MDS 1998 dues

Dues bills for 1998 memberships in The Movement Disorder Society were sent in early May. If you haven't paid your dues yet, please pay them as soon as possible.

If you have not yet received your MDS invoice, please contact Michele Puliti at the Administrative Secretariat (telephone: +1 609-423-7222, ext. 216, fax: +1 609-423-3420, or e-mail: mdshq@mds.smarthub.com) to make sure that the address we have listed for you is correct.

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Videotapes available

1. Toronto-Western Spasmodic Torticollis Rating Scale (TWSTRS) Training Videotape

2. Instructional Videotape for Motor Fluctuation Diaries in Parkinson's disease

For more information or to order videos, contact Michele Puliti, MDS Administrative Assistant, at the Administrative Secretariat.

Movement Disorders journal

If you are having any problems with delivery of your journal, *Movement Disorders*, please contact Administrative Assistant, Michele Puliti, at the MDS Administrative Secretariat (telephone: +1 609-423-7222, ext. 216, fax: +1 609-423-3420, or e-mail: mdshq@mds.smarthub.com).

Moving Along is supported by an educational grant from F. Hoffmann-La Roche Ltd., Basel, Switzerland

Moving Along

A *Movement* Disorder Society UPdate

Volume I, Issue 2 — Editors: Dr Bill Koller and Dr Eduardo Tolosa

Message from the MDS President

Organizations unite on World PD Day

It was recently my pleasure to welcome some of the major partners involved in helping people with Parkinson's disease (PD) to the dynamic and cosmopolitan capital of Catalunya, Barcelona in Spain. Recognizing that strength comes from unity, the Movement Disorder Society (MDS) together with the World Health Organization (WHO) organized a unique event with sponsorship from F. Hoffmann-La Roche Limited.

Entitled 'Uniting for Tomorrow', the meeting was held on Thursday April 2 to mark the 2nd World PD Day. The MDS is delighted with the endorsement for this meeting and continuing support received from the WHO, and look forward to further co-operation in the future. We are also very grateful that Dr J A Costa e Silva, Director of the WHO Division of Mental Health and Prevention of Substance Abuse, was able to participate in this special meeting.

A media conference was also held at the meeting which led to international press coverage that will help raise public awareness of the problems faced by people with PD.

In the special supplement to this issue of *Moving* Along, we are pleased to be able to share with you some of the advances discussed at this unique event through a series of presentation reports.

In the spirit of the meeting title, let us unite for tomorrow.

Sincerely,

Eduardo Tolosa
President

Partnership with the pharmaceutical industry

"If we work together, we really can improve the quality of life for people with PD." Mr William Burns, F. Hoffmann La-Roche Ltd.

The pharmaceutical industry has an important role to play in the alliance represented at this Barcelona meeting.

"Over many years there has been small stepwise progression in the knowledge we can bring to bear in this very debilitating disease. Advances in genetics will open another door for better diagnosis, which should, in turn, lead to better targeting of small molecules that can interfere with progression of disease," Mr William Burns, Head of Pharmaceutical Affiliates, European and International, from Roche, Switzerland, told delegates.

Part of Roche's duty and responsibility in this partnership is to ensure that any step forward is quickly available for patients. Over the past six months, Roche has been able to bring Tasmar® (tolcapone) to 25 countries. Tasmar® is a new agent which increases the effectiveness of levodopa, and reduces the quantity of levodopa required.

Communication is a further dimension that Roche can bring to the alliance. "We hope to use this skill to help patients, for example, through our sponsorship of the '*Awakenings*' Internet website*," said Mr Burns.

* The *Awakenings* website can be found at www.parkinsonsdisease.com

Hope and optimism for the future

Summing up the events of this exciting 2nd World PD Day, Dr Eduardo Tolosa, MDS President, said, "We believe that by working in partnership, it is possible to bring about the necessary changes that will result in the best possible quality of life for all those people living with, and affected by, PD. The meeting surpassed all our expectations."

"We look to the future with hope and with optimism. We expect to see major changes in the management of PD in the very near future."
Dr Eduardo Tolosa, Movement Disorder Society

This issue is dedicated to one of the Movement Disorders Society's pioneers, Harold L Klawans MD, who sadly died on March 30, 1998, aged 60.

