



THE NMDINFO



NEWS

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The Department of Physical Medicine and Rehabilitation, School of Medicine, University of California, Davis, 95616

Accomplishments: 1998—2003

This issue of The NMDINFO News provides a summary of the research accomplished by the Rehabilitation and Rehabilitation Center on Neuromuscular Diseases in the Department of Physical Medicine and Rehabilitation at the University of California, Davis during the grant period from 1998—2003. These studies were funded by The National Institute on Disability and Rehabilitation Research, United States Department of Education, Grant H133B980008-99.

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The mission of the Research and Training Center is to improve the lives of individuals with neuromuscular diseases by developing and evaluating new strategies that address lifelong needs for research-based medical care and counseling, psychosocial well-being, education, and independent living.

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Introduction

The Rehabilitation Research and Training Center in Neuromuscular Diseases (RRTC/NMD) at the University of California, Davis, School of Medicine, under the sponsorship of the National Institute on Disability and Rehabilitation Research (NIDRR), has been performing research on neuromuscular diseases since 1983. The goals of this center are consistent with the mission of NIDRR, which is to sponsor projects that will improve the lives of individuals with disabilities from birth through adulthood.

From 1998 through 2003 the RRTC/NMD, under the direction of Principal Investigator Craig M. McDonald, performed research that was focused on three major areas:

- interventions to preserve functional capacity of those with neuromuscular diseases;
- interventions to enhance their community integration; and
- provision of information on genetic testing.

A fourth area addressed was the provision of training and information services to health professionals and to the individuals affected by neuromuscular diseases. A major project was the sponsorship of a consensus conference that brought together an expert panel of scientists and clinicians to evaluate the state of scientific knowledge on the effect of exercise on healthy muscles and on muscles affected by neuromuscular diseases.

This publication is a summary of the accomplishment of each of the projects undertaken from 1998 – 2003.

Management of Muscle Wasting in NMD

Craig M. McDonald M.D.

Progressive muscle wasting is common to all progressive neuromuscular diseases (NMD) and may arise from both muscle degeneration due to the disease itself and disuse that is secondary to a sedentary lifestyle. Muscle wasting is an important factor that contributes to the reduced strength, increased fatigue, diminished mobility, respiratory insufficiency and decreased quality of life experienced by those with progressive neuromuscular diseases. These muscular disorders may have their origin in the muscle itself (muscular atrophies) such as myotonic

muscular dystrophy (MMD), fascio-scapulothoracic muscular dystrophy (FSH), limb girdle muscular dystrophy (LGMD), Duchenne muscular dystrophy (DMD), or Becker muscular dystrophy (BMD) or they may arise in the nerves that reach the muscles (neurogenic muscular atrophy), such as spinal muscular atrophy (SMA), amyotrophic lateral sclerosis (ALS), or Charcot Marie Tooth neuropathy (CMT). Another difference in these progressive neuromuscular diseases is that they may affect only a specific group of muscles (focal), such as FSH, or they may be more gen-

eralized, such as SMA. Evaluation of the effect of therapies on these diseases requires the ability to reliably measure the progression of the disease. Unfortunately, there has been no accepted method by which focal and generalized muscle wasting could be reliably determined and there have been no good methods to quantitatively evaluate the daily minute-by-minute activity of this group with neuromuscular diseases.

Evaluation and application of new technologies to individuals with neuromuscular diseases is a main goal of this project. The ability to measure activity and energy expenditure will provide a basis for the evaluation of therapies and interventions that may improve their quality of life.



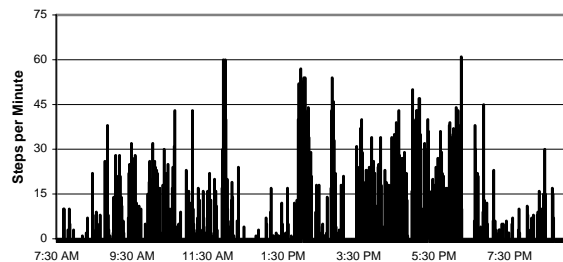
Minute-by-minute Step Rate

The first phase of our study addressed the issue of measuring the minute-by-minute step activity using the step activity monitor (SAM). The SAM is a small, unobtrusive device that is worn on the ankle. It is individually programmed by computer to define the length of time of data collection, the intervals at which data is collected and adjustments for different gait styles. The first groups studied were non-disabled control children and ambulatory boys with Duchenne muscular dystrophy. Each of the participants in these groups wore the SAM for three days while going about his ordinary daily routine. Figures below show one day of minute-by-minute activity for a representative non-disabled boy and for a boy with Duchenne muscular dystrophy.

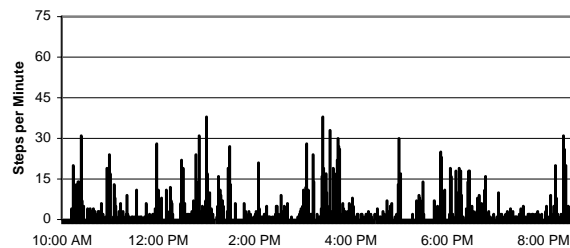
Our results demonstrated that, when awake during the 3 days of activity, the DMD subjects spent 32% more time inactive than the non-disabled boys as recorded by the SAM. When active, the DMD boys spent fewer minutes and took significantly fewer steps at moderate and high step rates than the non-disabled boys. As would be expected, the non-disabled boys took 42% more total steps each day than the boys with DMD.

