

The American Parkinson Disease Association

The American Parkinson Disease Association

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Finding the Doctor that's Right for You Fay Rhodes, Boston, MA

iagnosing Parkinson's disease (PD) can be a tricky proposition, even for a neurologist. The disease takes many different forms and there are other neurological disorders which look like Parkinson's disease in its early stages, among them-progressive sureanuclear palsy (PSP), multiple system atrophy (MSA), small strokes, diffuse Lewy body disease, Alzheimer's, etc. Before my diagnosis of PD, my nurse practitioner told me my shaking hand was "probably just nerves", and I hear stories all the time from Parkinson's patients who've even undergone orthopedic surgery before they were diagnosed.

Suggestion #1: Find a doctor whose ego isn't greater than his knowledge.

It's my experience that a lot of doctors find it difficult to admit they don't know something. A general practitioner — even a general neurologist - sees very few cases of Parkinson's disease over the years. In medical school they might have

and how many college lectures do you remember?! Also, the disease can be very tricky to diagnose.

> My first neurologist was competent enough to diagnose my condition, but he couldn't tolerate my questions. He considered an educated patient a problem. My second neurologist, the late Dr. Stephen Fink, was the Chair of the Neurology Department at **Boston University** Medical Center, yet he wasn't afraid to admit he didn't have all the answers.

Suggestion #2: Find a doctor who listens to you.

Treating Parkinson's disease requires a team approach by you, your doctor and, sometimes, your caregiver. Every Parkinson's patient is unique and responds uniquely to treatment. It took me a long time to find an agonist I could tolerate. Dr. Fink patiently worked with me as I experienced intolerable reactions to drug after drug. He didn't belittle me nor berate me when I took myself off medications which were making my life miserable; he accepted my input

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Electrical Stimulation of the Globus Pallidus

I nformation on electrical stimulation of the globus pallidus for the treatment of Parkinson's disease (PD), along with findings from 2 clinical trials that investigated the effectiveness of the treatment after 3-to-6-months (N Engl J Med 2001; 345:956-963) and 3 years (Mov Disord. 2002;17:803-807) are here reported.

The globus pallidus is a structure involved in motor control located inside the brain. It receives information from nerve cells that contain the neurotransmitter dopamine and is one of the primary brain areas in which information flow is disrupted. The dopamine cells degenerate in individuals with PD, leading to a disruption of information transmission in the nervous system. This breakdown in information transmission eventually leads to the tremor, rigidity, and slowness of movement symptoms that characterize Parkinson's disease.

When the flow of information to the globus pallidus is disrupted faulty information is transmitted to other areas of the brain and eventually to the muscles.

When patients undergo brain surgery, electrodes are implanted into the globus pallidus on each side of their brain. An MRI (magnetic resonance imaging) scan is often performed prior to surgery to give the surgeon a precise picture of the brain. The site chosen for electrode placement is usually determined by locating the position that produces maximum improvement in tremor, rigidity, and slowness of movement during a test stimulation. After the electrode implantation, a programmable stimulator is also implanted, usually near the collar bone.

The decision to use this treatment is made by the patient in consultation with his or her physician. Stimulation of the globus pallidus is typically offered only to those patients whose symptoms are no longer adequately controlled by medication.

The 3-to-6-month study included 38 such patients. The 3 year study included 6 patients who had Parkinson's disease for an average of 15 years. All were taking L-dopa, but despite this and other medications still had severe motor fluctuations

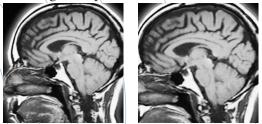
and dyskinesias (hyperactive motor problems) induced by I/-dopa administration.



The 3-to-6-month study found that electrical stimulation of the globus pallidus improved motor function, increased mobility, and reduced the amount of L-dopa needed at 3 months after implantation. Between the preoperative and 6 month visits, the percentage of time during the day that patients had good mobility, without involuntary movements, increased from 28% to 64%. This study used a design that permitted the investigators to conclude with some certainty that the treatment does work for the treatment of advanced Parkinson's disease.

In the 3 year study, motor symptoms were examined following L-dopa administration (L-dopa did not adequately control symptoms for these patients and induced motor hyperactivities of its own). Stimulation of the globus pallidus improved motor symptoms by 30% and these improvements continued for three years. During the first year of treatment, patients also reported a 30% improvement in their ability to engage in everyday activities, but these improvements gradually declined over the 3-year period. Additionally, the stimulation did not help cognition and communication, which actually became worse over the 3 years — possibly due to progression of the disease.