Moving Along is supported by an educational grant from F. Hoffmann-La Roche Ltd., Basel, Switzerland

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uniting for tomorrow

Moving Along

June 1998

A *Movement* Disorder Society UPdate

A WORLD PD DAY SPECIAL ISSUE

Special event to mark the 2nd World PD Day

'Uniting for Tomorrow' was a unique event held on Thursday 2 April and brought together specialists, researchers, patient organizations, and pharmaceutical industry representatives to discuss the latest developments in PD.

MDS President, Dr Eduardo Tolosa co-chaired the day's events and this supplement brings you presentation highlights from some of the world's experts in PD.

Joining together to fight PD

The morning programme was entitled 'Joining together to fight Parkinson's disease' and took place in the 'Ramón y Cajal' room at the Faculty of Medicine, University of Barcelona. This meeting was unique in that it was open to the general public, patients with PD, and carers.

To underline the patient participation in this session, Dr Tolosa unveiled a painting by Serra Llimona, a famous Catalan artist who has PD. The painting reflected the design of the 'Uniting for Tomorrow' logo in the sun against the Barcelona skyline.

Painting by Serra Llimona

PD beyond the second millennium

La Pedrera de Catalunya, the famous building in Barcelona by Gaudí, was the setting for the more clinical and scientific afternoon session: 'Parkinson's disease beyond the second millennium'. This part of the meeting was co-chaired by Professor Oscar Gershanik from the Centro Neurológico Hospital Francés, Buenos Aires, Argentina, and Professor Y Mizuno from the Juntendo University School of Medicine, Tokyo, Japan.

In his introduction, Professor Gershanik noted that although much has been learnt about PD in recent years, the challenge that awaits us beyond the turn of the century is still enormous.

"Will we be able to find the cause of PD? Will we discover specific biological markers that allow for an early and correct diagnosis even before clinical symptoms are evident? Will we understand the mechanisms of cell death in PD, therefore, allowing the use of effective neuroprotective strategies?" he asked the audience.

Exclusive announcement of gene discovery

Professor Mizuno later introduced the discussion of new and future treatment of PD. Following the discovery of an autosomal dominant gene for PD (alpha-synuclein) earlier this year, it was an honour that Professor Mizuno chose this meeting to exclusively announce the discovery of an autosomal recessive gene for PD (Parkin).

PD researchers need more brain tissue donations

More than 1000 people with PD have allowed their brain tissue to be donated to the UK Parkinson's Disease Society (PDS) Brain Bank, but there is a shortage of brain tissue from people who died from other causes, explained Dr Sue Daniel, Head of Neuropathological Research, PDS Brain Research Centre and Senior Lecturer in Neuropathology, Institute of Neurology, London, UK.

Almost 800 of the brains held at the London centre are from patients with movement disorders (635 Parkinson's syndrome, 137 dystonia and 18 Gilles de la Tourette syndrome) and the remainder are normal controls. The annual rate of donations is approximately 70 parkinsonian brains per year.

"Getting hold of control brains is a real problem for us. In an ideal world we would have one neurologically normal control for every Parkinson's brain," said Dr Daniel.

The neuropathology of specimens provides insight into conditions that may clinically masquerade as PD leading to erroneous diagnosis during life. "In the years 1987-1990, one in four brains with a clinical diagnosis of idiopathic PD were found to have other neuropathology. Today only one in eight cases are misdiagnosed," she explained.

Other current research is aimed at a better understanding of the molecular events underlying parkinsonian disorders. "Results of these studies are making a significant contribution to the understanding of disease aetiology and have important implications for effective therapeutic intervention and preventative treatment," said Dr Daniel. Donated brain material is used for in-house research projects and is also freely available to research groups worldwide.

Conditions most frequently misdiagnosed as PD	
Progressive supranuclear palsy	30%
Multiple system atrophy	26%
Vascular, lacunar state	20%
Tremor	11%
Alzheimer's disease	8%

Recent clues to the cause of PD

PD is characterized by a massive loss of dopaminergic neurons, yet not all dopaminergic neurons of the mesencephalon degenerate, said Professor Etienne Hirsch of the Clinique de Neurologie, Hôpital Salpêtrière, Paris, France.

