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Synapse

Winter 2004

Serving the Primary Lateral Sclerosis Community since 1997
Welcoming the SP Foundation since 2003

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Mission Just as the synapse is the point of neuron transfer between two nerve cells, this newsletter is intended to be the point of information transfer between individuals dealing with PLS or HSP and their caregivers. The focus of this quarterly newsletter will be on current advances in medical research and treatment, regional meeting reports, calendars of future meetings, help for caregivers and suggestions on how to enhance living with our diseases. *Ed. Note: This mission statement has been expanded to acknowledge the significant change which has occurred since the founding of the SP Foundation. The SP Foundation, created in 2002, is the only foundation dedicated exclusively to find cures for PLS/HSP. Today there is one patient community*

for those with HSP or PLS. Synapse - Winter 2004 Edition

PLS Symposium is set for June 4-6 The office of Dr. Teepu Siddique at Northwestern University has announced that the Symposium to define PLS, has been set for June 4-6, 2004 at Chaminade in Santa Cruz, CA. We have all worked hard to raise over \$36,000 seed money for this Symposium. The Symposium is about us, but not for us to attend. The Symposium is exclusively for the medical community to present papers and discuss matters relating to Primary Lateral Sclerosis. There will be a welcome dinner Friday night and multiple sessions Saturday with a Sunday morning session devoted to actually getting diagnostic criteria nailed down for publication. So far, 31 researchers from around the world have confirmed their attendance at the Symposium. We are awaiting confirmation from 20 more. The Les Turner ALS Foundation has generously offered a \$20,000 donation to the symposium! Thank you one and all for your efforts to help this important gathering of researchers happen!

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FUNDING

ExxonMobil Charity Campaign Set to Generate \$46,000 for SP Foundation

Ed Note: The following article will hopefully inspire others to encourage the corporations they work for to embrace SP Foundation as a major charity. SPF Board member Annette Lockwood has worked for ExxonMobil Corporation for 23 years (Mobil Oil prior to 2000). In 2002, ExxonMobil elected to conduct an Employees Favorite Charities Campaign (EFCC) for 2003 charitable donations instead of the usual United Way Campaign. The VP for the department that Annette works in spearheaded the inclusion of SPF in the campaign. Annette was selected as one of eight employees to be featured in a video that was used during the campaign. Although SPF was not on the list of charities for the first year, co-workers could write it in. The result was \$13,300 in contributions from her co-workers. Exxon Mobil Corporation provided a corporate match of \$5,660 which

made a 2003 grand

contribution total of \$18,960. In preparation for the 2004 EFCC, ExxonMobil invited the most popular charities from the previous year to participate in a Charity Fair. Each charity was given a table to display information and materials. On December 2, ExxonMobil presented Annette with a \$7,430 check which represented the Exxon Mobil Corporation match for the 2004 campaign. 2004 pledges from employees totaled \$20,081, for a grand total of \$27,511 to be donated in 2004, a 45% increase over 2003 contributions. Out of 157 charities that were selected, SPF was one of the top 20 charities selected.

and is due January 13. dale.rutschow@spfoundation.org **March 6, Raleigh, North Carolina Conference**

features leading Douglas A. Marchuk, Ph.D., Duke University, recipient of one of the first SPF Research Grant and a special PLS break-out session. Pat Croom - 919-553-3557 **March 12-13 Orlando, FL Connection** featuring a support group gathering and special break-out sessions for significant others to meet while those with HSP/PLS meet to talk about special topics and concerns.

kathigeisler1@aol.com or call: 978-256-2673 **April 2-3 Berkley Springs, West VA Ronnie's annual Spring Fling** weekend. frogrove@peoplepc.com 304-258-5275 -- needs TDD operator **April 24, Burlington, MA. Connection luncheon** at the Four Points Sheraton. kathigeisler1@aol.com or call: 978-256-2673 **May 1, New York Conference Tarrytown**

(Westchester County) featuring several educational workshops on treatment modalities as well as support group session. nosfatsugbob@netscape.net 914-997-1981. **June 4-6 Santa Cruz CA-Symposium to Define PLS.** A gathering of neurologists to clinically define PLS. **June 25-26 Chicago IL - Patient Connection and tour of Dr. Siddique's lab.** Welcome dinner Friday, Saturday 9am-12pm conference at Northwestern.

Teepu Siddique will be the speaker. He will give a preliminary report on the PLS Symposium and answer questions. Lunch following, with a tour of the lab from 1:15-2 pm More details will follow. Contact Jennifer Thomson mdmfoo@yahoo.com 858-481-5797 August 27-29 Boston, MA Team Walk for Our **Cures and National Conference** Plan now to attend our largest annual event. Noted speakers who are researchers on the cutting edge of our diseases, and our major fund raising event – Team Walk are the highlights of the weekend. Headquarters will be the Sheraton Four Points Hotel in Burlington, MA. The committee is meeting regularly to plan an event which will

EVENTS

Calendar of Events for the SP Community January 24 Denver CO. a Connection Luncheon will be held at the Saint James Church Hall \$15. Registration Fee covers lunch and the meeting

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be even better than the 2003 event! kathigeisler1@aol.com or call: 978-256-2673