These results were not surprising, but the importance of the study is the demonstration of the usefulness of the SAM in assessing the activity of disabled children. This method of analyzing minute-by-minute step activity can be utilized in future studies to evaluate the effectiveness of interventions that may improve the mobility of disabled and non-disabled children. By comparing a baseline assessment of daily activity before an intervention to daily activity following an intervention, the value of the intervention can be determined.

Non-Disabled Boy



Boy with Duchenne Muscular Dystrophy

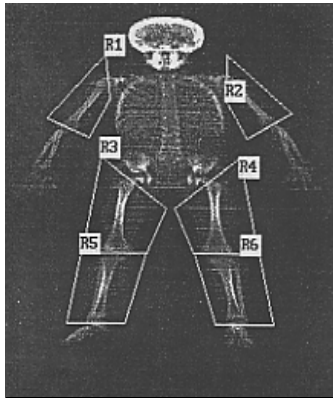


Heart Rate

In addition to measurement of the step activity, the heart rate of these two groups of boys was recorded during the three days. An interesting observation was that, when inactive, the boys with DMD had a higher heart rate than the non-disabled boys. Although the resting heart rate was higher, the maximum heart rate of the DMD boys was lower than that of the non-disabled boys. As the step rate increased, the heart rate of the boys with DMD increased, but at a slower rate than the rate of increase seen in the non-disabled boys. At the highest step rate the heart rate of the non-disabled boys was higher than the heart rate of the boys with DMD. It is known that as the dystrophy progresses, there is involvement of the heart. Further work is needed to understand the meaning of these preliminary results.

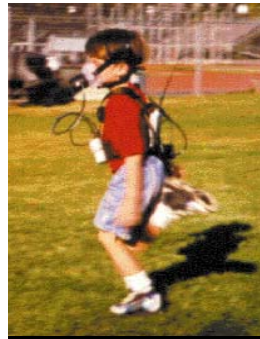
Body Composition

To evaluate the body composition of the groups of boys DEXA (Dual Energy X-ray Absorptiometry) was used. This method allowed the evaluation of both total body composition and the composition of regional areas of the body (upper arms, trunk, thighs, etc). Determinations were made of bone, fat and lean tissue (muscle). Results demonstrated that the percent body fat, as determined by DEXA, was negatively correlated with



DEXA scan showing definition of regional areas.

total step activity in the DMD group; the higher the percent body fat, the fewer the total steps taken each day.



Boy running with COSMED K4b².

The amount of muscle in the thigh was positively correlated with knee extension strength in DMD group. In the control group there was no relationship between either the body composition or the strength of the thigh and steps

taken per day. Therefore, the activity of the non-disabled boys is apparently not affected by their muscularity, while, not surprisingly, those boys with muscles affected by DMD demonstrate an effect of the disease on their daily activities.

Energy Expenditure

We also examined the energy expenditure of the two groups of boys while they walked for 10-minutes at a comfortable rate and while they sprinted (fast walking) for 100 meters. For this laboratory part of the study we used a small, portable device (COSMED K4b² breath-by-breath ambulatory metabolic measurement system) to determine oxygen consumption during these two exercises. The boys with DMD had a significantly higher oxygen cost during both the 10-minute walk and the sprint; it took them more energy to perform tasks similar to those performed by the non-disabled boys. Although their oxygen cost was higher, the boys with DMD walked only 48% as far as the non-disabled boys in 10 minutes and their sprinting speed was 37% of that of the non-disabled boys. The results of

(McDonald, Continued on page 8)

Exercise and Dietary Intervention in Slowly Progressive Neuromuscular Diseases (NMD)

David D. Kilmer, M.D.

Very little is known about the physical activity pattern of persons with neuromuscular diseases, but it is generally accepted that those with disabilities are at the forefront of having a sedentary lifestyle. Our past research indicates that persons with NMD are significantly more sedentary than a comparable group of controls. While they spend the same amount of time sleeping, NMD subjects were found to spend less time engaged in light, moderate, or strenuous activities while awake. Consequently, we found that NMD subjects have significantly lower 24-hr energy expenditure than control subjects. We also know from our own survey of 1169 persons with NMD that over 65% responded to the question "Did you feel full of pep in the last 4 weeks?" with "none of the time" or "a little of the time" and nearly 50% reported being dissatisfied with recreational activities in their lives.

This physical inactivity has been implicated as a major contributing factor in the deteriorating physical health of persons with disabilities and could be due to a lack of knowledge concerning the importance of exercise in overall health, limited access to transportation to and from the exercise site, inaccessible facilities and equipment, and a perception by some individuals that they are not able to exercise as a result of their disability. Furthermore, the medical profession's lack of working knowledge in this area, possibly coupled with the fear of doing harm, contributes to a general failure of the medical professionals to consider or promote exercise and nutritional interventions in persons with neu-

romuscular diseases.