A number of mechanisms may account for this difference. The density of astroglia (a mass of astrocytes considered as tissue) varies throughout the mesencephalon; being moderate in the dopaminergic cell groups which are the most severely affected in PD, and high in the least severely affected dopaminergic cell groups. This suggests a neuroprotective role of subpopulations of astrocytes.

"The factors involved in such neuroprotective effects may include the capacities of astrocytes to metabolize dopamine and oxygen free radicals," explained Professor Hirsch.

Other glial cells may exert a deleterious role. Microglia and/or subpopulations of astroglia are known to release cytotoxic compounds such as cytokines. This toxicity may be mediated by a direct mechanism involving specific receptors and pro-apoptotic transduction pathways, as shown for tumour necrosis factor.

Alternatively it may activate the production of inducible nitric oxide (NO) synthase, which may in turn, by producing NO, alter iron metabolism and induce oxidative stress. "The inhibition of such mechanisms may represent a target for treatments aimed at slowing down the pathological process," said Professor Hirsch.

New agents may prevent cell death in PD

The goal of neuroprotection is to prevent the degeneration of nerve cells in the substantia nigra pars compacta – a hallmark sign of PD. Current treatments are primarily directed at correcting the symptomatic consequences of the loss of these nerve cells. But according to Professor Warren Olanow, of Mount Sinai School of Medicine, New York, USA, innovative 'neuroprotective' drugs will soon be ready for clinical testing.

"A therapeutic strategy that can slow or halt degeneration of nerve cells, particularly if introduced at the earliest stages of the disease, could prevent the development of disability that accompanies the inexorable progression of PD," said Professor Olanow.

"Currently, agents are being explored in the laboratory and in the clinic that interfere with oxidant stress, mitochondrial dysfunction and excitotoxicity. More recently, there has been evidence that cell death in PD occurs by way of apoptosis. Towards this end, agents that block signalling for the initiation of apoptosis or the transcriptional and translational changes that are associated with this phenomenon might prove to be neuroprotective," said Professor Olanow.

Genes and gene therapy for PD

Interest in hereditary factors in PD has grown steadily as evidence has shown that a positive family history is a major risk factor for the disease.

Professor Mihael Polymeropoulos – whose team recently announced the discovery of a mutation in the alpha-synuclein gene in a group of families with PD (*Science* 1997; **276**:2045-7) – told the meeting he was committed to understanding the genetic causes of PD.

"One of these causes has now been resolved with the identification of the mutation in the alpha-synuclein gene," said Professor Polymeropoulos, of the National Human Genome Research Institute, National Institutes of Health, Bethesda, USA.

However, in common with other complex genetic disorders, this mutation only accounts for a minority of families with PD. "Beyond alpha-synuclein, what comes next?" asked Professor Polymeropoulos. Work on alpha-synuclein has suggested that the mechanism of aggregation of damaged proteins inside the neuronal cells of the substantia nigra may hold the clue to the pathophysiology and aetiology of PD.

"We have a few clues that the mutation leads to accumulation of protein which is the key event in the production of the pathology and symptoms of PD," he added.

Reviewing the role of gene therapy in the treatment of PD, Professor Pedro Lowenstein, Molecular Medicine Unit, University of Manchester, UK, described how gene therapy aims to utilize genes as drugs. "Its power resides in the capacity to deliver genes encoding novel or missing functions to the affected brain. On this theoretical point, gene therapy appears to be more powerful than pharmacology," he suggested.

In PD, gene therapy aims to deliver various gene products directly to the affected brain areas. These could be neurotrophic factors or enzymes necessary for the synthesis of the neurotransmitter dopamine.

Professor Lowenstein's group has inserted various neurotrophic and neuroprotective factors directly into adenoviral vectors and is currently testing their efficiency *in vitro* and *in vivo*.

"At the same time, we are improving the delivery systems, in order to achieve cell type-specific and regulatable expression of transgenes. We are also developing novel approaches to achieve long-term transgene expression. Any potential therapy for PD in humans will have to show its activity over many years. This constitutes an enormous challenge," he said.