Vancouver, British Columbia, Canada Contact JeanChambers 604-990-1060

MEDICAL UPDATES

NOTE: Local groups for related organizations such as the [MDA](#), [ALS Association](#), [National Multiple Sclerosis Society](#) and [Ataxia Foundation](#), may allow members of our community to attend their support groups. Please check out these resources. Additionally, these local groups are run by members of our community and other members of our community are specifically encouraged to attend: Ann Arbor, MI University of Michigan Every second Friday of the month, 6:30 pm - 8:30 pm, (in partnership with the NORD Michigan Chapter). Organized by [Joan Mathay](#), R.N., nurse of John K. Fink, M.D., the SPF Medical Advisor. 734-936-3087 **Norristown, PA** (nearly Philadelphia) 2nd Saturday of the month, 10:00 a.m. - 12:30 p.m., Mercy Suburban General Hospital. In partnership with the Ataxia Foundation local group. Contact [Liz Nusseur](#). 610-277-7722 **Garden Grove, CA** (near LA) - Monthly Support Group Meeting In partnership with the Ataxia Foundation local group. Contact [Kay Bell](#). **North Carolina South Carolina** - Quarterly Support Group Meeting Quarterly meeting alternates locations between Spartanburg, SC and Brevard/Asheville area in NC. In partnership with the Ataxia Foundation local group. Contact [Cece Russell](#). Areas where SPF volunteers hold meetings at least annually: Colorado: Contact [Dale Rutschow](#) 719-596-2087 Connecticut: Contact Dolores Carron 860-666 9862 Florida: Contact [Ann White](#) 717-279-0876 Idaho: Contact events@sp-foundation.org 978 256-2673 Massachusetts: Contact [Kathi Geisler](#) 978-256 2673 Texas: Contact [Marlene Doolen](#) 512-331-1953 West Virginia: Contact [Ronnie Grove](#) 304-258 5275 Wisconsin: Contact Annette Lockwood 703-493 8779

Two \$40,000 SP Foundation Grants Awarded The Spastic Paraplegia

Foundation, Inc. (SPF) announced the recipients of its first two Research Grants for investigation of upper motor neuron disorders. John K. Fink, M.D., Director, Neurogenetic Disorders Clinic, University of Michigan, was awarded a \$40,000 Grant for "A Molecular Genetic Analysis of Primary Lateral Sclerosis". Douglas A. Marchuk, Ph.D., Associate Professor of Molecular Genetics and Microbiology, Duke University, was awarded a \$40,000 Grant for "A Mouse Model of Hereditary Spastic Paraplegia". "I am very excited that our first awards are going to these two outstanding scientists," said Mark Weber, Esq., SPF President. "We are moving beyond discovering genes responsible for Primary Lateral Sclerosis and Hereditary Spastic Paraplegia to discovering the functions of the proteins created by those genes. This brings us one large step closer to the goal that we all desire - a cure. No other organization was focused on this group of motor neuron disorders, so we created the SPF to raise funds for research as well as meet patient needs of information and support," he adds. Some 20,000 people across the U.S. are estimated to be affected by one of these disorders. The organization's Scientific Advisory Board (SAB), which serves to review grant proposals as well as provide high-level medical and scientific guidance is chaired by Martha A. Nance, MD, Park Nicollet Clinic, St. Louis Park, MN. SAB members are Mary Kay Floeter, MD, PhD, Chief, EMG Section, National Institute for Neurological Disorders and Stroke (NINDS), National Institutes of Health (NIH), Bethesda, MD; Mark Gudessblatt, MD, South Shore Neurological Associates, Long Island, NY; Terry D. Heiman Patterson, MD, Professor of Neurology, Drexel

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University College of Medicine,
Philadelphia, PA; and Laura Ranum, PhD,
Professor of Genetics, Cell Biology and
Development, University of Minnesota.
Minneapolis, MN.

Baclofen & Learning Disturbance

Contributed by Dr. John Fink We (and many other neurologists and psychiatrists) have prescribed Baclofen, often in fairly high

dosages, to many children for treatment of spasticity and dystonia. In most instances, Baclofen is well tolerated without an obvious change in the individual's school performance. Known side effects of Baclofen include sedation (sleepiness) or paradoxically, hyperactivity, as well as memory disturbance. The occurrence of side-effects from Baclofen is related to a number of factors including the absolute dose and the rate of increasing dosage as well as individual variation. Some people (children or adults) are not able to tolerate even very small doses of Baclofen. Other individuals tolerate very large doses of Baclofen (if this high dosage is achieved gradually over many weeks). Baclofen (Lioresal) is chemically related to Valium. I would not be surprised to learn that in some individuals, Baclofen was associated with learning disturbance. I would suspect that this would be more likely to occur if a) other sedating medications were also used; b) the individual was taking a very high dose; or c) the dosage had been increased fairly rapidly. Certainly, I would suspect Baclofen to be a contributing factor if someone who had no prior learning disturbance, noticed learning disturbance after beginning to take Baclofen (or rapidly increasing Baclofen from a previously well-tolerated dose). As with all medications, we must pay attention to the appearance of adverse effects. With potentially sedating medications, such as Baclofen, this includes disturbance of memory, attention, school performance, sleep pattern, behavior, and mood.

dysfunction (HSP and PLS): "Spasticity: Physiologic Studies" Number: 01-N-0148

Summary: This study will provide information about changes that occur in the motor neurons of the spinal cord (the nerve cells that control the muscles) when the motor cortex (the region of the brain that controls movement) is unable to send messages

to the spinal cord and muscles in the normal way. This information will help elucidate how the nervous system adapts after injury or disease of the motor cortex. All participants will have electromyography (measurement of electrical activity in muscles) during nerve stimulation and transcranial magnetic stimulation. 2.

NIH is actively recruiting patients with ascending PLS for: "Movement Related Cortical Potentials in Primary Lateral Sclerosis" Number: 04-N-0017 Summary: This study will examine whether the motor cortex (the part of the brain that controls movement) works properly in patients with

primary lateral sclerosis (PLS). Healthy volunteers between 40 and 75 years of age and patients with ascending PLS may be eligible for this study. Patients with ascending PLS have a slowing of finger-tapping movements that corresponds to a particular abnormality of certain neuronal (nerve cell) activity. Participants perform a finger-tapping reaction time exercise while brain wave activity (electroencephalography, or EEG) and muscle activity (electromyogram, or EMG) are measured. Contacts: Patient Recruitment and Public Liaison Office Building 61 10 Cloister Court Bethesda, Maryland 20892-4754

Toll Free: 1-800-411-1222 TTY: 301-594-9774 (local), 1-866-411-1010 (toll free) Fax: 301-480-9793 Electronic Mail: prpl@mail.cc.nih.gov Note: Travel

expenses are covered on many NIH sponsored studies.