This study was designed to evaluate a simple, practical dietary and exercise program that applies the best knowledge currently available on diet and exercise to promote healthy behavior in adults with neuromuscular disease. Adults with NMD face the risk of declining strength, reduced aerobic capacity, and altered body composition due to the disease process. Consequently, they may be among the group most in need of function-enhancing activity and a healthy diet. To accomplish this change a program must be developed that is easily understood without the need for extensive training. To be readily incorporated into patients' daily lives it must also be practical, low-cost, and must lead to positive outcomes.

For those who are able to walk, even on a very limited basis, walking was used as the activity. A simple protocol was established based on each individual's abilities and baseline fitness. First, we measured how much walking each person did in their typical daily life by



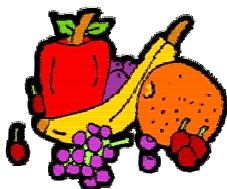
asking them to wear a pedometer for 3 days during their waking hours. We included two weekdays and one weekend day.

This allowed us to know how much walking activity each person was achieving on their own, and the average values ranged from 200 steps per day to over 10,000. We then gave each person a prescription that increased their walking by 25%, but on a gradual

basis. So if someone started with 100 steps, their training goal was to achieve at least 125 steps every day.

Each participant was given 2 pedometers (costing less than \$20) to take home, a primary and a backup in case of loss. At the end of each day, the number of steps accumulated was recorded in a notebook. Participants were monitored over 6 months, with frequent contact by telephone to check on progress, and a mid-way laboratory evaluation.

In addition to this activity prescription, we also assessed the diet of the participants at the start of the 6-month study. We monitored each participant's typical diet by asking them to record the type and amount of food ingested over 3 days. We also gave them surveys to determine what foods they liked and disliked. Comparisons were made with recommended nutritional guidelines such as the Food Guide Pyramid. Each participant was then given a short list of simple recommendations, typically no more than 3-5 specific suggestions, based on dietary analysis and discussion with the participant. The recommendations fell into common categories, such as increase intake of fruits, vegetables, and whole grains; reduce intake of calorie-dense foods like French fries, pastries, and other desserts; or reduce high sugar soft drinks. The participants also received nutritional support throughout the study. Outcomes evaluated were body fat, lean body mass (muscle), blood pressure, serum lipids (total cholesterol, high density lipoprotein, low density lipoprotein, triglycerides) and nutritional measures such as caloric intake based on a dietary log and a food frequency



questionnaire, macronutrients in diet, adherence to recommended dietary standards and measures of quality of life. This study was designed with an emphasis on simplicity and practicality, so that, if it proved successful, practicing health care providers, who may have no background in exercise or nutritional programs for those with NMD, could easily use it in their practices.

Preliminary Results

Preliminary results looking at the effect of the exercise program on daily activity found that the participants had a significant increase in their total daily step activity as determined by the total steps taken each day. After 3 months of the program the number of steps taken each day increased by approximately 26%, a significant amount. The simple twelve-week diet and exercise program resulted in a very small reduction in percent body fat after 6 months, which was considered a significant outcome because most Americans gain fat over 6 months (the phenomenon called "creeping obesity". The simple act of being enrolled in a monitoring program may have contributed to increased awareness (of activity and diet) on behalf of the participants. Although there was a significant increase in the activity of the participants, there was no demonstrated change in any of the serum lipid measurements at either 3 months or 6 months. There was a general trend toward improvement in the lipid measurements, but none was changed significantly. This preliminary data represented a small number of persons with NMD. It is possible that when there is analysis of the data from more patients,

(Exercise & Diet, Continued on page 18)

Exercise-related Fatigue and Injury in NMD Models

Mark A. Wineinger, M.D. (Memorial to Dr. Wineinger at www.nmdinfo.net)

The dystrophic *mdx* mouse has the same genetic defect as the boys with Duchenne muscular dystrophy. However, the mouse does not exhibit the clinical manifestations that are observed in the boys. Although muscles of the boys undergo progressive degeneration and infiltration with fat and connective tissue, this progressive degeneration is seen only in the diaphragm of the mice. Both the mice and the boys lack the large structural protein dystrophin in their muscles. This defect is felt to be responsible for the increased susceptibility of the membrane of the muscle to injury that leads to the degeneration.

A number of reports support the idea that free oxygen radicals can play a role in muscle injury and disease. Free oxygen radicals are normal products of muscle metabolism. There is evidence of lipid peroxidation and increased oxidative damage to proteins in the muscles of boys with DMD. Several studies of *mdx* mice have supported the potential role of peroxidation-related injury in the muscles. Since the lack of dystrophin puts the muscles at a mechanical disadvantage, additional stress on the muscles from exercise may cause increased production of free radicals. The cell membrane is a major source of lipids in the muscle. The oxygen radicals may react with lipids in the cell membrane and contribute to the susceptibility to membrane damage that is generally attributed to the lack of dystrophin.

To simulate the activity of the muscles we subjected muscles from the

mdx mouse to a fatiguing stimulation *in vitro* and measured the production of indicators of lipid peroxidation in a controlled environment and correlated these levels to the fatigue and weakness measured in these muscles.

