMC-6), September 2007 in Milan, Italy.

The International Myotonic Dystrophy Consortium *(*IDMC) is a group of scientists and clinicians with a shared interest in understanding all aspects of DM1 and DM2 with the long term aim of providing improved treatment for affected patients. Another unique component of the IDMC-6 meeting involves the participation of patients affected with DM. At the conference, patients can directly interact with investigators and clinicians to discuss symptoms which are most important to them.

The Registry staff and leaders presented information at IDMC-6 that described gastrointestinal (GI) symptoms reported by DM1 patients enrolled in the Registry. GI Symptoms in DM1 patients are common and often severe. The most common symptoms reported by Registry members were difficulty swallowing (68% of patients), acid reflux (48%), and constipation (43%). The Registry data suggests that GI symptoms are related to excess weight and the duration of the disease. More research is needed to understand the biology of these symptoms and to develop clinical guidelines and treatment.

We discussed our work on GI and other symptoms with DM patients at the conference. As our interaction with patient advocacy groups has increased, we have become increasingly more aware of the need to better investigate the symptoms most troublesome to patients. The development of accurate and reliable measurement tools for patient reported symptoms will help to improve treatment and quality of life for patients and family members.

Insight into the influence of gene activity on symptoms of FSHD
Published by University of Rochester researchers in the February 20th, 2007 issue of Neurology.

The development of a more thorough understanding of the biological processes that are disrupted in cells affected by FSHD has been a central goal for scientists involved in FSHD research.

It has been suggested that the DNA deletion on chromosome 4 affects the function of nearby genes. To explore this theory, Dr. Rabi Tawil and his colleagues at the University of Rochester collected tissue and blood samples from patients with FSHD as well as from patients with DM1 and subjects that were not affected with a muscle disease.

The researchers compared the activity of genes in skeletal muscle from the 3 groups of subjects. The researchers found that FSHD patients had an increase in gene expression (activity) in 44 different genes. Eleven of these genes have a role in the vascular (blood vessels) tissue of muscle and other cells. This increase in vascular gene activity was particularly notable in patients in the early stages of FSHD. These results may provide insight into the connection between the problems in the vascular tissue of the eye that commonly affect individuals with FSHD.

Annual Updates

Annual updates are sent to each member of the Registry every year. The purpose of the update is to identify changes in symptoms, medications and other factors related to your quality of life. It is also useful for updating our records if you have moved or changed your phone number. The Registry has been collecting annual update information for over six years, making our database one of the largest datasets available on the progression of DM and FSHD. The data from annual updates have been used to study the progression of congenital myotonic dystrophy, infantile FSHD, and gastrointestinal (GI) symptoms in DM1.

The Registry staff is pleased that so many of our members remain interested year after year. Over 75% of our members have returned at least one annual update. We hope to continue receiving such an excellent response. We encourage you to complete and return the form even if you do not have an opportunity to review your information right away. If there haven't been any changes in your information, we would still like to hear from you!

Developing accurate measurements of patient symptoms

The progress in muscular dystrophy research is encouraging, but it also presents many new opportunities and challenges. In the next few years we anticipate major advances in our understanding of the underlying causes for disease manifestations in both DM and FSHD and potential new treatment options. To identify treatments that are most effective, we need a better understanding of what symptoms matter most to patients. For example, which symptoms will respond best to new treatments? How do we measure potential reductions in pain? How do we measure fatigue? What symptoms matter most to you?

We and other researchers have worked to develop methods to accurately measure your strength and muscle mass. We must now expand our focus to include symptoms such as pain, fatigue and the impact of functional limitations on activities of daily living.

The current methods available to monitor pain, fatigue, functional limitations and other quality of life components were often developed without input from patients. These tests often overlook symptoms that most affect quality of life. Little research using these tests has been specific to DM and FSHD patients. Quality of life tests can also be very time consuming and require you to answers questions that may be irrelevant to your situation.

We need to understand your symptoms better to plan and develop more useful and appropriate measures of symptoms to use in future clinical studies and treatment trials. An essential part of that plan is asking for your help to better define the clinical course of your illness and to assist us in developing the best methods for measuring changes in symptoms over time. Prior to investigating different types of treatments in patients, we must decide on the best methods to determine the most effective therapy.

