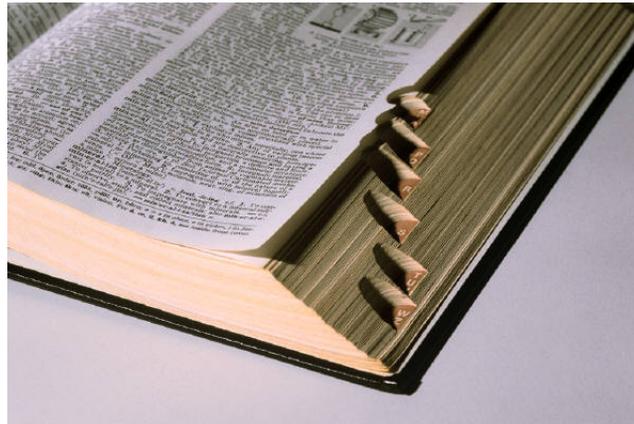




Alternative Therapies for ALS

Definition of Alternative Therapies

- Treatments for which there is no **good evidence**, that patients with ALS **use** instead of or in addition to treatments that are **proven** and recommended by **ALS experts**.



ALS Experts

- Neurologists that devote most or all of our careers to caring for PALS and researching ALS
 - Formal education
 - College, med school, internship, residency, fellowship, masters, doctor of philosophy
 - “Hands on” experience
 - Hundreds of patients, dozens of research studies
 - Strong personal commitment to PALS
 - Partnership for best possible outcome

Types of Evidence

- Large, randomized double-blind placebo-controlled trial
- Small, randomized double-blind placebo-controlled trial
- Large case series
- Animal study
- One or a few cases
- Hypothetical based upon mechanism

Best



Worst

Proven Treatments for ALS

- **Riluzole**
 - 2 Large randomized double-blind placebo-controlled trials
 - (Miller R, Mitchell J, Lyon M, Moore D. Riluzole for amyotrophic lateral sclerosis (ALS)/motor neuron disease. *Amyotrophic Lateral Sclerosis*, 2003;4(3), 191-206.)
- **PEG**
 - Case series
 - (Massine L, Corra T, Zaccala M, Mora G, DelPiano M, Galante M. Percutaneous endoscopic gastrostomy and enteral nutrition in amyotrophic lateral sclerosis. *Neurology*, 1995; 242, 695-698.)
- **BiPAP**
 - Case series
 - (Aboussouan LS, Khan Su, Meeker DP, Stelmach K, Mitsumoto H. Effect of noninvasive positive-pressure ventilation on survival in amyotrophic lateral sclerosis. *Ann Intern Med*, 1997;127, 450-453.)
- **Multi-disciplinary clinics**
 - Case series
 - Traynor BJ, Alexander M, Corr B, Frost E, Hardiman O. Effect of a multidisciplinary amyotrophic lateral sclerosis clinic on ALS survival: a population based registry 1996-2000. *J Neurol Neurosurg Psych*, 2003;74(9):1258-1261.

To More and Better Treatments

- We have a nice pipeline of candidate therapies
 - (Bedlack RS, Traynor BJ, Cudkowicz ME. Emerging disease modifying therapies for the treatment of motor neuron disease/ALS. Expert Opin Emerg Drugs 2007;12,229-252.)
- Will need volunteers to study these in trials and large series



Speed Bumps



- ALS is a rare disease
- Less than $\frac{1}{2}$ of the PALS in this country are ever seen in an ALS Clinic
 - (Khischenko and Bedlack, submitted.)
- Of those PALS that are seen, less than 10% are participating in research studies
- Participation does not appear to be influenced by the design of the research study
 - (Bedlack et. al. Scrutinizing enrollment in ALS clinical trials: room for improvement? ALS 2008;5:257-265.)

PALS Choose Alternative Therapies

- Approximately **50%** of PALS will try an alternative therapy
 - (Wasner M, Klier H, Borasio G. The use of alternative medicine by patients with amyotrophic lateral sclerosis. *J Neurol Sci*, 2001;191, 151-154.)
 - (Bedlack et. al. Scrutinizing enrollment in ALS clinical trials: room for improvement? *ALS* 2008;5:257-265.)