The goal of our study was to demonstrate that fatiguing exercise of the *mdx* muscles *in vitro* would increase the production of oxygen radicals and this increase would result in oxidation of lipid in the muscle membrane. The combination of biochemical techniques for measuring the reaction of reactive oxygen with muscle lipids and the *in vitro* physiologic studies of muscle strength and fatigue provided us with a powerful experimental methodology to determine the effects of oxygen radicals on muscle. This system also allowed the testing of the effectiveness of antioxidant compounds in preventing of the production of reactive oxygen and, therefore, the evaluation of their

use in prevention of muscle injury and fatigue. Since antioxidant compounds have been proposed to the general public as effective preventive and therapeutic agents for a variety of conditions and diseases, it is important to define their role in neuromuscular diseases.

Initially, we studied a small leg muscle because in previous studies it had exhibited the greatest reduction in strength and the greatest fatigability. Although the *mdx* muscle was weaker and fatigued much more rapidly than that of the normal mouse, using a vari-



ety of fatiguing stimulation protocols we found no difference in the lipid peroxidation in the two. There was also no difference when animals of different ages were studied to see if increasing age affected the lipid peroxidation. In none of these variations did we see the expected increase in lipid peroxidation in the leg muscle.

We then studied the diaphragm of *mdx* and control mice at various ages. There is a progressive deterioration of this muscle in the *mdx* mouse, that is similar to that observed in the muscles of the boys with DMD. The diaphragm of the *mdx* mice was weaker than the diaphragm of the control mice. When the diaphragm was subjected to a fa-

tiguing stimulation protocol, there was no effect of increasing age on the rate of fatigue in the control mice. However, the diaphragm of the *mdx* mice older than 8 months of age had increased fatigue and an increase in lipid peroxidation. Preliminary studies to reduce the observed peroxidation by the addition of the antioxidant n-acetyl cysteine *in vitro* were inconclusive. This is an area where much further work is necessary to determine first, if the peroxidation can be prevented *in vitro* and then, if this intervention is successful, to move to the whole animal to demonstrate the potential of an intervention with antioxidants as a means to delay the deterioration of the muscles in boys with DMD.



(McDonald, Continued from page 4)

the analysis of the daily minute-by-minute step activity of the two groups of boys are reflected in their ability as demonstrated in this laboratory study. On the average day the boys with DMD spend more time inactive and when they are active, their activity is less intense than the non-disabled boys. It takes more energy for the DMD boys to perform a level of activity similar to the non-disabled boys.

Summary

In summary, these preliminary studies demonstrate that the Step Activity Monitor, the DEXA analysis of body compo-

sition and the COSMED K4b² are instruments that can be used to provide meaningful information in examining activities in both the disabled and non-disabled populations. We have data currently under analysis using these techniques to evaluate adult subjects with neuromuscular diseases. These methods will provide an excellent means of evaluating interventions designed to improve mobility or to increase the efficiency of energy expenditure during daily activities in the disabled population.

Pain in Neuromuscular Disease

M.P.Jensen, Ph.D, G.T.Carter, M.D.

Although pain is a symptom commonly associated with several chronic debilitating neuropathic conditions, including diabetes and Guillain-Barré Syndrome, pain has not been described in the literature as a significant clinical problem in the major neuromuscular diseases (NMD). However, in our clinical experience many NMD patients complain of pain. This pain can have a negative impact on the functional abilities of those who experience it. There is a need for research to examine the frequency and extent of NMD-related pain and to examine the impact of this pain on psychological and physical functioning in persons with NMD.

Our goals in this project were to investigate the frequency, severity, and nature of pain in persons with neuromuscular disease; to investigate the relationship between pain, physical impairment, psychological well being and ability to perform activities of daily living; and to explore the effectiveness of pain therapies in the treatment of NMD-related pain.

In this project we documented that, with the exception of those participants with spinal muscular atrophy, persons with slowly progressive NMD experience significant pain that was comparable to the pain reported by subjects with osteoarthritis and chronic lower back pain. Those who reported significant pain also reported lower levels of general health, vitality, social function, and physical activity. To a lesser degree pain was related to increased fa-

tigue, reduced ability to cope adequately with stress, and sleep disturbances.

We investigated a variety of therapies designed to reduce or to better manage pain. Among these were physical therapy, nerve blocks, biofeedback/relaxation training, acupuncture, magnets, massage, chiropractic visits, hypnosis, counseling/psychotherapy, mexiletine, neurontin, tricyclic antidepressants, narcotics/opioids, acetaminophen, aspirin/ibuprophen, muscle relaxants including benzodiazapines, or carbamazepine.

We also found no single intervention that provided a great deal of pain relief for all patients, but many of the treatments appeared to provide at least some relief for some patients. The most common treatments utilized were over-the-counter analgesics: ibuprophen, aspirin, and acetaminophen. These

provided only moderate pain relief. Physical therapy, narcotic analgesics, and massage were the next most commonly used treatments. Only the latter two were associated with moderate relief and more than half of the patients discontinued their use. The least used treatment was chiropractic visits. These seemed to provide the greatest relief. We concluded that none of these treatments provided effective long-term relief for all of the patients. This means that any patient with NMD pain who is interested in pain relief deserves a trial of each pain treatment

None of the treatments studied provided effective long-term relief for all of the patients.