NIH Clinical Research Studies

1. NIH is actively recruiting patients with spasticity caused by selective corticospinal tract

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Milan MDA Conference Summary, November, 2003 <http://www.mndassociation.org/fullsite/symposium/milan/international2.htm> The site above will give the reader a lay persons synopsis of this important conference. For our Synapse readers without computers, I suggest you go to your local library, type in the above site, and print out the entire

summary. The following items were a part of this conference: Researchers investigating the fatal neurodegenerative condition amyotrophic lateral sclerosis (ALS) have pinpointed the first biomarkers for the disease. In addition to their diagnostic potential, the markers should shed light on the disease process itself, they report. Also known as motor neuron disease, ALS is a progressive degeneration of the motor neurons in the brain and spinal cord. These cells control the muscles used for locomotion, speaking, swallowing and breathing, and without them the muscles weaken and waste. Life expectancy from diagnosis is 2-5 years. Worldwide there are about 120,000 new cases diagnosed a year. There is one licensed drug treatment, riluzole, but it prolongs life only slightly, several other drugs are in trials. A total of 15 biomarkers for the disorder have been discovered by a team at the University of Pittsburgh, Pennsylvania, led by Robert Bowser. The researchers examined the cerebrospinal fluid (CSF) of 20 people recently diagnosed with ALS, and 20 controls. CSF is in close contact with motor neurons and brain cells called glia, which are also affected by ALS. The researchers analyzed the protein content of the CSF samples using a new mass spectrometry technique called SELDI-TOF (surface enhanced laser desorption ionization - time of flight). Analysis of the data revealed a panel of 15 proteins that predict ALS with 100% sensitivity, report Bowser's team. Specificity - the degree to which false positive predictions are eliminated - was around 85%, but this is expected to improve as more samples are

added to the dataset. Work is now underway to

sequence and identify the proteins. "We don't know at the moment if they are alterations or degradation products of existing proteins, or changes of protein expression, or whether these are novel proteins," said Bowser. "If some turn out to be well-known proteins, it could rapidly lead to new insights into the pathogenesis of ALS. If they are new proteins we would have to develop functional assays for them, which could take another year." It is not known why the motor neurons of ALS patients die, though researchers predict that programmed cell death, apoptosis, is probably involved. "We have various hints," said Bowser, "but we really don't know the key biochemical pathways to cell death. If some of the biomarkers are linked to particular pathways, it will point us towards those pathways as being

important. I think we will obtain some very important information." Once characterized, the biomarkers will be used to develop the first diagnostic test for ALS. Clinical diagnosis is difficult, hampering both patient care and research into new treatments. "In the lab we can diagnose ALS from a CSF sample in about six hours," said Bowser. A CSF-based test would enable doctors to assess the effectiveness of potential drug treatments in reducing protein abnormalities, though more research will be needed to see whether any such reductions correlate with clinical improvement. "We know that the pattern of biomarkers changes during disease progression, and we're currently trying to recruit more patients to study the pattern of that change," Bowser said. The team plan to analyse another 100-200 CSF samples in

the next few months. "Finding biomarkers is a top priority in ALS research," said Belinda Cupid, research coordinator for the UK-based Motor Neurone Disease Association. "This work is timely, and the techniques used are novel and elegant. However, until the proteins are identified they can't yet be confirmed as specific ALS biomarkers." Every year the contribution of an eminent neurologist who also runs an active research program is recognized by awarding the Forbes

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Norris Award. This year the award was made to Dr Bob Brown of Massachusetts General Hospital in Boston, USA. He is particularly known for encouraging international collaborations - many careers of well-respected North American and European researchers have been enhanced from a period as a visiting scientist in his laboratory. In light of this award it was fitting that Dr Bob Brown had been invited to give the closing presentation of the Symposium. He started his upbeat talk by asserting, "We have 10 more therapeutic targets than we had 10 years ago". These include targeting other cells in addition to motor neurons. Dr Brown also suggested that these drugs will probably involve "different agents acting in concert". One of the hurdles for developing drugs to treat MND is their adequate delivery

into the brain and spinal cord. In the remainder of his talk Dr Brown highlighted a number of new developments that could solve this problem. These included the potential of both gene and stem cell therapies respectively. "There is a sea change coming in ALS research," he concluded.

of the current study, which was presented at the San Francisco meetings of the American Neurological Association in October, should help understand principles of regrowth that apply to all types of nerves. "Of course our goal down the line is therapy," he says. In this study, Hvke's team used a model system of chronic nerve injury. The researchers severed a nerve in the leg, letting the free piece deteriorate for six months. Then, they connected a new, freshly-cut nerve to that segment to see if repair and regrowth through it was still possible. Most important, they injected neural stem cells from mice to the nerve area. The happy result was that, in models using the stem cells, nerve fibers grew from the healthy nerve through the formerly injured section. And though it wasn't 100 percent, electrical activity was restored. Recordings of nerve activity in the foot showed messages were getting through the previously injured leg nerve. Hvke believes the success was due, in part, from stem cell secretion of a potent growth factor called GDNF. The team also had strong signs that natural systems that suppress nerve growth - nature's way of preventing nerve overgrowth - were damped down as a result of having stem cells at the injury site. "There's still work to do," says Hvke. "We'd like to improve

the recovery of nerve function so it's higher than 25 percent. We also need to identify more precisely what combination of growth factors and other agents are missing in chronically denervated nerves." "Dr. Hvke's team has provided solid work that shows nerve repair is a worthwhile direction for ALS research to take," says Jeffrey Rothstein, director of the Packard Center for ALS Research at Johns Hopkins. "We intend to help him continue."