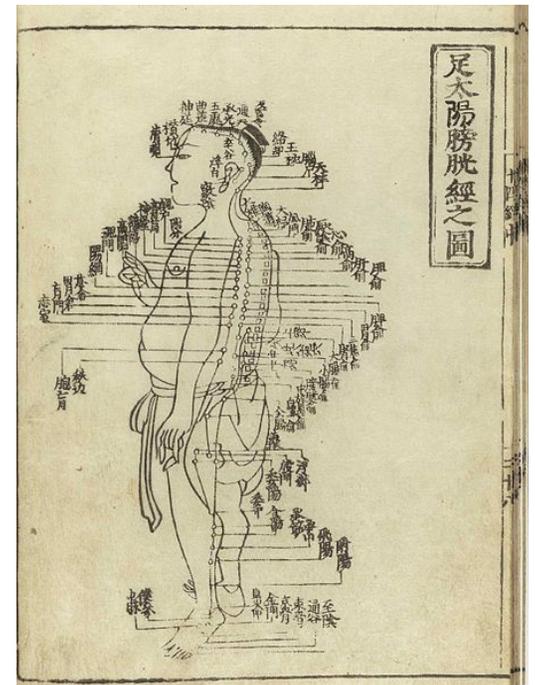
PALS Choose Alternative Therapies

- Why?
 - Frustration over lack of cure
 - 10% believe they will find a cure, 20% believe they will find something to make them better, 50% believe they will find something to slow progression
 - (Wasner M, Klier H, Borasio G. The use of alternative medicine by patients with amyotrophic lateral sclerosis. *J Neurol Sci*, 2001;191, 151-154.)
 - “Peer pressure”
 - “I have ALS, what further harm could come to me?”

Specific Alternative Therapies Often Used By PALS

Acupuncture

- Almost ½ the PALS in one survey have tried this
 - (Wasner M, Klier H, Borasio G. The use of alternative medicine by patients with amyotrophic lateral sclerosis. *J Neurol Sci*, 2001;191, 151-154.)
- Not clear how it could influence any event thought to be important in how ALS starts or progresses
- No trials or large series
- Case reports of improved cramps, breathing
- Risks: bleeding, infection, punctured organs
- Cost: \$100, unlikely to be covered by insurance



Amalgam Removal

- Amalgams are 50% mercury
- Patients with amalgams are exposed to mercury vapor and have mildly increased urine mercury levels
 - Normal urine mercury <2mcg/L
 - Toxic urine mercury 50-300mcg/L
 - Every 10 surface increase in amalgams increase urine mercury by 1mcg/L



Amalgam Removal

- Mercury vapor poisoning causes weakness **with** gum disease, numbness, kidney problems, lung problems, behavior problems, memory loss
 - ([Clarkson TW, Magos L, Myers GJ. The toxicology of mercury--current exposures and clinical manifestations. N Engl J Med, 2003;349,1731.](#))
- Multiple large studies fail to show any difference in neurological problems between patients with amalgams versus those without
 - http://www.ada.org/public/media/presskits/fillings/testimony_marshall.pdf
- Replacement of amalgams is painful, expensive (\$2500-5000 for every 10 surface replacement), and causes a spike in urinary mercury levels!



Atypical Lyme Disease Treatment

- Lyme disease causes rash, joint pains, and rarely weakness **with** numbness, psychiatric changes
- No good evidence that Lyme can ever cause a picture that looks like ALS
- CDC has recommended a standardized 2-step process for Lyme testing
 - Elisa, followed by western blot



Atypical Lyme Disease Treatment

- “Lyme and ALS” yields 600k hits on Google
- Some are “Lyme centers”
 - Use bizarre testing with high false positive rates
 - Use bizarre therapeutic regimens with many side effects
 - Treatment in these centers is expensive and may not be covered by insurance



Jemsek Clinic files for bankruptcy

Preeminent AIDS specialist sued for purported Lyme misdiagnosis

by Donald Miller



Dr. Joseph Jemsek will no longer be treating HIV/AIDS patients.