(Pain, Continued on page 15)

Role of Personal Strivings in the Community Integration of Individuals with NMD

Robert A. Emmons, PhD

Personal strivings describes a model of community integration that is based on personal goals. These goals are what a person is characteristically trying to do or be and they provide access to what he/she is potentially capable of becoming. This framing of subjective quality of life outcomes such as personal well being in terms of goals leads to new possibilities for understanding adaptation to physical disabilities and offers substantial advantages for addressing the psychosocial needs of persons with disabilities and for ultimately improving the quality of their lives.

Asking each person directly what he/she wants out of life assists in identifying current priorities and commitments; precisely where they are in terms of functional abilities, current perceptions of their overall quality of life, and their concerns for the future. This direct personal

input gives each person with a disability a voice in examining what he/she wants out of life in various areas, including home, work, recreation, and relationships and it allows each person to set goals that are appropriate for his/her physical and emotional abilities or limitations at the time of goal setting. This framing of subjective quality of life outcomes in terms of goals leads to new possibilities for understanding adaptation to physical disabilities. It better equips each person to identify sources of frustration and futile effort, particularly when trying to meet the expectations of uninformed external individuals. Individuals with a high sense of well-being tend to pursue goals that are im-

portant and meaningful, moderately difficult and challenging, fueled by optimistic expectations, supported by others, and free from conflicts arising from competing goal concerns or interpersonal obstacles. Goals make life meaningful, valuable, and purposeful. They lie at the heart of what it means to live a life of quality; they are, therefore, central to quality of life research.

The outcome of setting goals for people with disabilities is the achievement of a realistic sense of what is both possible and desirable in terms of physical and emotional adaptation to disability and any limitations a disability may present. In doing so they are better equipped to identify sources of frustra-

tion and futile effort, particularly in trying to meet uninformed external expectations.

The purpose of this clinical study was to test the applicability of a goals-based model for the enhancement of community integration of persons with neuromuscular disorders. This approach offers substantial advantages in addressing the psychosocial needs of persons with disabilities to ultimately improve their quality of life. We hypothesized that there would be connections between personal goal systems and well-being in this sample of persons with NMD. Striving systems that are characterized by predominantly negative, avoidance strivings will be related to lower satisfaction ratings and a greater frequency of unpleasant emotions. Strivings that are perceived as highly valued, attainable, and provide

this study tested a goals-based model for the enhancement of community integration

meaning and purpose will be those that contribute most strongly to a sense of well-being.

We utilized the Personal Strivings Assessment Packet to evaluate subjective well being rather than standard, questionnaire measures of community integration. Preliminary results showed that this goal-based method was the strongest predictor of overall levels of well being (life satisfaction, positive affect, and vitality) of any of the other goal variables examined. The strongest predictors of life satisfaction were community integration through goals, perceived meaningfulness of the goals, and low goal difficulty. In addition, a goal-based measure of spirituality (self-ratings of the degree to which the goal brings the person closer to God) was predictive of life satisfaction and positive emotionality. The degree to which pain interfered with the person's ability to work toward his/her goals was predictive of psychological distress (negative effect). However, a direct self-report of degree of pain recently experienced was unrelated to subjective well-being. Another predictor of a negative result from the goal setting was the amount of interpersonal strain caused by the striving. These results, taken as a whole, suggest that a goal-based approach to community integration is viable and invites further exploration into the role of personal goals as workable clinical units of analysis for understanding the quality of life in the lives of persons with neuromuscular disease. However, in this study little information has been provided as to what factors are critical to achieving a high quality of life. Facilitating the patient's identification of personally meaningful, attainable strivings and developing workable strategies for their accomplishment becomes a pri-

Participants in the quality of life intervention experienced more high-energy positive moods

ority for rehabilitation providers.

In an additional study, the participants in the initial study were divided in thirds as listed:

- *quality of life intervention.* They kept daily records for 21 days recording their moods, health behaviors (sleep duration and quality, pain and pain interference with daily activities, exercise), difficulty in activities of daily living, positive life events (things for which they were grateful) and global ratings of life satisfaction, optimism for the upcoming day, and feelings of connectedness to others and wrote down up to 5 things in their lives for which they were grateful or thankful.
- indicated a person to whom they were grateful.
- control group who did no listing each day.

We found that the group with the quality of life intervention, when compared to the control group, experienced more high-energy positive moods (such as enthusiasm, alertness, and vitality), a greater sense of feeling connected to others, more optimistic ratings of one's life, and better sleep duration and quality. A number of the participants wrote to us expressing how valuable this daily monitoring procedure was for them, and how it led to an increased appreciation for the goodness in their lives. The transformative power of positive emotions has been documented in much recent research. Our participants report that such "magical" moments or periods of time, described by many as states of increased spiritual connectedness, were triggered by the genuine experience of heartfelt positive emotion. The experi-

(Strivings, Continued on page 15)

Risks and Benefits of Genetic Testing in Persons with Hereditary NMD

T.D.Bird, MD

Genetic testing by DNA analysis is becoming a common occurrence in the practice of medicine. It is most frequently being used in the diagnostic evaluation of symptomatic patients. The use of genetic testing is less well understood in the identification of asymptomatic gene carriers, who often may be tested decades before the onset of symptoms. This project addressed an important and timely issue: the risks and benefits of genetic testing of asymptomatic persons in families with hereditary neuromuscular disorders. Nationally, more than 200,000 individuals are at risk for the NMD disorders and could be eligible for genetic testing. The social, psychological and economic fallout from such testing is largely unknown. The impact is likely to vary widely depending on the characteristics of the diseases, the individuals and the local social milieu. It behooves us to carefully measure and evaluate these risks and benefits in order to adjust the testing process appropriately to assist individuals, families and society in coping with the results. It is critical for society and the health care profession to assess and monitor the impact of DNA testing on factors such as general patient well being, family planning, employment and access to insurance in these disorders.