New Study Gives Hope for Nerve Regeneration <http://www.alscenter.org/>

A study by a Packard Center scientist and his colleagues at Johns Hopkins makes an important step toward repair of nerves after they've been long damaged. The work, which involved rat models and stem cells from mice, is the first to

show that nerve regeneration is possible, as long as six months after injury. The repaired nerves recovered about a quarter of their lost function. For some time, Center investigator Ahmet Hvke has studied the changes that occur in nerve cells after injury. He's primarily focused on the peripheral nervous system (PNS)-nerves extending from the spinal cord out to skin, muscles and organs-where nerve repair is more likely to occur than in the spinal cord proper or the brain. "But even in the PNS, getting a piece long-damaged nerve to regrow would be highly unusual," says Hvke. The results

Nerve Regrowth Trials Oxford BioMedica Says It Will Start Nerve Repair Therapy Trials Within a Year British gene therapy company Oxford BioMedica said it was on

track to start clinical trials during 2004 of a novel therapy designed to restore nerve function after spinal cord injuries. It said early

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Pseudobulbar Affect Trials If you laugh or cry uncontrollably and inappropriately, you may be eligible to participate in a clinical trial for a medication that is being tested to control these symptoms. Go to <http://www.pseudobulbar.com/> or call 1-800-669 0281 to learn more.

pre-clinical work in mice showed that its Innurex product induced a high level of nerve regrowth, indicating its potential to be a first-in-class product for nerve repair. Innurex uses a viral vector to carry the RAR B2 gene to nerve cells at the injury site, causing them to grow and forge new nerve connections. Prof. Alan Kingsman, chief executive, said in a statement that proof of principle had been established in less than two years and the product was now "on course for clinical development within the next 12 months". He told Reuters Health it would be administered to patients who had just been injured after an accident rather than to patients who had long been paralysed, because old scars at the injury site may impede nerve repair. Kingsman said nerve regrowth in the animal experiments was "an order of magnitude greater" with Innurex compared with the results of other

groups using other nerve repair mechanisms. The company acquired exclusive rights to the RAR B2 gene from King's College London where the initial observation that this gene could programme nerve cells to regrow in vitro was made. Professor Malcolm Maden, head of the King's programme, said: "The combination of the RAR B2 gene and the very efficient Lenti Vector delivery system has produced a high level of axon regrowth. There is every chance that this is enough for restoration of function to damaged nerves and the company should have functional data shortly".

<http://www.oxfordbiomedica.co.uk/news/2003>

- [ob-22.htm](#)

Diffusion Tensor Imaging in the Diagnosis of PLS Ulug AM, Grunewald T, Lin MT, Kamal AK, Filippi CG, Zimmerman RD, Beal MF. Department of Radiology, Weill Medical College of Cornell University, New York, New York. **PURPOSE:** To evaluate the utility of MR diffusion tensor imaging in diagnosing primary lateral sclerosis (PLS). **MATERIALS AND METHODS:** Five patients who met clinical criteria for a diagnosis of PLS, and two patients with possible PLS of less than three years duration and eight normal volunteers were studied using MR diffusion tensor imaging. **RESULTS:** All seven patients showed decreased diffusion anisotropy and increased diffusion constant in the PLIC, with complete separation from a normal control group, including patients early in the course of the illness. **CONCLUSION:** Quantitative diffusion tensor imaging appears to be a useful test to detect upper motor neuron damage and hence to help to establish the diagnosis of PLS. *J. Magn. Reson.*

Imaging 2004;19:34-39. Copyright 2003
Wiley-Liss, Inc. SOURCE: J Magn Reson
Imaging. 2004 Jan;19(1):34-9.
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=14696218
&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=14696218&dopt=Abstract)

Web Sites about Medicare Changes

Contributed by Dolores Carron

www.kff.org/medicare/rxdrugdebate.cfm List of
resources on the new Medicare drug benefit
[www.sites.stockpoint.com/AARP/drugbenefit.
asp](http://www.sites.stockpoint.com/AARP/drugbenefit.asp) Calculate potential Medicare drug benefit
www.needymeds.com Lists patient assistance
programs www.destinationrx.com Search
engine to comparison shop for drugs
www.rxaminer.com Offers free cost-cutting
advice.

Botulinum (Botox) for Spasticity

Contributed via Mark Several uses of Botox
for reducing spasticity are summarized
below: Fried GW, Fried KM. Magee
Rehabilitation Hospital, 6 Franklin Plaza,
Philadelphia, PA 19102, USA.
gfried@mageerehab.org

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Spasticity is commonly seen after spinal
cord injury, and a large percentage of
patients with spinal cord injury will need
treatment to control it. Although oral
medications do a fair job of controlling

spasticity in most patients, some patients will need additional forms of treatment. In many cases, oral medications alone do not adequately control spasticity or the patient cannot tolerate the side effects. In these instances, botulinum toxin may help control the spasticity for approximately 3 months after injection. The amount of botulinum toxin and the injection sites can be tailored to meet individual patient needs. Botulinum toxins can reduce spasticity, improve function, and reduce the amount of needed assistance.

SOURCE: Phys Med Rehabil Clin N Am. 2003 Nov;14(4):901-10.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?c=md=Retrieve&db=PubMed&list_uids=14580044

&dopt=Abstract

Westhoff B, Seller K, Wild A, Jaeger M, Krauspe R. Department of Orthopaedics, Heinrich-Heine University Duesseldorf, Duesseldorf, Germany.
westhoff@med.uni-duesseldorf.de
Intramuscular botulinum toxin A injections are beneficial for the treatment of functional shortening of the iliopsoas muscle, but it is difficult to achieve precise needle positioning and injection. As a solution to this we present an ultrasound-guided injection technique for the iliopsoas muscle using an anterior approach from the groin. The procedure was performed 26 times in 13 patients (seven males, six females; mean age 11 years, SD 9 years 8 months; age range 4 to 31 years), 10 times bilaterally. Indications were functional iliopsoas

shortening due to cerebral palsy (17 hips), hereditary spastic paraplegia (four hips), and Perthes disease (five hips). In all cases the iliopsoas muscle was identified easily by ultrasound; the placement of the injection needle and injection into the site of interest were observed during real time. No complications were encountered. Botulinum toxin A (BTX-A) injections have become established as a standard procedure for the treatment of functional shortening of different muscles in persons with spasticity or dystonia (Kessler et al. 1999, Bakheit et al. 2001, Kirschner et al. 2001). SOURCE: Dev Med Child Neurol. 2003 Dec;45(12):829-32. <http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&listuids=14667075&dopt=Abstract>