CONTENTS

The Movement Disorder Society's 5th International Congress on Parkinson's Disease and Movement Disorders

October 10-14, 1998, New York

Make your plans to travel and attend this important event while rooms are still available in the headquarters hotel, The New York Hilton and Towers. A record 1140 abstracts were received and will be presented in poster format over the five-day congress. In addition, there will be 10 half-day plenary sessions with invited talks on parkinsonism, dystonia, chorea, ataxia, childhood diseases and tremors.

Dr. Anders Bjorklund will present the Stanley Fahn Lecture this year. Other highlights include over 50 breakfast seminars with limited attendance, two video sessions and over 40 exhibiting companies with the latest in treatment and technologies available worldwide.

Socially, the Congress has been structured to allow you and your colleagues to enjoy all that New York has to offer. We are making blocks of Broadway Theater tickets available, as well as creating a unique Welcome Reception and Gala Banquet for your pleasure.

The complete registration brochure is available on the web at www.movementdisorders.org/congress/congress.html or by fax on demand by calling 609-423-3427, ext. 704 and requesting document #210. When asked for your fax number, US callers must enter 1 + area code + your fax number, and non-US callers must enter 011 + country code + city code + your fax number. You can also request information to be mailed to you by calling 609-423-7222, ext. 350 or emailing mdshq@mds.smarthub.com.

We look forward to seeing you in New York for a most rewarding educational experience and opportunity to see old colleagues and meet new friends.

Applications now being accepted for satellite meetings in 2001

The MDS Secretariat is now accepting applications from meeting organizers who wish to receive MDS sponsorship for scientific meetings in the year 2001. Application forms are available upon request from the Administrative Secretariat by mail, fax, or e-mail. Completed applications must be submitted to the Administrative Secretariat by August 1 1998. All completed applications will be referred to the Education Committee which will make recommendations to the International Executive Committee.

The International Executive Committee will announce those meetings selected as MDS-sponsored meetings for the year 2001 during the 5th International Congress on Parkinson's Disease and Movement Disorders to be held October 10-14 1998 in New York City.

1998 MDS Officers/ International Executive Committee Meetings

June

MDS International Executive Committee/Officers Strategic Planning Meeting
June 30-July 3,
Aiguablava, Spain

October

MDS 5th International Congress on Parkinson's Disease and Movement Disorders
October 10-14,
New York, NY, USA

MDS Officers/ International Executive Committee Meeting
Friday, October 9

MDS Business Meeting
Monday, October 12, 12.45pm

November

Financial Affairs Committee/Officers
November 14-15, *venue TBA*

MDS-sponsored meetings, 1999

INTERNATIONAL MOVEMENT DISORDER SOCIETY SATELLITE MEETING ON MUSCLE STIFFNESS

August 26-29, 1999
Sheraton Mirage Resort
Port Douglas, Australia

Local Organizing Committee: Professor Philip D. Thompson
Meeting Secretariat: Conference Action Pty Ltd., PO Box 1231, North Sydney NSW 2059, Australia.
Fax: +61 9956 5154

INTERNATIONAL SYMPOSIUM ON GAIT DISORDERS

September 4-6, 1999
Prague, Czech Republic

Convenor: Associate Professor Evžen Růžička, MD, PhD
Symposium Secretariat:
A. Kürfurstová, c/o Czech Medical Association J. E. Purkyne, PO Box 88, Sokolská 31, 120 26 Prague 2, Czech Republic.
Telephone: +420 2 29 72 71, 29 68 89
Fax: +420 29 46 10, 242 168 36
E-mail: KURSFURSTOVA@CLS.CZ
Website: http://congress.cls.cz/gaitdisorders

INHERITED ATAXIAS

October 13-15, 1999
Seattle, Washington, USA

Contact: S. H. Subramony, University of Mississippi

New drugs making impact on PD

New drugs for PD are helping overcome important limitations of levodopa, Professor Werner Poewe, Department of Neurology, University of Innsbruck, Austria, told the audience of 'Uniting for Tomorrow'.

"When first introduced in the 1960s, levodopa had a dramatic impact on the level of symptomatic control, progression of disability, and early mortality in PD. Thirty years later, levodopa is still regarded as the gold standard of therapeutic efficacy of all antiparkinsonian drugs," said Professor Poewe.

However, he added that the 'honeymoon' period of levodopa treatment is regularly followed by late failure with progression of axial symptoms, drug-induced dyskinesias and fluctuations in response.