CHARLOTTE — Dr. Joseph Jemsek is well known in this city's HIV/AIDS community — he's been specializing in the treatment of infected patients for several years.

"He's been working in the field since the early '80s," says Dr. Frederick Cruickshank. "In fact, he was the first doctor in the area to diagnose and treat HIV/AIDS patients." In the past year Jemsek has turned his focus to the treatment of Lyme Disease, although additional Jemsek doctors continued to oversee HIV/AIDS patients.

Jemsek was disciplined by the N.C. Medical Board this past summer for "unorthodox diagnoses and treatment" of Lyme disease. He filed for bankruptcy in the last week of October on behalf of his clinic, which is located in Huntersville.

According to a report in The Charlotte Observer Federal court documents show the clinic owes more than \$2 million to its top 20 creditors, including about \$22,000 to the Mecklenburg County tax collector, \$1.2 million to Scottish Bank and \$716,000 to First Citizens Bank. Bankruptcy law gives the clinic 120 days to file a reorganization plan.

The bankruptcy filing allows the clinic to continue to operate, despite the debt.

In light of multiple patients' complaints of misdiagnoses, the death of one patient and the charges of "unorthodox diagnoses and treatment," insurance agencies have terminated agreements with Jemsek, which means patients will now be required to pay for all services up front. What's more — the Jemsek Clinic won't be treating AIDS patients any longer.

However, two HIV/AIDS specialists who joined Jemsek earlier this year, Cruickshank and Dr. Octavio Cieza, have opened their own office specializing in patients with HIV/AIDS, the Rosedale Infectious Diseases Clinic.

Cruickshank confirms that all patients are welcome.

"We're accepting patients with Medicaid and Medicare, standard health insurance and the uninsured."

Currently Rosedale is operating in the Jemsek building, but plans to move to a new location in the near future,

Chelation

- Mutations in gene for Cu/Zn SOD1 can cause ALS
 - Pathological *gain in function*
- Copper may be critical for this enzyme's function
 - By depleting copper through chelation, may inhibit function
- In FALS1 animal model, penicillamine delays disease onset, doesn't affect survival
 - (Hottinger, A.F., Fine, E.G., Gurney, M.E., Zurn, A.D., and Aebischer, P. (1997) The copper chelator dpenicillamine delays onset of disease and extends survival in a transgenic mouse model of familial amyotrophic lateral sclerosis. *Eur J Neurosci*, 2006;9(7),1548-1551.)

The *NEW*
Chelation Miracle



When sailors painting military ships were contaminated with lethal levels of lead, the U.S. Navy relied on a newly discovered remedy to quickly eliminate deadly toxins from the bloodstream...



Within a short time,
their arteries went
from this...
... to this

...Not only did this inexpensive therapy save the lives of the sailors, but it miraculously flushed out dangerous plaque and toxins clogging their arteries.

Chelation

- Other heavy metals are toxic to motor neurons in animals and cultures
- Heavy metal poisoning causes weakness **with** sensory loss, pain, blue gums, hair loss, skin rash, anemia, etc
- Measurements of heavy metal exposure in PALS are inconsistent across studies
 - Some studies show reduced levels of certain metals, and one showed prolonged survival in PALS with higher lead levels!

The *NEW*
Chelation Miracle



When sailors painting military ships were contaminated with lethal levels of lead, the U.S. Navy relied on a newly discovered remedy to quickly eliminate deadly toxins from the bloodstream...



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Chelation

- Chelation can alter the distribution of metals in the body, including shifting more into motor neurons
 - (Ewan K, Pamphlett R. Increased inorganic mercury in spinal motor neurons following chelating agents. *Neurotoxicology*, 1996;17, 343-349.)
- One case of ALS with elevated mercury, chelation reduced mercury levels but did not alter disease course
 - ([Praline J](#), [Guennoc AM](#), [Limousin N](#), [Hallak H](#), [de Toffol B](#), [Corcia P](#). ALS and mercury intoxication: a relationship? *Clin Neurol Neurosurg*, 2007;109(10), 880-3.)