Bell KR, Williams F. Department of Rehabilitation Medicine, University of Washington School of Medicine, 1959 NE Pacific Street, Box 356490, Seattle, WA 98195, USA. krbell@u.washington.edu

BT is likely effective in controlling spasticity in the smaller muscles of the arm and hand, although there has been only one large controlled trial. For lower limb spasticity, the outcomes are more mixed. No large randomized, controlled trials have been done, and the larger size of the muscles results in a decreased ability to treat widespread spasticity. For more focal treatment in the legs and feet, however, and when combined with other denervating agents or physical modalities, BT is probably effective. Careful analysis is warranted

before performing any chemodenervation on a limb muscle or muscles. SOURCE: Phys Med Rehabil Clin N Am. 2003

Nov;14(4):821-35.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?c=Retrieve&db=PubMed&list_uids=14580040

[&dopt=Abstract](#)

ALS2 Gene Mutation & PLS, HSP & ALS Unstable mutants in the peripheral endosomal membrane component ALS2 cause early-onset motor neuron disease. Koji Yamanaka *, Christine Vande Velde *, Eleonore Eymard-Pierre, Enrico Bertini ,Odile Boespflug-Tanguy, and Don W. Cleveland * *Ludwig Institute for Cancer Research and Departments of Medicine and Neuroscience, University of California at San Diego, 9500

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Gilman Drive, La Jolla, CA 92093; Institut National de la Santé et de la Recherche Médicale Unité Mixte de Recherche 384 et Fédération de Génétique Humaine Auvergne, Faculté de Médecine, 63001 Clermont-Ferrand, France; and Unit of Molecular Medicine, Bambino Gesù Children's Hospital, 00165 Rome, Italy. Edited by Fred H. Gage, The Salk Institute for Biological Studies, San Diego, CA, and approved October 28, 2003 (received for review August 15, 2003). Mutations in ALS2, carrying three putative

guanine exchange factor (GEF) domains, are causative for a juvenile, autosomal recessive form of amyotrophic lateral sclerosis (ALS), primary lateral sclerosis, and infantile-ascending hereditary spastic paralysis. Endogenous ALS2 is shown here to be enriched in nervous tissue and to be peripherally bound to the cytoplasmic face of endosomal membranes, an association that requires the amino-terminal "RCC1 (regulator of chromatin condensation) like" GEF domain. Disease causing mutants and a naturally truncated isoform of ALS2 are shown to be rapidly degraded when expressed in cultured human cells, including lymphocytes derived from patients with ALS2 mutations. Thus, mutations in the ALS2 gene linked to early-onset motor neuron disease uniformly produce loss of activity through decreased protein stability of this endosomal GEF.

SOURCE: Proc. Natl. Acad. Sci. USA, 2003 Dec 10 [Epub ahead of print].

http://www.pnas.org/cgi/content/abstract/2635267_100v1

and Intensive Care, University Hospital of Geneva, Switzerland Objectives: To report an unusual cause of intrathecal drug delivery failure in baclofen pump device. Study design: A case report of an SCI patient treated with intrathecal baclofen, presenting a drug withdrawal. Methods: We present a case of a 38-year-old male with complete T9 spastic paraplegia for 15 years, treated with intrathecal baclofen for 11 years. He recently presented to our centre with a spastic hypertonic episode, associated

with rhabdomyolysis. Results: Standard investigations were unrevealing. However, a CT scan performed after injecting a radio-opaque solution by the side port of the pump, showed an unexpected catheter migration into the subdural space. Surgical revision reversed withdrawal symptoms. Conclusions: Subdural catheter migration must be considered in the differential diagnosis of intrathecal drug delivery system failures. We recommend the use of the CT scan after contrast injection, to detect the localization of the distal catheter tip and confirm the normal diffusion into the subarachnoid space. SOURCE: Spinal Cord December 2003, Volume 41, Number 12, Pages 700-702

CAREGIVING

Baclofen Pump Dysfunction Contributed by Mark Weber Subdural catheter migration may lead to baclofen pump dysfunction

Y Pasquier¹, A Cahana² and A Schniderly¹ ¹Spinal Cord Unit, Clinic of Reeducation, Department of Clinical Neuroscience, University Hospital of Geneva, Switzerland ²Interventional Pain Unit, Department of Anesthesiology, Pharmacology

Resources for Caregivers Submitted by Gary

King The Family Caregiver Alliance is a nationwide organization based in San Francisco. www.caregiver.org Following is just a portion of the section of one of the files they have on-line. This summary is the conclusion of the file on "Taking Care of You; Self-Care for Caregivers."

Learn and use stress-reduction techniques. ~Attend to your own healthcare needs.

Get proper rest and nutrition. ~Exercise regularly.

Take time off without feeling guilty. ~Participate in pleasant, nurturing activities.

Seek and accept the support of others.

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Nor look into your eyes. To see the flame of living there,
Bright and strong, Alive! If I do not see the person
Who in that body dwells Who thinks and dreams and hopes,
And in whose heart love swells. An inner person much like me.

If this I do not
find, But turn and
go away,
Then the Handicap is
mine!

LIVING WITH PLS/HSP

-Seek supportive counseling when you need it, or talk to a trusted counselor or friend.

Identify and acknowledge your feelings. Change

the negative ways you view situations. **Set goals.** The site contains a **wealth** of practical information for **caregivers**, as well as links to other related sites such as:

www.eldercare.gov The Eldercare Locator is a national toll-free directory assistance public service of the U.S.

Administration on Aging that helps people locate **aging services** in every community throughout the United States. (800) 677-1116 during the hours 9 a.m - 8 p.m. (ET) Monday - Friday. The primary goal of **the** service is to promote awareness of and improve access to state, area agency and local community aging programs and services. Since its inception in 1991, more than 660,000 calls been received from families, friends, caregivers, aging professionals and older persons **seeking** direction on where to begin to look for aging services and programs.