The hereditary neuromuscular disorders provide a broad assortment of diseases on which to assess the impact of genetic testing. This is because they affect several different parts of the nerv-

ous system resulting in a wide range of quite variable symptoms and signs, may last many decades, may or may not reduce life span, frequently do not produce cognitive or behavioral deficits and may be perceived quite differently by various family members. In the last seven years genes have been discovered for and testing is available for myotonic dystrophy (MMD), three types of autosomal dominant Charcot-Marie-Tooth neuropathy (CMT) and six types of hereditary ataxia (HA). MMD, CMT and HA have a very broad range of possible degrees of "severity".



The results of testing for myotonic muscular dystrophy, Charcot Marie Tooth dystrophy and hereditary ataxias will likely have different implications than those for other diseases such as colon and breast cancer, where the disease outcomes are different and treatments may be available.

Potential benefits of genetic testing include:

- specific diagnosis of carrier status (positive or negative),
- reduction of anxiety,
- useful information for family planning, financial planning and career plans.

Potential risks of genetic testing include:

- increased anxiety and depression
- threats to insurance, employment
- threats to personal relationships.

The long range goals of this study were to: (a) better understand the moti-

vating factors and decision making processes underlying subject participation or nonparticipation in genetic testing, (b) identify factors influencing both personal and societal responses to genetic testing and (c) develop procedures and strategies to improve the implementation and long-term care and counseling of subjects undergoing genetic testing.

In this study, we found that a common motivation for genetic testing was suspicion that one may be developing early signs of the disease. Many of those with positive tests did show subtle, non-specific signs of the disease on examination. However, some who believed that they had early symptoms of the disease were relieved to discover that they had not inherited the genetic condition. Another important motivation was family planning, making a decision about whether or not to have children.

The response to the testing was generally good. There was a trend for anxiety levels to decrease following testing in both those with a positive test and those with a negative test. An interesting finding was the absence of major depression in the study population. This was in contrast to the findings in Huntington's disease and familial Alzheimer's disease. This is possibly due to the difference in the cognitive effect of the groups of diseases. Those with NMD generally do not exhibit the severe cognitive effects seen in Huntington's and Alzheimer's diseases. Another factor was that those deciding to pursue genetic testing were a highly self-selected group, mainly college-educated, middle-aged females with children. Further study is needed of the psychological make up of this group.

Genetic testing poses a consider-

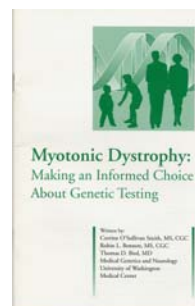
able concern over the potential for discrimination in acquiring health insurance. Although in this study we did not find this discrimination, the state in which it was conducted has a law preventing discrimination in insurance. Some of the participants were denied long-term insurance. This aspect also requires further study.

As a part of this study, informational booklets were written:

- ◆ Myotonic Dystrophy: Making an Informed Choice about Genetic Testing
- ◆ Facioscapulohumoral Muscular Dystrophy: Making an Informed Choice about Genetic Testing
- ◆ Spinocerebellar Ataxia: Making an Informed Choice about Genetic Testing

These booklets are designed to provide background information on genetic testing with an emphasis on the issues involved in genetic testing for these three diseases. They are available in pdf format on the Internet at <http://nmdinfo.org/rrtc/publications/genetictesting.asp> or <http://depts.washington.edu/neurogen/>.

These results should not be generalized to other studies and any person considering genetic testing should receive counseling from trained, experienced genetic counselors.



Enhancing Medical Students' Attitudes & Knowledge about Disabilities

N.K. Seyden, M.S., R.T. Abresch, M.S., D.D. Kilmer, M.D.

Although the goal of rehabilitation has been to help people with disabilities "live happily and productively on the same level as and with the same opportunities as their neighbors," several studies have shown that physicians believe that individuals with severe disabilities have a poor quality of life. In contrast, our previous research, conducted on individuals with severe neuromuscular diseases, indicates that many severely disabled individuals perceive that they have a high quality of life. This discrepancy in opinion has been shown to alter the care that a person with a severe disability receives.