The most serious adverse effect associated with electrical stimulation of the globus pallidus is intracranial



hemorrhage, observed in 18% of patients in the 3- to-6-month study. Infection was also observed in several cases.

In the 3-year study, patients experienced nausea, thoracic pressure and an abnormal burning, tingling, or prickling sensation in some part of their body. These symptoms eventually disappeared.

The conclusion drawn from the 3-to-6-month study was that stimulating the globus pallidus on both sides of the brain produces significant improvement in motor function in those patients with PD whose condition cannot be further improved with medical therapy.

This article was adapted from Dr. Daniel Truong's article in "Glory B" Newsletter, Dec./Jan. 2003.

<u>MEDICATION</u>

MEDICATION CHANGES

There are three important things that physicians consider when evaluating medical treatment for Parkinson's patients.

First, are there significant side effects from the medications? It becomes a matter of determining what is worse: the symptoms being treated or the side effects from the treatment. Fortunately, most of the side effects of the medication for Parkinson's disease (PD) are mild. Some of the major side effects include: low blood pressure, dizziness or a feeling of fainting when standing, severe nausea, inability to urinate, confusion and hallucinations. These are managed with a reduction in dose, choice of another agent, or use of another drug to minimize the side effect; for example, flucortisone (Florinel®) to treat low blood pressure; quetiapine (Seroquel[®]) or clozaril (Clozapine®) to treat hallucinations.

The second determination of whether a medication change is indicated is the presence of fluctuations. Usually at five years after starting levodopa, at least half of the patients with PD no longer have a smooth transition from dose to dose. Periods of good control (ON time) alternate with periods when symptoms worsen (OFF time). That's when one dose of levodopa runs out of steam before the next one starts working.

Many patterns of fluctuation are more complicated, especially when OFF time combines with dyskinesias, these are extra

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P R E S I D E N T ' S M E S S A G E

Dear Readers,



In my statement at the close of our fiscal 2002/ 2003 year, I am gratified to report that the American Parkinson Disease Association continues to meet its goals, and objectives set forth earlier this year.

In July, the APDA network of Chapter Presidents and Information & Referral Center Coordinators will join with the national headquarters staff, management, and Scientific Advisory Board members at the National Conference, in Portland, Maine. At this symposium, we will share information, coordinate strategies, engage in a series of informative lectures, and focus on ways to carry on our important work serving the Parkinson community.

Under the guidance of APDA's Scientific Advisory Board, we continue to aggressively pursue our research efforts to develop the best approaches for diagnosis prevention, and treatment of this disease. To emphasize this effort and commitment, APDA has, once again, awarded research grants, postdoctoral awards, Roger Duvosian and summer medical student fellowships for studies on Parkinson's disease.

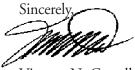
The Corporate Development unit has moved forward with a series of programs that will provide increased awareness and additional funding for our work while developing cooperative partnerships and spurring new corporate initiatives.

Efforts continue with "Play Ball for APDA," a nationally sponsored fund raising program in association with Minor League Baseball. The program to be held in APDA Chapter markets is targeted to become a yearly fund raising event. A national prototype program "Staten Island Eats" scheduled for September is a food and wine sampling show featuring the best restaurants, winery's and bakeries in a local market — in this case Staten Island, New York — as a fund raising tool.

The first APDA broadcast Telethon in October will set the tone for a new era in fund raising initiatives for the association. And finally, APDA will shortly break ground for our new national headquarters to close out an active and productive year.

We look forward to a new fiscal year with the renewed inspiration and continued determination to provide the means and the tools to ease the burden of those afflicted and to find a cure for this disease.

Once again, all of this would not be possible without your continued support, caring, and perseverance, and I thank you personally.



Vincent N. Gattullo

PARKINSON'S NEWS

People with Parkinson's (PWP) and their loved ones now can subscribe to a program called the New Hope for Parkinson's Program. This monthly newsletter developed by Medtronic offers the latest medical and wellness information.

It includes a web site and gives subscribers the opportunity to connect with other patients. The newsletter not only reports the latest scientific findings, but also explores other topics related to health and well-being.