The *NEW* Chelation Miracle



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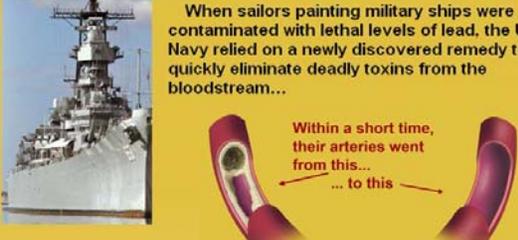
...Not only did this inexpensive therapy save the lives of the sailors, but it miraculously flushed out dangerous plaque and toxins clogging their arteries.

Chelation

- Risks: abnormal heart rhythm, kidney failure, respiratory failure, seizures, allergic reaction, death all reported
- Costs: few thousand dollars first month, about a hundred every month thereafter, unlikely to be covered by insurance

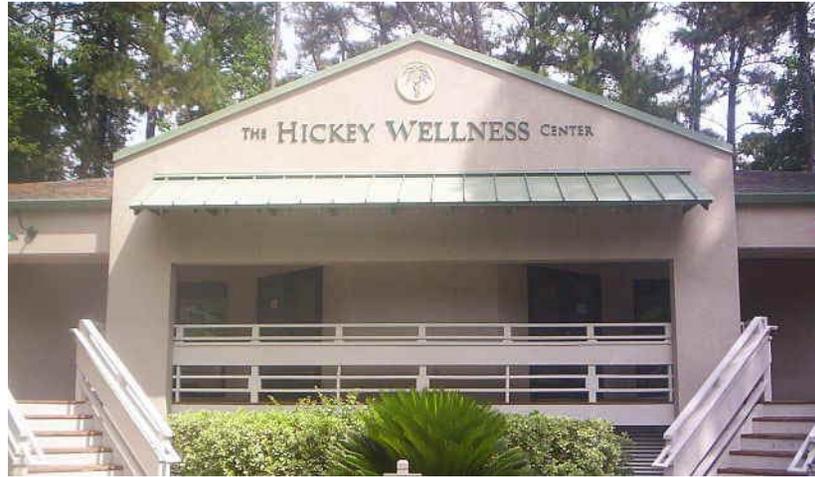
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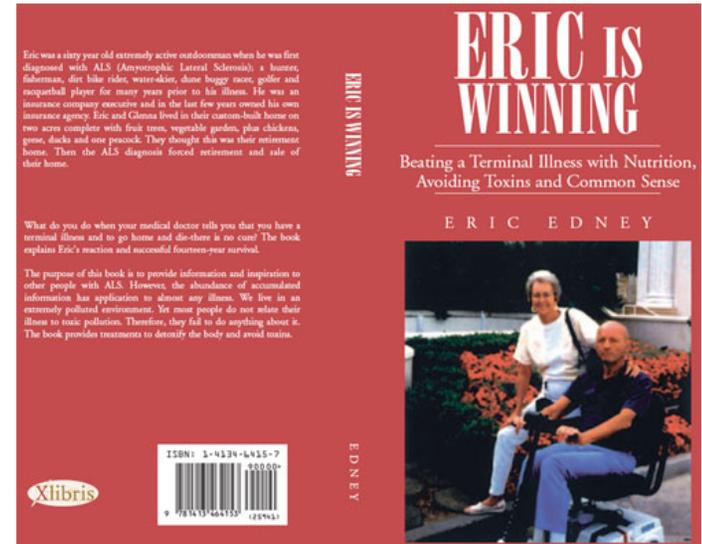
Chinese Herbs

- Complex combinations of herbs, minerals, plant extracts
- No rational hypothesis or data for use in ALS
- CDH found many contaminated with toxins
 - (http://www.organicnews.com/news/article.cfm?story_id=153.)
- Cost \$30-1000 per month, not covered by insurance



