

Forbes Norris ALS Center

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From the Desk of Robert G. Miller, M.D., Medical Director

A number of very recent developments have inspired hope in all of us here at The Forbes Norris MDA/ALS Research Center. Both patients and members of the health care team battling ALS need every infusion of hope available.

Landmark Meeting

In June, more than 150 international leaders in ALS research convened in Tarrytown, New York, to consider new approaches to finding effective ALS treatments. Research experts in a variety of disease related fields described clinical trials participation levels in their disciplines. Approximately 33% of ALS patients currently participate in clinical trials. Many disciplines have a much higher rate of participation, for example, as many as 80%–90% of cancer patients participate in clinical trials. The experts concluded that the low level of ALS patient participation did not allow research to move forward quickly enough to identify new possible therapies. Patients should be made more aware of the advantages of participating in a clinical trial. These advantages include: engendering hope; possibility of direct personal benefit; helping advance the field; helping others; and having one's finger on the pulse of leading-edge research.

Read more about this landmark ALS clinical trials conference inside this edition of the *Forbes Norris ALS Center News*.

New Developments

Novartis, a pharmaceutical research and development corporation, is about to launch global clinical trials of another drug directed toward apoptosis. This new drug has shown impressive results in the laboratory and represents another potential step forward for effective ALS disease therapy. The Norris ALS Center and other large centers around the world will be part of this exciting new trial.

A recent report in *Science Magazine* by Jeffrey Rothstein, M.D., Ph.D. and his collaborators demonstrated the effectiveness of insulin-like growth factor, IGF-1, when linked to a virus and injected into muscle. The research study demonstrated how gene therapy could effectively slow disease process substantially. A large national trial of IGF-1, sponsored by the National Institutes of Health (NIH), is now underway at a number of ALS research centers across North America, including the Norris ALS Center.

The momentum is building and there is room to be hopeful and even optimistic that in the not too distant future we will find effective treatment for this devastating disease.



A handwritten signature in black ink, appearing to read 'R. Miller'.

Robert G. Miller, M.D.
Norris ALS Center Director



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Meet The Norris ALS Center Clinical Director

Deborah Sorrell Gelinás, M.D.



Every so often one realizes how lucky they are, and the Norris ALS Center is no different. The Forbes Norris MND/ALS Research Center realized its luck when they discovered the exceptional gift they had received with the arrival of Dr. Deborah Gelinás at the Center in 1993 as its Clinical Director.

Brought in to fill the enormous shoes of the late Dr. Forbes Norris, an internationally recognized authority on ALS, Dr. Gelinás has shown her exceptional skills in clinical management and research. "I am committed to ALS patients and compassionate to their profound array of ever-changing problems," she says.

Dr. Gelinás has dedicated her life to this exceptionally difficult and oftentimes demoralizing, long-term disease and its problems. She is relentless in her pursuit for improvement, always seeking better clinical techniques to improve the patient's quality of life. This unique combination of commitment, compassion, and expertise has garnered her an increasing load of speaking and writing engagements around the country and the world. However, this huge load of professional obligations does not bother this exceptionally competent and innovative "super" woman physician.

Born in Massachusetts, Dr. Gelinás is from a large, loving family of six sisters, one of whom developed a neurological problem early in life. This prompted Dr. Gelinás'

interest in medicine at an early age. She excelled in all levels of school, graduating from McGill University and then New York Medical College with honors.

Following a stint as Director of the Neurology Unit at Letterman Army Hospital in San Francisco and being the mother of three children, Dr. Gelinás was delighted to receive an offer to stay in San Francisco. She accepted an invitation from Dr. Miller to assist in the burgeoning Norris ALS Clinic at California Pacific Medical Center.

Upon meeting the renowned Dr. Norris, she found her true calling, involvement in this clinical and basic science program. "The first time I saw the desperation in the eyes of these patients, I knew where I belonged," she says. Dr. Gelinás saw how ALS patients, desperate for help in coping with an incurable, increasingly disabling disease, could have a better quality of life. Using aggressive symptomatic interventions and an empathetic caring hands-on approach, she saw how this could greatly impact patient's lives, allowing them to retain hope and dignity.

She sought to emulate the compassionate level of care set by Dr. Norris. This has set the tone for patient care at the Norris ALS Center and also the model standard of ALS clinical management around the world.

The Norris ALS Center is extraordinarily proud of Dr. Gelinás, her work and her commitment to the ALS community. She has expanded her professional horizons by developing new clinical approaches in research, which will ultimately evolve into new applications for better care of ALS patients and their families.

U P C O M I N G E V E N T S

11th Annual International ALS/MND Symposium

November 13 – 19, 2003

Milan, Italy

This is the only International ALS Scientific Symposium devoted solely to all aspects of ALS. It consists of concurrent sessions addressing the most important basic research and clinical management of ALS. Participants, including patients, families, and health care professionals from all disciplines, come from all over the world. For more information on this event visit the International ALS/MND Alliance Website at www.als/mndalliance.org/symposiums.