The Eldercare Locator is absolutely **FREE**. There is no **charge** to use the service, and there is no **charge** for the information. Individuals calling this service or using the website have access to state and local information & referral service providers identified for every ZIP code in the country.

The Handicap Is Mine

Contributed by Rita DiClemente

If I look upon your twisted hands,

The braces on your feet. If
I hear the funny sound you
make

When you try to speak. If I
watch you as **you** as you try to

walk

With wobbly,
weaving gait. And
seeing others walk
away

For you they cannot wait.
If I look upon your outer
shell,

And imperfections there
I find. And turn and go upon
my way,

The Handicap is
mine!

Disabilities Act Protects Service Animals, too Contributed by Katherine Wisheart

The following article is forwarded to you by the Great Lakes ADA and Accessible IT Center for your information: By Allan Appel disabilities columnist As far as The Americans with Disabilities Act is concerned, a service animal is to be treated like a person. The law's prohibition of discrimination against people with disabilities applies to their service animals as well. Businesses cannot prevent people with disabilities from taking their service animals onto the premises. Hotels, restaurants, bars, sports facilities, taxicabs, retail stores and more are all included. In other words, if a customer is allowed in an area, that right extends to his or her service animal. Even if a state or local ordinance says otherwise, this federal rule prevails. Period. That includes not segregating the person with a service animal from other customers. Or exacting a cleaning fee or surcharge for possible "accidents." It is, however, permissible to charge a customer for damage caused by the animal — as long as it is customary to similarly

charge people without disabilities for damages they cause. And Seeing Eye dogs are not the only service animals protected by the ADA. The law includes any animal trained to assist a person who has a disability. Some animals alert hearing-impaired people to sounds. Others provide balance to

If I do not see beyond the shell,

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people with mobility impairments. And others may pull a wheelchair or carry things. Most

service animals are equipped with harnesses to help them perform duties. Removal of that harness or other paraphernalia usually indicates to the animal that he is off work. If there is any doubt about an animal's status, ask the owner. Although most owners have documentation about the animal's status, it is not required for the owner to produce that documentation as a condition to being served. These rules do not travel on a one way street, however. While on the business' premises, the owner is responsible for the animal's care and supervision. If the service animal's behavior directly threatens others or is otherwise out of control, the animal may be expelled from the premises. A service animal is really just another working stiff, trying to

do his job. He is not a pet. So don't treat him like one. Allan Appel can be reached c/o Scripps Treasure Coast Newspapers, 800 W. Indiantown Road, Jupiter, FL 33458, or by e-mail at aappel223@yahoo.com. www.canineassistants.org Toll Free Telephone: 800-771-7221 Canine Assistants is a non-profit organization, founded in 1991, which trains and provides service dogs for children and adults with physical disabilities or other special needs. In addition to physically assisting those with disabilities, Canine Assistants service dogs are instrumental in removing many of the barriers faced by the disabled in today's society. One recipient made the value of this skill quite clear when asked by a reporter what she liked most about her service dog. Immediately, she responded, "My dog makes my wheelchair disappear."

Blessed are you that never bids us 'hurry up and more blessed are you that do not snatch our tasks

from our hands to do them for us, for often we need time rather than help. Blessed are you who stand beside us as we enter new ventures, for our failures will be outweighed by times we surprise ourselves and you. Blessed are you who ask for our help, for our greatest need is to be needed. Blessed are you when by all these things you assure us that the thing that makes us individuals is not our peculiar muscles, nor our wounded nervous system, but is the God-given self that no infirmity can confine. Blessed are those who realize I am human and don't expect me to be saintly just because I am disabled. Blessed are

those who pick things up without being asked. Blessed are those who understand that sometimes I am weak and not just lazy. Blessed are those who forget my disability of the body and see the shape of my soul. Blessed are those who see me as a whole person, unique and complete, and not as a 'half and one of God's mistakes. Blessed are those who love me just as I am without wondering what I might have been like. Blessed are my friends on whom I depend, for they are the substance and joy of my life.

Beatitudes for Friends of Disabled People

Marjorie Chappell Blessed are you who take time to listen to defective speech, for you help us to know that if we persevere, we can be understood. Blessed are you who walk with us in public places and ignore the stares of strangers, for in your companionship we find havens of relaxation.

Cruise Tips for the Handicapped *Ed. Note: I misplaced the name of the author, sorry!*

We're back from our 7-day Caribbean cruise on the world's largest cruise ship, Mariner of the Seas (Royal Caribbean). It's probably the most handicap-accessible facility around, on sea or land. Every door opens automatically, and every public restroom has a button to push on the outside wall to open the door, another button inside to open the door to the toilet stall, a huge stall that accommodated my scooter, and another button

inside the stall to open that door again. Same for leaving the restroom--button on the wall. This was so great for my husband, who

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has to always open and hold the outside door and gets dirty looks from other women. Our cabin was huge, again large enough to accommodate my scooter. Same for the toilet. Since this was the maiden voyage, there were glitches that need to be ironed out. If you enjoy cruises, this is certainly the most handicap-friendly ship. My biggest complaint was that there were no non sports activities offered while at sea, not even a movie or trivia game. Everything revolved around

climbing their rock wall, ice skating, playing miniature golf and all the other things we can't do anymore. Since even many able-bodied people can't do these things, I hope they'll offer more on future cruises. Hope this "review" helps anyone looking for a cruise in the future.

adversity--boiling water--but each reacted differently. The carrot went in strong, hard and unrelenting. However after being subjected to the boiling water, it softened and became weak. The egg had been fragile. Its thin outer shell had protected its liquid interior. But, after sitting through the boiling water, its inside became hardened. The ground coffee beans were

unique, however. After they were in the boiling water they had changed the water. "Which are you?" she asked her daughter. "When adversity knocks on your door, how do you respond? Are you a carrot, an egg, or a coffee bean?" Think of this: Which am I? Am I the carrot that seems strong, but with pain and adversity, do I wilt and become soft and lose my strength? Am I the egg that starts with a malleable heart, but changes with the heat? Did I have a fluid spirit, but after death, a breakup, a financial hardship or some other trial, have I become hardened and stiff? Does my shell look the same, but on the inside am I bitter and tough with a stiff spirit and a hardened heart? Or am I like the coffee bean? The bean actually changes the hot water, the very circumstance that brings the pain. When the water gets hot, it releases the fragrance and flavor. If you are like the bean, when things are at their worst, you get better and change the situation around you. When the hours are the darkest and trials are their greatest, do you elevate to another level? How do you handle adversity?