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Series of Series	REGISTER NOW to receive the monthly New Hope for Parkinson's Newsletter.		
Active Archaesedors	* art terms		

The New Hope Program will offer insights from the country's leading movement disorders clinicians and other experts including PWPs themselves.

The first issue will be published in June 2003 and will include a recap of recent scientific findings on PD and the special profile of a woman who had dedicated her life to finding a cure for PD.

PWP and their loved ones may subscribe to the electronic version of the newsletter by logging onto the New Hope web site at www.NewHopefor Parkinson's.com. They may subscribe to the printed version by calling the New Hope for Parkinson's Program subscription line at 1-800-675-5752, or simply completing the enclosed business reply card. ■

Finding the Doctor that's Right *c*₀

and simply prescribed the next drug in his arsenal.

I have a friend, Dot, who cared for her Parkinsonian mother-in-law for many years. Whenever she took her to the local neurologist, the doctor would direct all his questions to Dot. That is downright offensive behavior. On the other hand, there is a neurologist in Boston renown for being so focused on empowering the patient that he prescribed a "wife-ectomy"!

Once I thanked Dr. Fink for listening to me without taking offense. His response was simply, that he found he could learn a lot from his patients if he was willing to listen. What a healthy attitude!

Suggestion #3. If possible, see a movement disorder specialist.

Those of us who live in the Boston area are blessed to have access to many excellent movement disorder specialists, however, in many parts of the country this is not the case. Your area APDA Information and Referral Center coordinator can give you the names of all the movement disorder specialists in your area. A movement disorder specialist is the kind of doctor who will have the most experience with Parkinson's disease and those diseases which mimic it. Many patients find that traveling a long distance to obtain a second opinion from a movement disorder specialist pays off in peace of mind.

Suggestion #4.

Take responsibility for yourself.

My first neurologist did not want educated patients. He suggested that I do not look for information on the Internet, and was offended when I asked questions about my treatment. Thankfully, I've learned that he's not typical. A good neurologist encourages his patients to learn as much as possible about the disease. Knowledge keeps hope alive and teaches you how to function at maximum capacity in your world. Finding another neurologist was an important act of taking responsibility for myself.

It's important that you find a doctor you are comfortable with. If you come away from your appointments feeling worse than when you went in, that may be a sign that it's time to find someone new. Even a general practitioner who's willing to learn with you may be better for you than a neurologist who isn't. Last week I met a couple who said they were thrilled with their doctor. He "had no personality," but really knew his stuff. For them, it was a good match.

You may never find the perfect fit, but you always have the responsibility to make the choices that are best for you. Don't abdicate that responsibility just because you have Parkinson's dis-

ease. 🗖



MEDICATION

Continued from Page 3

movements caused by the brain. Specifically, the receptors for dopamine become overly sensitive to the effects of levodopa. This leads to twisting, gyrating, and dance-like movements of different parts of the body. Many people with PD are not bothered by mild dyskinesias and, if that is the case, the symptoms should be tolerated. End-ofdose problems can be improved by taking levodopa more frequently, switching to the extended-release preparation, or adding entacapone or a dopamine agonist. Likewise, reducing, substituting, adding, or eliminating anti-PD medications can minimize dyskinesias. For patients with disabling fluctuations, deep brain stimulation is also a good option.

The third scenario that indicates to the physician that a patient is in need of a medication adjustment is that they are no longer able to function at a level they find acceptable. Commonly, people with PD are often at their best during an office visit, potentially leading to an underestimation of their problems.

So, tell your neurologist how you're doing: specifically medication side effects, fluctuations, and your level of personal and professional function.





Enrico Fazzini, D.O., Ph.D

Assoc. Prof. Neurology New York University, N.Y., University of Nevada, Las Vegas, NV, N.Y. Institute of Technology, Old Westbury

> I am a 64-year-old male. I have been to three different doctors in the last month. Two of the

doctors think that I have early Parkinson's disease but did not start me on any medication. The other doctor did not think that I have Parkinson's disease. Are there any tests that will confirm that I have Parkinson's disease? If yes, how do I go about getting them?