Recently a number of new drugs have been introduced into clinical practice with the aim of improving long-term control in PD. These include the catechol-*O*-methyl-transferase (COMT) inhibitor, tolcapone, and newer dopamine agonists, such as cabergoline, ropinirole, and pramipexole.

COMT inhibitors can successfully smooth out fluctuations in levodopa response and may potentially improve the long-term outcome of levodopa treatment when co-administered in de-novo patients. Professor Poewe described how COMT inhibition with tolcapone reduces the 'wearing-off' phenomenon, and prolongs 'on' time in fluctuating parkinsonian patients while allowing a reduction in daily levodopa dosage, thereby improving the efficacy of long-term therapy.

CONTENTS

Informal carers 'are no longer there'
A European patient's perspective

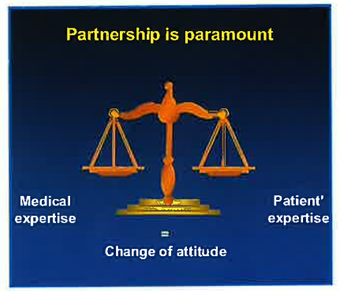
For decades, the care of people with PD has relied on 'informal carers'. However, in many countries, the number of such carers is dwindling, Mary Baker, MBE, President of the EPDA, reminded 'Uniting for Tomorrow'.

"Two thirds of informal carers are women, but falling birth rates, and proper career structures mean they are no longer available," she explained.

Never before has it been so important for the voice of patients' organizations to be heard. "In order for the providers of service to deliver appropriate and cost-effective care, it is important that they listen to the voices of the voluntary organizations and recognize the necessity for changing attitudes and the reassessment of education and training," she said. The voluntary organisations should also be listening to the voices of patients and convey those needs as swiftly as possible to the policy makers, she added.

"Unity and collaboration are essential if we are to get best practice."
Mary Baker, European Parkinson's Disease Association

"We need to combine the knowledge and clinical observations of the doctors with the experiences of those people living with, and impacted by, chronic neurological illness on a daily basis. It is only then that it will be possible to achieve an integrated picture of the challenges of managing a chronic neurological illness such as PD," concluded Mrs Baker.



Innovative surgical treatments

There has been a resurgence of interest in surgical treatments for PD, said Professor Jose A Obeso, Clínica Quirón, San Sebastián, Spain.

This renewed interest has stemmed from a better understanding of the pathophysiological basis to parkinsonism and the experimental demonstration that inactivation of the subthalamic nuclens dramatically alleviates parkinsonism in monkeys.

There are three current surgical approaches:

- Grafting human embryonic dopaminergic cells into the striatum
- Lesioning the globus pallidus or, rarely, the thalamus
- Implanting electrodes in the subthalamic nuclens or globus pallidus to block neuronal activity by chronic depolarisation.

"Surgery is no longer seen as negative. For many years, like most of you, I was led to believe that surgery was the failure of intelligence to solve the problem. Now I think the future for surgery in PD has changed radically and now we have many tools to interfere with specific mechanisms which may lead to regeneration and halt progression of the disease. This will be a great endeavour until the actual aetiology of the disease is known," said Professor Obeso.

He added that future innovative surgical techniques may include:

- Lesioning of structures such as the subthalamic nuclens
- Stimulation of new targets such as the external pallidus
- Grafting of embryonic cells from other species (xenotransplants)
- Grafting of genetically determined cells to correct major deficits caused by the disease and express neurotrophic factor to halt disease progression.

PD is a 'priority' for WHO

PD is a priority for the WHO Neurology and Neuroscience Program, said Dr J A Costa e Silva, Director of the WHO Division of Mental Health and Prevention of Substance Abuse.

"PD currently affects around 1% of people aged over 65 years; however, this proportion will rise as the average life span increases. Steps to increase public awareness of PD as an important health problem should be pursued vigorously," he told delegates.

He also added that widespread dissemination of information to the health authorities, medical schools, and teaching hospitals was required.

Neuroscientific developments make positive impact in PD

Recent scientific advances have made a tremendous impact on our understanding of PD, Dr William Koller, Department of Neurology, University of Kansas Medical Center, Kansas City, USA, told 'Uniting for Tomorrow'.