Carrot Egg and Coffee Bean Author

Unknown A young woman went to her mother and told her about her life and how things were so hard for her. She did not know how she was going to make it and wanted to give up. She was tired of fighting and struggling. It seemed as one problem was solved a new one arose. Her mother took her to the kitchen. She filled three pots with water and placed each on a high fire. Soon the pots came to a boil. In the first, she placed

carrots, in the second she placed eggs and the last she placed ground coffee beans. She let them sit and boil, without saying a word. In about twenty minutes she turned off the burners. She fished the carrots out and placed them in a bowl. She pulled the eggs out and placed them in a bowl. Then she ladled the coffee out and placed it in a bowl. Turning to her daughter, she asked, "Tell me, what do you see?" "Carrots, eggs, and coffee," she replied. She brought her closer and asked her to feel the carrots. She did and noted that they were soft. She then asked her to take an egg and break it. After pulling off the shell, she observed the hard-boiled egg. Finally, she asked her to sip the coffee. The daughter smiled as she tasted its rich aroma. The daughter then asked, "What does it mean, mother?" Her mother explained that each of these objects had faced the same

Social Security - Disability Contributed by Vaughn Hickman I had no problem with getting long-term disability (after three months of short-term). Likewise I had no problem getting SS Disability. My long-term insurance company paid \$1,000 to a company that specializes in helping to get the SS started. I had to wait for six months, then I got a back check. The long-term insurance company's incentive to help is because they get to reduce their payments to you for every \$ of SS you receive. After six months of receiving SS, you are also eligible to apply for Medicare regardless of your age. It then becomes your Primary Medical

Insurance and you can (usually) get your normal Health Insurance at a reduced cost, because it then becomes a supplement to Medicare. Contributed by Bonnie McIsaac I am a former disability analyst/hearing officer for Social Security. I did the job successfully until PLS crept in my life and I needed to retire. If you are receiving disability income (SSI or SSD) - you are allowed to work and receive up to \$750.00 per month.

The Uninvited

Guest Written by Thurza
Campbell

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h
e

An uninvited guest it
seems

Has set up residence Within
our home and life has changed

Profoundly ever since. The
nervy guest pretends she's me.

She's volatile; then cries.
She kills our conversations. How?

With her persistent drive She's
stilled my tongue and forces me

To find some other means
To say "I love you" "How are
you?"

She's making me too lean.
She tries hard every day
and night

To make me fall down flat.
But now I'm careful when I
walk

My walker handles that.
She forces me to find new
ways

To do what e're I would.
I've tried to make her go
away but

She's settled in for
good. But now we know
she isn't me

And we can vent
our ire At PLS and
nothing else.

Together we'll conspire To
have her be the whipping
boy

When life's frustrations loom And
laugh at her - share fun in life .

And thus defeat her gloom. *Dedicated
to Heather who pointed out to me on
11/24/03 that the disease is what we each
get angry with, not each other.*

A PLS Mind-Body Debate on Falling Contributed by Dale Last evening as we were getting dinner ready, I had the revelation... No matter how much "mind fog" "dullness" etc. we get from this, our minds are still many, many times faster than our bodies. In our home we have a 4.5 foot divider between the kitchen and dining area. It has a counter top about a foot across which is great because we put everything up there and walk around and "set the table". My wife was

finishing heating some veggies; I went around to the dining area and starting moving the food/dishes from the counter to the table. I am standing facing the wall, to my right is the counter, the left the table. I was turning back and forth and then stopped waiting for the last dish. I am just standing there talking to Jen (wife) and I can feel myself slowly falling backwards. My mind is going, "tighten up some muscles to bring me back over center", Body(in it's disease/drug induced haze): "what?" Mind: "hurry up, your going to go over!" Body: "Ok, ok, I can do this..." Mind: "HURRY you are going over, either tighten up the muscles or take a step back!" Body: "Hey, don't help, I can do this, I use to know how, just hold on. what's the rush man???..." By this time I can feel myself going back on my heels, it won't be long before I go over, my mind is panicking but my body, well it's has it's own mind... Mind: "Reach out and grab the counter!" Body: "No, no that's not it, there's more to it then that, just hold on, don't help I know I can handle it, I have done it for years. Now where is that check list, I have it around here somewhere. Let's see, oh yes, balance and falling, step 1..." Mind: "DO SOMETHING!" Body: "oh yes, ok, we are getting over center start tightening up muscles, but we are too far over center to pull us back to center so take a little step

back and reach out and grab counter." Mind: "Thank GOD!"

Body: "See, I knew I could do it!"