> The diagnosis of PD is made using
> history and

examination. Patients have a history of low voice volume, excess drooling, slowness with dressing, washing and feeding, slow gait, flexed posture, small handwriting, tremor at rest, masked facial expression, and freezing when attempting to walk. On examination this slowness of movement, cogwheel rigidity, resting tremor and gait abnormality is seen without the presence of weakness or sensory loss. An MRI of the brain is done to rule out structural abnormalities such as strokes or tumors. If the diagnosis is still in doubt medication of L-Dopa is given and the patient is re-examined a few weeks later to determine if any improvement has occurred. (Improvement using L-Dopa is highly suggestive of PD.)

I have Parkinson's disease for 2 years now. I have been reading about all the various vitamins. What are the advantages of taking coenzyme Q10, Vitamin B12, Vitamin C or Vitamin E? If I should start on these vitamins, what dosage should I be on?

There has never been found to be any scientific

evidence that Vitamin E is beneficial. Coenzyme Q10 has been found to be beneficial at slowing disease progression at doses of 1200 mg/day. Vitamin B12 deficiency can lead to weakness, vibration loss and dementia but not PD. Vitamin C deficiencies have not been found to be associated with PD.

> My wife is 68 years old. She has had Parkinson's disease for the last 15 years. I have read about all

the surgeries. Can you tell me the potential benefits of pallidotomy, deep brain stimulation, and stem cell therapy?

> Stem cell therapy remains experimental

in the treatment of PD. There is no control over the degree of growth of the dopamine-producing tissue once it is placed in the brain. Pallidotomy can be performed on one side of the brain in order to reduce dyskinesia and improve tremor and bradykinesia. Bilateral pallidotomies lead to too many side effects and not enough benefit. Subthalamic nucleus deep brain stimulation is a safe and effective method for reducing the "on/off" fluctuations in response to medications in patients who cannot be stabilized on a regimen of medicines and who remain sensitive to the effects of L-dopa.

DEPRESSION AND PD

Depression is a very common complication of Parkinson's disease (PD) and it causes considerable personal suffering. Symptoms of depression include not only sadness, but also difficulty sleeping, excessive worrying, problems with appetite, lack of interest and motivation and social isolation.

While many patients receive antidepressant medications from their doctors, it is not clear which antidepressant is best, or even how well antidepressants work in patients with PD.

A total of 75 patients will receive one of three treatments (two antidepressants and a one



placebo). Patients will be treated for up to six months and will receive careful evaluation of both their neu-

rological and depressive symptoms.

The study will take place at Robert Wood Johnson Medical School in New Brunswick, NJ and interested patients should call the coordinator of the study, Allison Dicke, at 1-877-795-4673 toll free, or at 732-235-5886



Do you have blurred vision, dry eyes, difficulty reading? Do you have these problems even though your eye exams reveal normal or near normal corrected vision and no obvious eye disease? If you do have these difficulties, are they improved after a dose of Parkinson's disease (PD) medication? If so, your visual problems may be Parkinson's related.

The cause may also be a side effect of one of your medications. Many medications, including Parkinson's medications, cause dry eyes: anticholinergic medications (Artane and Cogentin) are especially likely to cause this problem. On the other hand, your eyes may be dry because you stare without blinking and artificial tears may provide temporary relief, if that is the cause.

The retina of the eye contains special nerve cells containing dopamine. Animal studies, and limited human studies, indicate that the retinas of PD patients may have reduced dopamine content. These studies suggest that some eye problems may vary depending on whether the patient is in an "on" or "off" period.

"Seeing" is a complicated process, not at all like photography. A number of different eye movements are at risk of being degraded by Parkinson's.

After the retina has sensed the image and passed the information to the

brain, it is processed in various ways by the visual cortex, a very large, complex part of the brain. The function of the visual cortex is to "make sense" of the mass of data that the retina has passed on.

Some PD patients are said to have problems with visual perception, but the significance and cause of their difficulties are not well understood.

Visual acuity using the standardized distance letters in eye charts has been found to be poor in PD patients when tested under low light intensity. Fairly intense lighting is required for the visual acuity and reading comfort of many PD patients.

Some PD patients suffer from double vision. This most frequently occurs because the muscles of the two eyes are not looking at exactly the same spot. Perhaps it is not surprising that a condition that affects the muscles, and frequently one side more than the other, causes double vision.

Ability to see clearly is enormously important if one is trying to keep in touch with friends and the outside world. Visual complaints can erode one's quality of life and complicate attempts to stay "connected" socially, yet visual impairment is often overlooked or neglected.