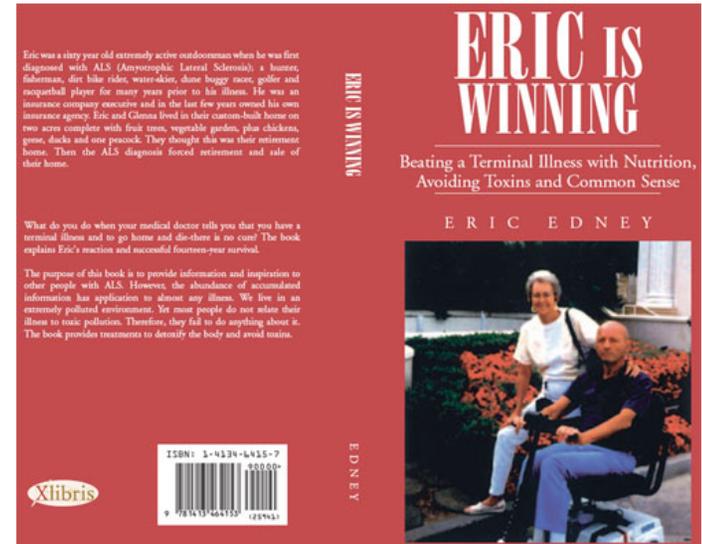
“Eric is Winning”

- Eric is convinced that neurodegenerative diseases are caused by pesticides and heavy metals
- 2 phases
 - 1: Stop progression
 - 2: Restore the body



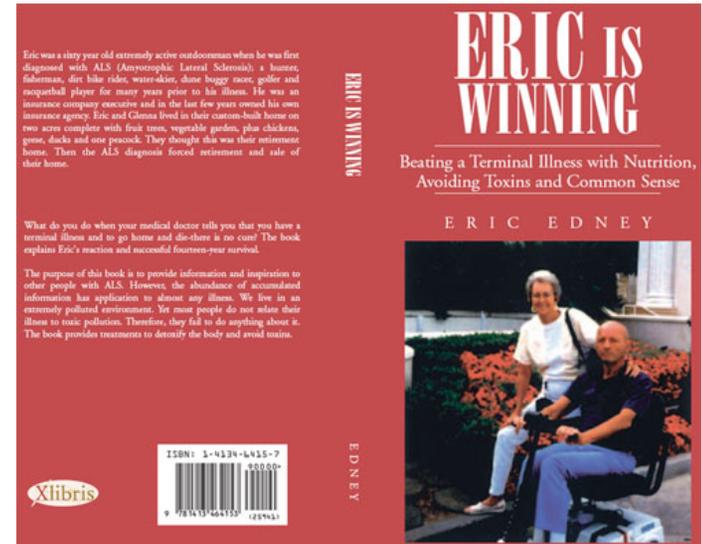
“Eric is Winning”

- Phase 1 components:
 - Divorce present MD and find “specialist” in alternative medicine
 - Purify colon and liver
 - Colloidal silver, clay, psyllium, enemas
 - Detoxify body
 - Chelation, clay foot baths, ionic foot baths, colon hydrotherapy
 - Eliminate toxins
 - Amalgam removal, avoid prescription drugs, eat only organic foods, alkalinize the urine, take anti-oxidants, take glutathione



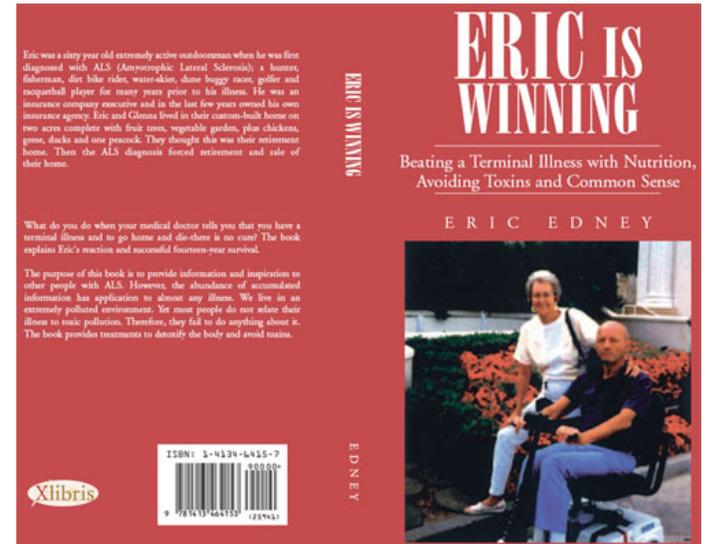
“Eric is Winning”