Landmark ALS Clinical Trials Conference Yields Significant Hope for Future

“Reaffirmed hope for successful ALS clinical trials” might have been the ultimate message to emerge from the major ALS conference, “ALS Clinical Trials – The Challenge of the Next Century,” held in June 2003 in Tarrytown, New York.

Chaired by the renowned **Hiroshi Mitsumoto, M.D.**, Director of the Eleanor and Lou Gehrig MDA/ALS Research Center, and sponsored by Columbia University’s Department of Neurology, the Muscular Dystrophy Association, the NINDS, and the National Institutes of Health. The meeting attracted scientists, clinicians, families, advocacy groups, industry representatives, various ALS organizations and groups, the NIH and FDA.

Together, this group examined some of today’s major issues facing the ALS medical community. These included:

- The high incidence of failure in past trials of potential therapies.
- Trial design, outcome measures or end points, and the need for “negative” studies.
- The impact of fewer industry sponsored trials on the immediate future.
- The growth of investigator-driven drug trials and their impact.
- The complex problems associated with “high throughput” assay discoveries.
- The strength and limitations of animal models as predictors of human results.
- “Fast track” potential therapies and satisfy current FDA requirements.
- The emergence of several ALS study groups and their roles in trials.
- The state of stem cell research and potential gene therapy.

A unique and particularly valuable aspect of the conference was the recognition that ALS scientists could learn from other disease advancements and the processes used which have resulted in treatment success. This foresight brought several medical specialists from other fields to

present valuable lessons that can be applied to future ALS studies. Additionally, representatives from the FDA and the NIH offered specific recommendations, assurances, and services to aid investigators in gaining approval for their grants.

A successful meeting always addresses future “action issues” to assure success of the hoped-for goals. This meeting’s “action issues” for the future included:

- Commitment to hold meetings to share information, stimulate ideas, and build collaborations.
- Improve trial design and the conduct of clinical trials, including administrative issues that more efficiently expedite the time between grant approval, actual funding, and trial onset.
- Continue current efforts, including drug screening efforts, stem cell and gene therapy research, and development of better animal models.
- Promote “gene environment” studies to better understand sporadic ALS.
- Explore the concept of a national ALS study group, possibly by merging the current ALS study groups to foster better, larger, more inclusive studies.
- Obtain more input and involvement from ALS organizations and advocacy groups.
- Promote a more inclusive approach by encouraging and training the next generation of young interested investigators.

The success of this landmark meeting was reflected in the pervasive sense of hope among the scientists in finding effective therapies for ALS in the near future.

The Forbes Norris ALS Center News is published twice a year. For more information or to be removed from the mailing list, please call (415) 750-4406.

RESEARCH AGENDA



Basic Research

Dr. Mary Abood: Her research study “Amyotrophic Lateral Sclerosis: Delayed disease progression in mice by treatment with a cannabinoid” has been accepted for publication by the journal *Amyotrophic Lateral Sclerosis and other Motor Neuron Disorders*. She has received a supplemental award from the National Institute of Neurological Diseases and Stroke (NINDS) to continue these studies in mice.

Dr. Nancy Lee: Research investigation has narrowed down the identification of the earliest molecular changes in the nervous system to early microglia dysfunction involvement in ALS. Current research suggests that microglia perform dual roles of neuroprotection as well as an immune function to kill and remove damaged neurons. While both these functions are critical and essential to the well being of our central nervous system, she believes dysfunction of the microglia contributes to the degeneration of motor neurons in ALS. She is concentrating on enhancing the neuroprotective role and blocking the neurodegenerative role of the microglia system in order to block the progression of ALS.

Dr. Jian Liu: In her research lab, she is focusing on studying the genetic model of ALS: mutations in the copper/zinc superoxide dismutase (SOD1) gene. Using rodent models of ALS, she recently discovered that mutant SOD1s (bad protein) are specifically mislocated and recruited to spinal cord mitochondria. Currently she is trying to understand how this misregulation and further damage in mitochondria of the affected tissues occurs, as well as to find ways to protect them against toxicity and preserve their function.

Current Clinical Research Trials

Working in all aspects of basis science and clinical research, including clinical drug trials, is an important part of fighting and winning the war against ALS. Participation in research is a difficult personal medical decision. If you are interested in participating in any of our current research studies, please contact our Research Nurse, Jason Mass at **(415) 600-3967**.

Myotrophin Phase III (IGF1) Study — 24-month placebo-controlled study to determine whether Myotrophin slows the progression of weakness in ALS.

Minocycline: Phase III — 13-month trial testing the possible benefit of minocycline, an oral antibiotic, in

controlling programmed cell death, apoptosis. This is a placebo-controlled study requiring monthly visits.

THC346: Phase IIb — Evaluation of the effects of THC346 on ALS symptoms. 10- to 17-month trial enrollment. This is a placebo-controlled study requiring monthly visits.

Creatine Study — Trial testing whether creatine treatment results in increased and sustained muscle strength, in addition to the possibility of slowing progressive muscle deterioration. This study requires 12 visits over a 9-month period.