The goals of this project were to have medical students assess their perception of the life satisfaction of individuals with severe neuromuscular diseases; to determine if their attitude would affect their potential treatment; and to assess their knowledge of the physical, mental, social and vocational needs of persons who are severely disabled. To accomplish these goals, medical students had a four-week "hands on" medical rotation working with patients in rehabilitation treatment in the Physical Medicine and Rehabilitation Department (PM&R). This training included a short course where materials were presented on the barriers to access faced by those with disabilities, problems in living independently with personal care assistance, how care is provided and paid for, use of assistive devices and technological developments, sexual and repro-

ductive health needs of the disabled, physical and substance abuse issues for wheelchair users, aging with a disability, public policy issues, and availability of national resources. The students completed a questionnaire at the beginning of their PM&R training period to provide baseline information. After exposure to the training material and four weeks of personally working with patients in rehabilitation, they repeated the questionnaire to ascertain whether the program had made a difference in their knowledge and attitudes toward disability.

The majority of medical students reported that, prior to this rehabilitation training, they were not aware of the health care needs and living concerns of individuals with disabilities. They incorrectly assumed that individuals with severe disabilities have low self-esteem, negative attitudes, and feelings of failure and uselessness. In addition, they had a limited understanding of what it means to live

with a disability (i.e., barriers encountered, risks to health, understanding the concept of independent living with personal care assistance, knowledge of resources available, and the laws and rights of individuals with disabilities).

The training program changed the attitude and knowledge of these future physicians toward people with disability and, surprisingly, changed their perception of their own lives. They were unaware of the housing difficulties,



Nancy Seyden, M.S.

the problems posed by the need for personal care assistants, the gynecological and abuse issues of wheelchair users and their lack of knowledge of agency resources for the disabled (SSI, SSDI, IHSS, etc.). They also found that the disabled were healthier and had an easier and more rewarding life than their original perception. After exposure to the day-to-day situations faced by the disabled, the students were more satisfied with their own housing and transportation and felt that their own lives were more interesting and more enjoyable.

As future physicians this new understanding and attitude should help them

The training program changed the attitude and knowledge of these future physicians toward people with disability and, surprisingly, changed their perception of their own lives.

to improve their communication with people with disabilities and improve their ability to provide better services to

individuals with long-term disabilities. Identifying where gaps exist in the students' knowledge and how issues might be considered that affect health, quality of life, and community integration of individuals with long-term disabilities will provide information that can be used to complement existing course-

work. The data gathered will be used to further refine the curriculum and determine whether or not the program should be replicated at other medical and nursing schools.

(Pain, Continued from page 9)

to determine which treatment or treatments are most effective for him/her. The findings from this study suggest that, in their order of effectiveness, the following treatments provide pain relief: chiropractic manipulation (tried by only a few patients), narcotic analgesics, muscle relaxants, massage, acupuncture, ibuprophen/aspirin, hypnotic analgesia, neruontin, physical therapy, counseling, tricyclic antidepressants, biofeedback/relaxation training, acetaminophen, carbamazapine, and



magnets.

We anticipate that the independence and quality of life of persons with slowly progressive NMD will be improved by a better understanding the relationship between pain and the performance of activities of daily living. As our results are disseminated, physicians will become more aware of the problem of pain in NMD and will address it in their practices to provide their patients with the opportunity for a reduction in their pain and, as a result, an improved quality of life.

(Strivings, Continued from page 11)

ence of deep appreciation for another's kindness increases the perception of connectedness to others and perhaps with all of humanity. Our research provides objective evidence of what we

have long known intuitively, that positive emotional states may indeed be key to optimal functioning, enhancing nearly all spheres of human experience, including a sense of integration or connectedness.

Meeting Information Needs to Enhance the Community Integration of Individuals with Neuromuscular Conditions

R.T. Abresch, M.S., N.K. Seyden, M.S.

Despite twenty years of effort since passage of the Rehabilitation Act of 1973, individuals with disabilities continue to experience problems in accessing information and services and in receiving maximum benefits from the health care, social service, and rehabilitation systems. This inability to obtain access to information on disability-related topics may be due to geographical and physical inaccessibility, lack of knowledge by professionals, poor inter-agency communication, a fragmented service delivery system, resource restrictions or to the continued use of traditional patterns of service provision, especially to minority groups. There is an urgent need for access to disability related information and services, and a need to improve the quality and availability of resources, especially in the areas of attendant and home health care, respite care and financial support.

In this project our goal was to determine the extent of knowledge individuals with neuromuscular diseases had about disability-related services, to assess their specific information needs and to assess their use of disability-related information and services. The second goal, after establishing the needs of those with neuromuscular disease, was to assess the information that is available and to develop an extensive Disability Resource Guide to meet those needs.

Our survey of 566 individuals with

neuromuscular diseases found that more than half of those surveyed had difficulty obtaining information on the following subjects: health care, medical research, diet and nutrition, computers, recreational opportunities, advocacy issues and durable medical equipment. Familiarity with availability of disability related services was also quite low with fewer than 40% of those surveyed familiar with Independent Living Centers, vocational rehabilitation services, transportation services for the disabled, evaluation and assessment services, and information and referral services. If individuals are not familiar with the services available to them, they are not able to access them.