- Phase 2 components:
 - “Live cell therapy”
 - Animal embryo cell extracts
 - B1
 - HGH shots
 - Starbucks Chai Soy Milk Latte
 - Laser beam therapy



“Eric is Winning”

- Many of these are known to be dangerous
- Cost over the course of ALS: \$40k
 - Not covered by insurance



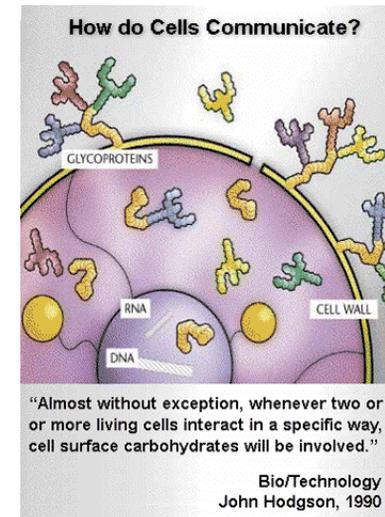
Glyconutrients

- *Heart disease, cancer, stroke, diabetes and most of the other major killers in society today can be classified as 'diseases of the uninformed.' They are nonetheless lethal but only to those who have not heard about prevention and natural cures. Unfortunately, this includes your loved ones and friends as well as the great majority of the Western world.*

– Dr Helena Toth Hardy. N.D. C.N.C,
www.glyconutrientsreference.com/

Glyconutrients

- Sugars used by cells to make glycoproteins and glycolipids, which are important in how cells communicate
- No good evidence that these are a problem in ALS, nor that treatment with GN helps
- \$100-150 per month, not covered by insurance



High Dose Vitamins

- There is evidence of oxidative stress in ALS, thus antioxidant treatment sounds attractive
- High dose vitamin E delayed disease onset in FALS1 animal model
- A thorough review of literature showed no benefit of vitamin E or other antioxidants across studies in PALS
 - (Orrell RW, Lane JM, Ross MA. Antioxidant treatment for amyotrophic lateral sclerosis / motor neuron disease. Cochrane Database Syst Rev 2004(4):CD002829.)
- Co-Q 10 recently shown to be futile in PALS

High Dose Vitamins

- Some vitamins may actually be harmful in large doses
 - Vitamin B6 toxicity causes painful neuropathy
 - Review of published studies of healthy persons taking vitamins suggested treatment with beta-carotene, vitamin A or vitamin E was associated with earlier death
 - (Bjelakovic G, Nikolova D, Gluud LL, Simonetti RG, Gluud C. Antioxidant supplements for prevention of mortality in healthy participants and patients with various diseases. *Cochrane Database of Systematic Reviews* 2008, Issue 2. Art. No.: CD007176. DOI: 10.1002/14651858.CD007176)

•

Stem Cells

- Offer great hope for modifying, perhaps even reversing progression in PALS
 - Deshpande et. al. 2006
 - Rats paralyzed by Sindbis virus (kills motor neurons)
 - Mouse ES differentiated into motor neuron precursors, injected into lumbar spinal cord along with dbcAMP (anti-myelin repulsion factor), rolipram (PDE4 inhibitor); GDNF secreting cells in sciatic nerves, CsA
 - Videos

Stem Cells

- Source? Amount? Location? Replace glial cells or neurons? Additional meds?
- HUMAN TRIALS PREMATURE AT THIS POINT!!!