Rollator Walkers

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1-866-909-2273 is available from this

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rDeluxeSuper.htm Momentum

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3 Salt Lake City, UT 84101...800 644

2263 is a manufacturer. One vendor who

carries their walkers is

<http://www.grogans.com/servlet/shop> Toll Free

1-800-365-10

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said, "How about going to lunch in a half hour?" She would gasp and stammer, "I can't. I have clothes on the line. My hair is dirty. I wish I had known yesterday, I had a late breakfast. It looks like rain." And my personal favorite: "It's Monday."...She died a few years ago. We never did have lunch together. Because Americans cram so much into their lives, we tend to schedule our headaches. We live on a sparse diet of promises we make to ourselves when all the conditions are

perfect! We'll go back and visit the grandparents when we get Stevie toilet-trained. We'll entertain when we replace the living-room carpet. We'll go on a second honeymoon when we get two more kids out of college. Life has a way of accelerating as we get older. The days get shorter, and the list of promises to ourselves gets longer. One morning, we awaken, and all we have to show for our lives is a litany of "I'm going to", "I plan on", and "Someday, when things are settled down a bit." When anyone calls my 'seize the moment' friend, she is open to adventure and available for trips. She keeps an open mind on new ideas. Her enthusiasm for life is contagious. You talk with her for five minutes, and you're ready to trade your bad feet for a pair of Rollerblades and skip an elevator for a bungee cord. My lips have not touched ice cream in 10 years. I love ice cream. It's just that I might as well apply it directly to my stomach with a spatula and eliminate the digestive process. The other day, I stopped the car and bought a triple decker. If my car had hit an iceberg on the way home, I would have died happy. Now...go on and have a nice day. Do something you WANT to.....not something on your SHOULD DO list. If you were going to die soon and had only one phone call you could make, who would you call and what would you say? And why are you waiting? Do you run through each day on the fly? When you ask "How are you?" Do you hear the reply? When the day is done, do you lie in your bed with the next hundred chores running through your head? Ever told

your child, "We'll do it tomorrow." And in your haste, not

Seize the Moments Author Unknown Too many people put off something that brings them joy just because they haven't thought about it, don't have it on their schedule, didn't know it was coming or are too rigid to depart from their routine. I got to thinking one day about all those women on the Titanic who passed up dessert at dinner that fateful night in an effort to cut back. How many women out there will eat at home because their husband didn't suggest going out to dinner until after something had been thawed? Does the word "refrigeration" mean nothing to you? How often have your kids dropped in to talk and sat in silence while you watched 'Jeopardy' on television? I cannot count the times I called my sister and

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COOKBOOK CORRECTIONS

see his sorrow? When you worry and hurry through your day, it is like an unopened gift.... Thrown away... Life is not a race. Take it slower. Hear the music before the song is over.

Cookin' for a Cure Corrections

Pills Contributed by Linda Gentner

A row of bottles on my shelf Caused me to analyze myself. One yellow pill I have to pop Goes to my heart so it won't stop.

A little white one that I take Goes to my hands so they won't shake.

The blue ones that I use a lot Tell me I'm happy when I'm not. The purple pill goes to my brain And tells me that I have no pain. The capsules tell me not to wheeze Or cough or choke or even sneeze. The red ones, smallest of them all Go to my blood so I won't fall.

The orange ones, very big and bright Prevent my leg cramps in the night. Such an array of brilliant pills Helping to cure all kinds of ills. But what I'd really like to know.... Is what tells each one where to go! Goes to my heart so it won't stop.

A little white one that I take Goes to my hands so they won't shake. The blue ones that I use a lot Tell me I'm happy when I'm not. The purple pill goes to my brain And tells me that I have no pain. The capsules tell me not to wheeze Or cough or choke or even sneeze. The red ones, smallest of them all Go to my blood so I won't fall. The orange ones, very big and bright Prevent my leg cramps in the night. Such an array of brilliant pills Helping to cure all kinds of ills. But what I'd really like to know..... Is what tells each one where to go!

Pg. 9 Marinated Mushrooms - change to read "dried" thyme Pg. 17 Banana Orange Salad -add to ingredient list

2 (11-oz.) cans Mandarin oranges (drained) Pg. 25 Fish Chowder - change to read frozen cod "or" other fillets

Change to read 2 soup cans milk Pg. 27 Harvest Pumpkin and Zucchini Soup Change to read 3 cups zucchini "cubed" 31 Potato Salad with Tarragon Vinaigrette

Change to read "wine" vinegar Pg. 37 Tabbouleh - add Yield: 10 servings Pg. 49 Ratatouille - change to read "dried" basil

Change to read "broil until cheese melts" Pg. 54 Beef Burgundy - should read 2 lbs. stewing beef Pg. 57 Broccoli & Bacon Quiche - should read: Layer broccoli, bacon, onion and cheese (not eggs) Pg. 59 Chicken and Dumplings - should read baking powder (not soda)

(also change to baking powder in first line) Pg. 68 Escarole Soup with Meatballs - change title Italian Wedding Soup Pg. 75 Light Salmon Loaf Dill - put * after "fresh dill"

Should read 1 can salmon (not cup). Yield: 4 servings Pg. 82 Picanti Biscuit Bake - add to ingredient list:

1 can (2-1/4 oz.) sliced ripe olives (drained) Pg. 90 Vegetable Lasagna - change to read "dried" oregano Pg. 113 Berry Bread Pudding - change to read strawberries, chopped" Pg. 113 Berry Cobbler - add to ingredient list: 34 c. flour

http://sp.foundation.org/assets/pdf/cookbook_corrections.pdf

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World Geography of **ALS, PLS & HSP** Created
and compiled by Frank Reyerse *Ed Note: Frank
created this chart from data patients have sent him.
If you are not in his data base and would like to be,
click on: <http://geocities.com/freyerse/>*

Fri, Jan 2, 2004

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COUNTRIES PLS HSP ALS COUNTRIES

Australia Argentina Belgium Brazil China Greece Germany Holland India Italy Ireland | Israel
Mexico New Zealand Pakistan Russia South Afrika Spain Sweden Switzerland
Turkey JUnited Kingdom 0 COUNTRIES

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To
WAB

PLS/HSP/ALS Members Data Base

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USA2 PLS|HSPALS CANADA

HSPALS USAT PLS HSPALS P USA2 Aberta

Alabama

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Alaska

Mississippi Manitoba

Arizona

Missouri New Brunswick

Tarkansas

Montana Newfoundland

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Nebraska Northwest I

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Nevada Nova Scotia

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IDelaware

1 New Jersey Ontario

Florida

New Mexico Prince Edward 1

Georgia

New York Quebec

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North Carolina Saskatchewan

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Illinois

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