The National Institutes of Health (NIH) has embarked on an ambitious goal to develop questions and methods that quickly and more accurately assess your quality of life and measure changes during treatment. In the next year, we plan to pursue studies involving interested members of the Registry to test these new questionnaires related to quality of life in patients with DM and FSHD.

Opportunities for Unaffected Family Members

Membership to the National Registry is not limited to patients diagnosed with DM and FSHD. We also encourage unaffected family members to apply. Relatives, spouses, and care caregivers that have no symptoms of illness can join. We have enrolled nearly 150 unaffected family members.

There are several reasons for including unaffected family members in the Registry. A patient's quality of life can be altered due to the symptoms associated with muscular dystrophy and the influence can extend beyond the patient. The psychosocial and economic impact on the family and caregivers has yet to be studied in DM and FSHD. Previous research in other diseases such as, Duchene muscular dystrophy, has highlighted the additional stress that can be placed on a family. The Registry data on unaffected family members provides a resource for investigators seeking people for these types of important studies.

Additionally, unaffected family members that have not received genetic testing may be at risk for these illnesses even if they do not currently have any symptoms. For example, older adults often have symptoms that go unnoticed or are attributed to other conditions and are only diagnosed after other family members are affected with more severe symptoms. The symptoms of DM and FSHD can be very diverse even within the same family. The long term monitoring of "at risk" family members will help us better understand the progression of these diseases.

Finally, family members that have negative DNA testing for DM and FSHD can help researchers identify other genes that may vary between affected and unaffected individuals. These secondary genes do not directly cause DM or FSHD but may influence the onset and severity of the illness or may provide protection against developing the disease.

Fields Center for FSHD and Neuromuscular Research

We have exciting news about FSHD research! The University of Rochester has received a generous and long-term donation from a private donor, Mr. Richard Fields. The formation of the Fields Center for FSHD and Neuromuscular Research was announced on October 25, 2007. This kind donation has enabled the development of an "FSHD Center without walls" combining the University of Rochester's expertise and resources with their research partners at Leiden University Medical Center in the Netherlands. Dr. Rabi Tawil of the University of Rochester and co-investigator of the National Registry is the Director of the Fields Center.

This exciting new project provides the opportunity for an international group of scientists and clinicians to collaborate and offer their expertise to advance research in the area of FSHD. The aim of the Fields Center is to better understand the complex genetic mechanisms that result in FSHD, to improve the current guidelines for diagnosing FSHD, and to enhance clinical guidelines to improve care for patients.

Several research projects have been planned to investigate the relationship between clinical symptoms of FSHD with biological data from genetic tests and muscle biopsies. The first study will collect DNA samples from individuals affected with FSHD with the goal of identifying new variations in the deletion area on chromosome 4 which may help reveal what gene is responsible for FSHD.

In 2008, the National Registry will assist the Fields Center to recruit patients that may be interested in participating in this important research. "The real key to this project will be our ability to interact with a large population of patients who will be able to guide us toward a more clearly focused understanding of the disease," says Dr. Moxley, Principal Investigator of the Registry. If you are interested in learning more about the Fields Center, please visit their website at http://www.fieldscenter.org.

We will notify eligible Registry members by mail when the opportunity to participate in this research becomes available!

Website Updates

The staff of the National Registry is contacted by many patients and their families with questions regarding their diagnosis and what they can do to help find a cure. Our website was developed to make information about common questions readily available. We strive to provide current and reliable information about DM and FSHD, as well as encourage people to join the Registry. To support these goals, we have planned several enhancements to the website over the next few months.

- Genetic counseling is an important step in the diagnostic process for many patients with DM and FSHD. However, it can be a challenge to locate clinicians that are familiar with these rare illnesses. To help with this process, we will be posting the names and contact information for several genetic counselors through out the United States with experience counseling families affected by muscular dystrophy.

- The Registry aims to enroll a diverse group of patients and remove any potential barriers to participation. In early 2008, application materials for the Registry will be translated into Spanish. A portion of our website that describes the purpose and goals of Registry will also be translated. The Spanish application forms will be available to download from our website or by contacting the Registry office.

- Registry enrollment has gone digital! We have developed a new option to request an enrollment packet through our website. This online application request form allows interested individuals to request an application to join the Registry by simply entering in their contact information. All of the information provided is sent directly to the Registry staff via a secure internet connection. Once your request is received, an application packet is mailed to the address provided.