Stem Cells

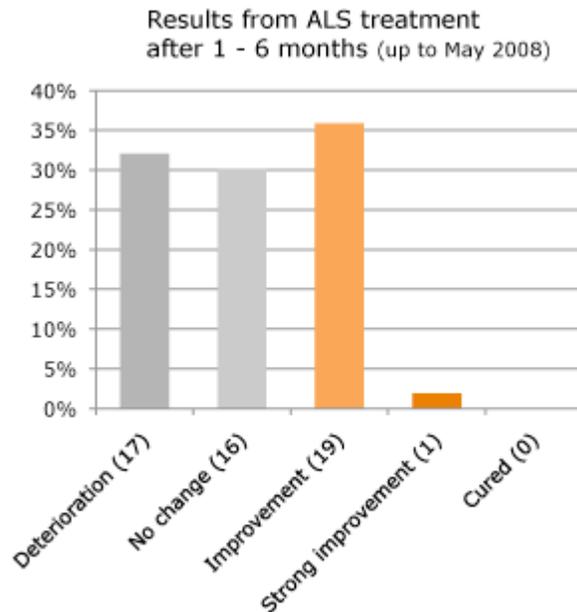
- “ALS and stem cells” yields 854,000 hits on Google
- Some are “clinics” offering “stem cell therapy” to PALS

Stem Cells

- Dr. Huang, Institute of Beijing
 - Human fetal olfactory cells injected into brains and spinal cords of PALS
 - Dr. Van den Berg investigated 12 cases in 2007
 - No ethics committee involved or proof cells survived
 - \$30-40,000 out of pocket per patient
 - 5/12 reported transient improvement, followed by progression (other 7 no improvement)
 - Blood clots, pneumonia, permanent ringing in ears
 - Chinese government has since closed this clinic down

Stem Cells

- XCell Center (<http://www.xcell-center.com/>)
 - Autologous bone marrow cells harvested and injected (into spinal fluid?); 7545 euro/treatment



-16 out of 53 patients reported no change in muscle spasticity, sensation, mobility or feeling of wellbeing after the treatment.

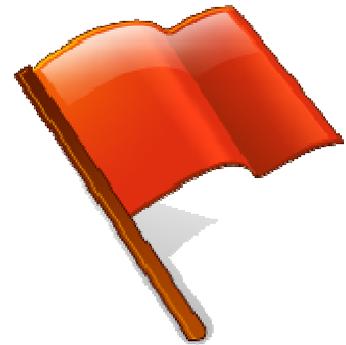
-19 out of 53 patients reported an overall improvement, with improved mobility (legs, arms) and/or improved breathing and or/ improved strength. Some patients reported a regaining of muscle strength and/or an improvement of balance, sleeping or a reduction of spasms.

-One patient reported a strong improvement, with a marked improvement of mobility, breathing, speech and swallowing.

-17 out of 53 patients reported a perceived deterioration of the quality of their life. A majority of these patients saw a reduction of mobility, strength, speech/swallowing or balance. The treatment could neither stop nor reverse the advance of the ALS symptoms. It is believed that the treatment has not adversely affected the patients.

How to Assess Other Alternative Therapies

- Discuss any options with your ALS expert
- “Red Flags”
 - Evidence is only case report(s)
 - Subjective improvements
 - Large up front out of pocket cost
 - Lack of follow up
 - “Cure all” for diverse diseases



A Cautionary Tale

- Minocycline
 - Affects mechanisms relevant in ALS
 - Prolongs survival in FALS1 model
 - Well-tolerated in PALS



A Cautionary Tale

- Minocycline
 - Large DBRPCT slow to enroll
 - Many PALS elected to take minocycline off-label rather than participate in trial
 - When finally finished, PALS on minocycline progressed 25% faster than those on placebo!



Studies for NC PALS 09/06/08

- www.clinicaltrials.gov
- Now recruiting in or near NC
 - Validation of Biomarkers in ALS (Duke, WFU)
 - Safety and Efficacy of AVP-923 in PBA Patients with ALS or MS (Duke, CMC)
 - Electrical Impedance Myography As an Outcome Measure in ALS Trials (WFU)
 - Safety and Tolerability of KNS-760704 in ALS (UVa)
- Coming soon in NC
 - Lithium
 - Exercise
 - Ceftriaxone Phase 3
 - Arimoclomol