To fill this information gap we developed a web based 'Resource Guide On Disability'. The guide serves two purposes: to teach individuals and their families how to find disability-related information on the Internet and to provide one place with easy access to information on disability. This allows individuals to better manage their disability and their health, and to optimize their quality of life. Broad categories covered in the Resource Guide include 'Getting Internet Information,' 'Federal Programs and Governmental Assistance,' 'Technology, Products, and Adaptation,' 'Disability Resources,' 'Medical Resources,' 'Resources for Kids,' and 'Northern California Resources.' The guide was developed for all who are

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Consensus Conference:
Role of Physical Activity and Exercise Training
in Progressive Neuromuscular Diseases (NMD)

On September 30 – October 3, 2001 the RRTC in Neuromuscular Diseases hosted a consensus conference to discuss the state of the science on the Role of Physical Activity and Exercise Training in Progressive Neuromuscular Diseases. The conference brought together 22 scientific leaders from the fields of exercise sciences and medical rehabilitation to exchange information and develop a consensus statement.

The role of exercise in the rehabilitation of individuals with neuromuscular disease is controversial. Maintaining or improving muscle strength is a major functional concern for those with loss of strength and loss of cardiorespiratory (aerobic) endurance that is secondary to neuromuscular disease. Determining whether or not exercise helps or causes further injury in muscles undermined by a progressively disabling genetic disease is complicated by a number of factors, not the least of which is the widespread belief among lay people and professionals alike that, given ample opportunity, the body can often heal itself with a self-help remedy, such as exercise. Exercise has been shown to be effective in improving or maintaining strength and endurance at particular points in the disease process, but many questions remain. The use of exercise for the many different NMD is not known. A copy of the background material and literature review on which the conference was based is available at: <http://nmdinfo.org/training/lectures/conf2001.pdf> and a copy of the program is at: <http://nmdinfo.org/training/lectures/conf2001-program.pdf>.

The conference opened with remarks by Wm.F.Fowler, Jr.,MD, followed by a patient's perspective on NMD by William Lewis, MD, a cardiologist at UC Davis who has fascioscapulothoracic dystrophy, and an overview of the conference by Craig M. McDonald, MD, principal investigator at the NIDRR RRTC on NMD.

The first day's proceedings centered around presentations on "**Adaptations to Exercise Training in Able-bodied Humans and Animals.**" Presentations on whole organ system adaptations were followed by presentations of adaptations at the cellular and molecular levels and on muscle injury due to exercise in able-bodied humans and animals.

The second day's proceedings were centered on "**Adaptations to Exercise Training in Humans and Animals with Neuromuscular Diseases.**" Fatigue as a response to exercise testing and electrical stimulation was presented first, followed by adaptations to disuse atrophy, cardiopulmonary training and resistive training in humans with NMD and then by adaptations to training and simulated exercise in animal models of NMD.

The third day of the conference was devoted to three simultaneous round table discussions, which were, followed by presentations of these summary discussions to all in attendance:

- Fatigue Response to Exercise Testing and Electrical Stimulation
- Adaptations to Exercise Training in Humans
- Adaptations to Exercise Training

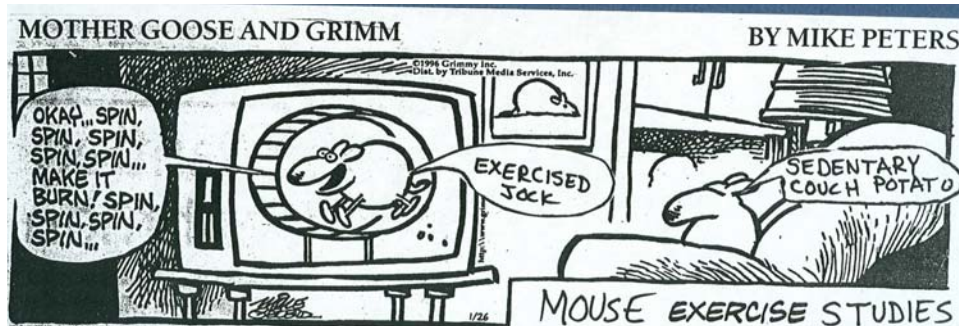
and Simulated Exercise in Animal Models of NMD

General recommendations for those with NMD are:

- Adopt an active lifestyle.
- Moderate intensity resistive exercise will usually result in modest increases in strength if the weakness is not severe and the disease progression is relatively slow.
- Moderate aerobic exercise training programs may be recommended without any deleterious effect.
- Individuals with NMD will have a variable response to training depending on their degree of weak-

ness, the rate of progressions of their weakness, their fatigability and their level of conditioning.

Conference proceedings have been published as a special supplemental issue of the **American Journal of Physical Medicine and Rehabilitation (Volume 81, November 2002, Number 11(supplement))**. Permission was granted allowing unrestricted web access to 11 of the 18 conference presentations. Available on the web site are written and audio transcripts of these and the slide presentations. These are available at <http://www.nmdinfo.net/training/lectures/>



(Exercise & Diet, Continued from page 6)

reductions in the serum lipid measurements may be observed. Although further study is needed, these preliminary results give an indication that a simple, home-based dietary and exercise regimen may be successful in improving the health status and quality of life of patients with slowly progressive neuromuscular disease.

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disabled, whether they have been disabled for a significant period of time or are newly disabled, for the families of those who are disabled and for those working in the health professions. The Resource Guide on Disability is currently available on the web site of the Department of Physical Medicine and Rehabilitation at UC Davis. <http://rrtc.ucdavis.edu/pm&r/resourceguide.htm>



Achievable goals are important for those with NMD.
See page 10.