Many visual complications of PD can be treated with standard PD medications. ■

APDA NEWS

Information on Parkinson's Disease

Single copies of the following publications may be obtained free of charge by writing to the national APDA office or by calling the toll free number 1-800-223-2732 or Fax 1-718-981-4399.

EDUCATIONAL BOOKLETS

- 1. Basic Information about Parkinson's Disease 4 page brochure (English, Chinese, Spanish)
- 2. Parkinson's Disease Handbook Symptoms, causes, treatment, 40 page booklet (English, German, Italian, Portuguese, Spanish, Russian)
- **3.** PD "n" Me-Coping with Parkinson's disease 70 page booklet (English)
- 4. Be Active A suggested exercise program for people with Parkinson's disease, 25 page booklet (English, German, Italian)
- 5. Be Independent Equipment and suggestions for daily living activities, 32 page booklet (English, German, Italian, Spanish)
- 6. Speaking Effectively Speech and swallowing problems in Parkinson's disease, 34 page booklet (English)
- 7. Good Nutrition in Parkinson's Disease 26 page booklet (English,Italian, Swedish)
- 8. Young Parkinson's Handbook 78 page booklet (English)
- 9. How to Start a Parkinson's Disease Support Group 24 page booklet (English, Italian)
- 10. Aquatic Exercise for Parkinson's Disease A 20 page booklet for patients and their families (English)

EDUCATIONAL SUPPLEMENTS

Hospitalization, Helpful Hints, Living Will, Oral Health Care, The Family Unit, Helping Your Partner, Nursing Homes, Long Term Care Insurance, Recreation and Socialization in Parkinson's Disease, Comtan Questions & Answers, Use of Comtan in the Treatment of Parkinson's disease, PD and The Emergency Room

CARELINK

(A cooperative APDA - GSK project) You can now contact the APDA Information and Referral Center closest to you by dialing the toll free number **1-888-400-2732**

APDA WORLDWIDE WEB SITE

www.apdaparkinson.org for PD, I&R Centers, Chapters, Support Groups, Education and Information Material, Meeting Dates, Publications, Medical Abstracts, Video Library, Udall Bill, etc.

WORLD PARKINSON DISEASE ASSOCIATION WEB SITE

www.wpda.org/ A weekly updated source of world news



FISCAL YEAR 2003-2004 RESEARCH FUNDING

The number of research grants and fellowships submitted to APDA for funding during fiscal year 2003-2004 was considerably higher than the number submitted in the past.

The recommendations and scores submitted by the Scientific Advisory Board (SAB) under the chairmanship of Dr. Wooten were reviewed by the Executive Committee of the association, and a grand total of 30 awards made. The new grants are listed at p. 8 and include: three Roger Duvoisin Fellowships, 12 Research Grants, 10 Post-Doctoral Fellowships, and five Summer Medical Student Fellowships. The results obtained by the Centers for Advanced Research were also reviewed and approved by the SAB.

The material contained herein concerning the research in the field of Parkinson's disease and answers to readers questions are solely for the information of the reader. It should not be used for treatment purposes, but rather as a source for discussion with the patient's own physician.