QR-334 Study — Open-label trial for ALS patients with excessive saliva problems. Trial participants receive real medication in either lozenge or aerosol form. The study requires 2 visits over a 5-week period.

Magnetic Resonance Study — Measuring the concentrations of several chemicals in the brain helps us understand the possible causes of ALS, including the role of abnormal glutamate levels in the brain. Glutamate may serve as a reliable indicator of specific impairments in early detection and evaluation of new drug therapies.

ALS Gene Study — This study focuses on finding the causes of ALS through an examination of both genetics and environmental risk factors. Blood samples from individuals with ALS and their parents and/or siblings can be drawn at your local community laboratory.

“ALS Care” Database — North American voluntary patient care database serves as a tool to help us better understand clinical practices for ALS patient care and the relationship between medical practices and clinical outcomes.

The Vest — In conjunction with six United States ALS centers, this study is being conducted to determine the mucous expectoration efficacy of a chest vibrating mechanical device, “The Vest.” If you would like more information on this study please contact **Felecia Hart, R.N. (415) 600-3604**.

Exercise Study — Measures the effects of regular exercise on muscle strength, endurance and mood, and quality of life. Study requires 4 visits per week over a 4-month period.

The ALS Research Foundation Celebrates 20th Anniversary

2002 marked a memorable year in the Bay Area ALS community: The ALS and Neuromuscular Research Foundation in San Francisco celebrated its 20th Anniversary. It was a poignant and lovely evening, with much reminiscing on the 20 years of creating, developing, supporting, and maintaining the goals of a non-profit foundation. The Foundation is devoted to researching the cause of ALS and supporting the needs for creating an effective patient care program to aid those who suffer the indignities of this disease.

In attendance were original founding and current board members of the Foundation, including **Mrs. Esther Quement**, Board President, and **Regina Mastrantonio**, who together with her late husband, **Anthony**, and Mrs. Quement helped establish the Foundation with **Dr. Forbes Norris**, **Dr. Eric Denys** and **Dee Holden Norris**, current Executive Director. Joining current Board members, **Drs. Bob Miller**, **Deborah Gelinas** and **Bob Fallat**, were heads of the current ALS Basic Science team at CPMCRI, **Drs. Nancy Lee**, **Mary Abood**, and **Jian Liu**.

Generous testimony was paid to everyone for a job well done over the years, which has directly led to the success of the Foundation. This success is measured by the Foundation's role in helping to found and support the Forbes Norris ALS Research Center at California Pacific Medical Center, one of the largest and best-staffed ALS



clinical centers in the country, and a model program for other ALS centers around the country. This standard for clinical management of ALS is equaled by the ALS basic science program, which continues to make significant contributions to the molecular understanding of why motor nerves die.

The Foundation has been supported over the years by the generosity and commitment of its donors and volunteers. This generosity has helped to sponsor a variety of activities from fundraising events to hosting visiting dignitaries and international symposia. It has been a remarkable 20 years for a small foundation, and with the continued commitment and the dedication of this extraordinary board and its leadership, we plan on a long and successful future.

Patient's Corner:

Update on the Medicare Homebound Restriction

David Jayne, founder of the National Coalition to Amend the Medicare Homebound Restriction for Americans with Significant Illness (NCAHB), continues his fight for the rights of "homebound patients." Recently Rep. Edward Markey and Rep. Christopher Smith introduced H.R. 1874, legislation to exempt severely and permanently disabled individuals from Medicare restrictions limiting their ability to travel away from home without losing their home health benefits. H.R. 1874 is a compromise bill creating a pilot program to test whether this exemption would result in increased costs to the Medicare program, as claimed by the Center for Medicare and Medicaid Services.

Call (202) 224-3121 or go to <http://www.house.gov> to contact your Representative, or <http://www.senate.gov> to

contact your Senator regarding H.R. 1874. Let's all join in the fight to loosen "homebound restrictions" and keep our needed home care services.

Traveling With ALS? YES!!!

Don't let anything stop you from pursuing your traveling dreams! With planning and patience most trips are not insurmountable. Joined by travel companions and a dedicated travel agent, you can go just about anywhere. Choosing a travel agent who understands the needs of persons with disabilities and knows the vacation facilities that specialize in wheelchair accommodations can make traveling a relaxing and enjoyable event. Most agencies that specialize in disability travel can be found by searching the Internet. They not only set up the travel arrangements, but also the excursions in your vacation location.

Traveling with a disability is not easy, but with extra pre-planning and research it is completely doable and well worth the experience. Kudos to all who accomplish incredible things against incredible odds. The Forbes Norris ALS Center applauds you.



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The Gift of Giving

The Forbes Norris MDA/ALS Research Center is totally dependent upon private donations to support its patient services programs. It is supported, in part by the generous donors for ALS to the California Pacific Medical Center Foundation.

For more information on the Foundation or on ways you may give to the Forbes Norris MDA/ALS Research Center to support their services, please call Dee Norris at (415) 600-3608.

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