These advances include:

- Understanding the role of genetics with the discovery of gene defects and, in some cases, of familial PD
- A marked increase in our knowledge of the cascade of pathological events that eventually result in neuronal injury
- A significant improvement in drug therapy with the introduction in the past six months of four new drugs for the treatment of PD. This includes a new class of compounds, the COMT inhibitors, and three new dopamine agonists, two of which have distinct receptor agonist profiles.
- A resurgence of interest in surgical treatments including pallidotomy and deep brain stimulation of areas such as the thalamus, globus pallidus, and subthalamic nucleus
- The discovery that apoptosis is the precise mechanism of neuronal cell death in PD.

"More research is now being undertaken into PD than at any other time in history. Sometimes it seems there are daily advances in our understanding. These advances will translate into better care for our patients. I believe that a cure for PD is within our grasp in the not too distant future," said Dr Koller.

Patient associations – the US perspective

The US National Parkinson Foundation (NPF) now funds 38 centres of excellence in the USA and 13 other PD research centres throughout the world, according to NPF Director, Mr Emilio Mendoza.

The NPF has joined with the Parkinson Outreach Program to provide physical, occupational, and speech therapy, plus an array of social services at more than 40 sites in the USA.

"This ambitious project was initiated less than three years ago, and has already established multiple service sites in all regions of the country.

"While aggressively seeking the cause and cure for PD, we are deeply committed to in-depth services to enhance quality of life for those affected," said Mr Mendoza.

Global Survey of Parkinson's Disease

The Global Parkinson's Disease Survey (GPDS) – the first international quality of life study to involve people with PD, their carers and physicians – is now underway, Professor Leslie Findley told 'Uniting for Tomorrow'. It is one of the first examples of the successful collaboration between the organizations which are committed to helping patients with PD, including the WHO, European Parkinson's Disease Association (EPDA) and Roche.

The survey aims to investigate those factors which influence the quality of life of people with PD, other than disease severity and drug treatment. "Identifying and prioritising these factors will enable us to provide a universal management framework for all involved in the provision of care," said Professor Findley, Consultant Neurologist and Professor of Health Sciences at the South Bank University, London, UK.

Approximately 1000 people with PD will be drawn at random from the patient lists of 200 clinicians across countries in Europe, America and Asia. A further 800-900 carers will also be included in the survey. Trained interviewers will question carers, patients, and physicians face-to-face using specially designed forms.

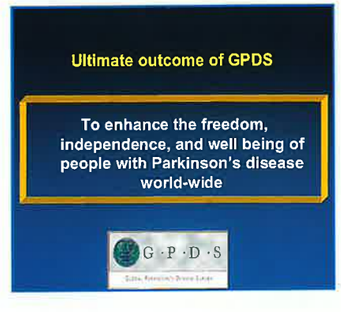
The pilot stage of the GPDS is underway and the full survey will start this summer, with results available by the end of the year.

Professor Findley stressed that the information from the Global Parkinson's Disease Survey is essential to make best use of the limited resources available for the management of PD.

"The Global Parkinson's Disease Survey will help optimise care and use resources economically." Professor Leslie Findley, London

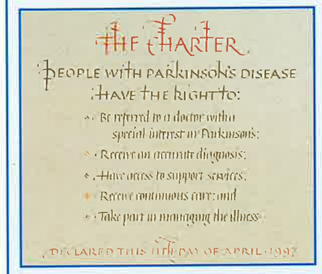
Factors to be examined in the GPDS

- Attitudes of the patient, caregiver and healthcare professionals
- Delivery of diagnosis
- Infrastructure of support
- Patient/carer support groups
- Drug therapies
- Non-drug therapies, surgery, and complementary therapies
- Access to information
- Communication between patients and their care team and support groups



World Charter is reaffirmed

The five key principles incorporated into the World Charter on PD, first declared on April 11, 1997, were reaffirmed when speakers and delegates re-signed the Charter in Barcelona.



The World Charter on PD

The Charter states that people with PD have the Right to:

- Be referred to a doctor with a special interest in PD
- Receive an accurate diagnosis
- Have access to support services
- Receive continuous care
- Take part in managing the illness.

One of Dr Tolosa's PD patients, Mr Gregorio Santos, signs the Spanish Charter