THE PRINTING OF THIS NEWSLETTER WAS FUNDED BY AN EDUCATIONAL GRANT FROM GLAXOSMITHKLINE

APDA Additional Research Funding for Fiscal Year 2003-2004

Roger C. Duvoisin, M.D., Fellowsh		
M. Maral Mouradian, M.D.	UMDNJ Robert Wood Johnson Medical School <i>(New Brunswick, NJ)</i>	Cytotoxicity and Chaperone-Medicated Modulation of Parkin Aggregation
Gregory A. Petsko, Ph.D.	Brandeis University (Waltham, MA)	Structural and Functional Studies of DJ-1, the Protein Whose Gene is Mutated in Autosomal Recessive Early-Onset Parkinson's Disease
Ke-Zhong Shen, M.D., Ph.D.	Oregon & Health Sciences University (Portland, OR)	Mechanism Underlying the Effect of High-Frequency Stimulation of the Subthalamic Nucleus in Rats with Unilateral Dopamine Denervation
Research Grants		
Dean Dluzen, Ph.D.	Neoucom (Rootstown, OH)	Testosterone: Potential Facilitator of Nigrostriatal Dopaminergic Neurodegeneration
Marc W. Fariss, Ph.D.	Washington State University (Pullman, WA)	Protective Role of Mitochondrial Alpha Tocopherol in Rotenono Induced Experimental PD
Curt R. Freed, MD	University of Colorado HSC (Denver, CO)	Role of DJ-1 in Dopamine Neuron Death and its Interaction with Alpha-Synuclein
Ming Guo, MD, Ph.D.	UCLA School of Medicine (Los Angeles, CA)	Role of DJ-1 Gene in Dopaminergic Neuronal Survivial
Ashok N. Hedge, Ph.D.	Wake Forest University (Winston-Salem, NC)	Parkin and Neurodegeneration
Cameron C. McIntyre, Ph.D.	Emory University (Atlanta, GA)	Electric Field Generated by Deep Brain Stimulation
Jean-Christophe Rochet, Ph.D.	Purdue University (West Lafayette, IN)	Effect of DJ-1 on Oxidative Stress and Alpha-synuclein Aggregation in Parkinson's Disease
Michal K. Stachowiak, Ph.D.	University of Buffalo (Buffalo, NY)	Does Inactivation of the FGF-2/FGFR1 Signaling Underlie Neuronal Degeneration in Parkinson's Disease? The Implication for New Therapeutic Targets
Mona J. Thiruchelvam, Ph.D.	University of Rochester (Rochester, NY)	Neonatal Pesticide Exposure and Parkinson's Disease
Zuo-Zhong Wang, Ph.D.	University of Pittsburgh (<i>Pittsburgh, PA</i>)	A Clonal Dopaminergic Cell Line for Transplantation Therapy of Parkinson's Disease
Jin Xu, Ph.D.	Caritas Št. Elizabeth's Medical Center <i>(Boston, MA)</i>	Functional Studies of DJ-1 in Human Dopaminergic Cells
Jianhua Zhou, Ph.D.	University of Massachusetts (Worcester, MA)	Interaction Between Parkin and REPA on Protein Ubiquitination and Degradation
Post-Doctoral Fellowships		
Stephanie Baulac, Ph.D.	Brigham and Women's Hopital (Boston, MA)	Implication of DJ-1 in PD Study in Mammalian Cells, Human Brain, and Zebra Fish
Srinivasbharath Mukunda, Ph.D.	Buck Institute For Age Research (Novato, CA)	Role of Thiol Oxidation of Mitochondrial Complex 1 During Glutathion Depletion in Dopaminergic Cells as a Model for Parkinson's Disease
Sic Lung Chan, Ph.D.	National Institute of Aging <i>(Baltimore, MD)</i>	Neuroprotective Action of the Novel ER Stress Protein Herp in Models of Parkinson's Disease
Amanda Eberz, Ph.D.	University of Pennsylvania (Philadelphia, PA)	Effect of Oxidative Stress on Calpain Cleavage of Wild Type and Pathological Forms of Alpha-Synuclein
Sherwin E. Hua, MD, Ph.D.	Johns Hopkins University (Baltimore, MD)	Objective Measurement of Rigidity and Bradykinesia during Intraoperative STN Microstimulation to Optimize DBS Targeting
Cecile Martinat, Ph.D.	Columbia University (New York, NY)	Stem Cell-Derived Neurons and the Environment: Extrinsic Regulation of Terminal Differentiation
Tianhong Pan, Ph.D.	Baylor College of Medicine (Houston, TX)	Is Reduced Nurr 1 Expression in Human Peripheral Blood Lymphocytes a Biomarker of Parkinson's Disease?
Helen Walden, Ph.D.	St. Jude Children's Research Hospital <i>(Memphis, TN)</i>	Structural Studies of Parkin
Anat Ben-Zvi, MS	Northwestern University (Evanston, IL)	Identification and Characterization of the Toxic Form(s) of Parkinson Aggregates

Summer Medical Students Fellowships			
Brett Bordini	University of Wisconsin Medical		
	School (Madison, WI)		
Maher Khan	Chicago Medical School		
	(Chicago, IL)		
Elise Malecki	University of Maryland		
	(Baltimore, MD)		
Eleanora Marnes	Finch University of Health		
	Sciences (Chicago, IL)		
Mark Richardson	Medical College of Virginia		
	(Richmond, VÄ)		