



NEWSLETTER N°5, November 2007

# EuroMyasthenia



Dear Colleagues

This newsletter is naturally dedicated to our friend and colleague John Newsom Davies who has left us orphans in the world of Myasthenia Gravis. We have all been very shocked by his sudden death in a car crash during a visit to Romania in the context of his work on the clinical protocol on early thymectomy study.

John was a "father" to most of us. All researchers and clinicians working in the field of MG had the opportunity to meet him and exchange ideas. He was always very pleasant, gallant, and professional, with a sense of humor that many of us could appreciate, and he was exceptionally talented in inciting people to pursue their research in MG. I met him for the first time in Vienna at an "autoimmunity meeting" in 1980, before I started working on MG. I remember how I enjoyed his encouragements, guidance, and advices. I am sure than many of us had a similar experience.

Even after he officially retired, John continued working and trying to get clear and definite information about the effects of thymectomy on MG symptoms. This project was a real challenge for him and for all of us, and he gave it all his energy and even his life. Indeed, it is just after his visit to a hospital where he met a MG specialist that the fatal accident occurred. Clearly, we can say that he died "on duty".

Unhappily, John will not see the results of the early thymectomy program that was so important to him. To honor his memory, we must keep this protocol going and think of him when we get the final results. Our thoughts go to his wife Rosemary to whom we wish a prompt recovery and to Amelia, Imogen, and Tom, John, we miss you a lot.

Sonia

*Sonia Berrih-Aknin*, Coordinator

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## GuardianUnlimited

John Newsom-Davis was killed in a car accident in Romania. He was professor of clinical neurology at Oxford (1987-98) and one of the most distinguished clinical neurologists and medical scientists of his generation. Newsom-Davis was born in Harpenden, Hertfordshire. He was educated at Sherborne school, Dorset, and, later, after training as a fighter pilot during a period of national service in the RAF, at Pembroke College, Cambridge, and Middlesex hospital medical school, from which he qualified MB BChir in 1960. After a variety of training posts including a period at the Cornell medical centre, New York, he became, in 1970, consultant neurologist at the Royal Free hospital and National hospital for Nervous Diseases, in London. From 1980 to 1987, he held the post of clinical research professor of neurology at the Medical Research Council. In 1987, attracted by the impending development of the multidisciplinary Institute of Molecular Medicine (later the Weatherall Institute), he moved to Oxford, where he was appointed professor of clinical neurology.

As well as building up an excellent clinical department, with his long-standing collaborator Angela Vincent, he assembled a strong team of neuroscientists in the institute, where he pursued his later work on aspects of autoimmune and genetic disease of the nervous system. Newsom-Davis was also an outstanding teacher and communicator, loved and admired by generations of medical students, house staff and young clinical scientists. His ability to convey the excitement of his field to general audiences led to his appointment as president of the biomedical section of the British Association for the Advancement of Science in 1982. He played a major role in the development of neurology and was president of the Association of British Neurologists (1999-2000) and editor of the journal *Brain* (1997-2004). He was a founder fellow of the Academy of Medical Sciences and gave his time generously to many other institutions, including the Medical Research Council and the Royal College of Physicians. His international reputation is reflected in his honorary membership of the American Academy of Neurology and his election as a foreign member of the Institute of Medicine of the US National Academy of Sciences. (continued, next page)

## GuardianUnlimited

His contributions to the neuro-sciences were widely recognised by named lectureships and awards; he was elected a fellow of the Royal College of Physicians in 1973, a fellow of the Royal Society in 1991, and awarded a CBE in 1996. His other major interest was in music, particularly opera. And although he was loathe to admit it, he was also an excellent cook; he was equally reticent about his prowess as a pilot in the RAF. Newsom-Davis was a delightful, outgoing character. Eternally youthful, he continued both his clinical and research activities at Oxford after his retirement in 1998 and remained a major figure in the neuroscience community. In 1963 he married Rosemary Elizabeth Schmid, an educational psychologist who worked in child development. She survives him, along with their son, two daughters and seven grandchildren, who formed a close-knit and extremely happy family. (*The Guardian*, by David Weatherall, 21st September 2007)

## THE INDEPENDENT

John Newsom-Davis was one of a small number of physicians who in the 1970s began to apply advances in basic science to clinical problems...His greatest contribution was to identify auto-immune mechanisms and appropriate treatments in neurological diseases.....Myasthenia gravis affects the signalling junction between nerves and muscles, leading to muscle weakness which can be life-threatening. Work in the United States, also performed by Newsom-Davis, Ricardo Miledi and colleagues, showed reduced signalling protein in the junction in patients' muscles, and that this was most likely caused by antibodies that search out and destroy this protein.



A logical but previously untested treatment was to remove the offending antibodies, which was performed by Newsom-Davis, Anthony Pinching and Keith Peters using a procedure called plasma exchange. This produced a remarkable clinical effect, even in patients who had been partly paralysed for many years, and further work convincingly demonstrated that the antibodies to the receptor protein were the cause of the disease, which could also be treated with drugs that suppress the immune system.

In addition, genetic studies with Alastair Compston and Richard Batchelor helped to define distinct subgroups of myasthenia, including the younger patients in whom the thymus gland is enlarged, which Newsom-Davis and colleagues went on to show was a source of immune dysfunction and actively produced some of the harmful antibodies. He then hypothesised and demonstrated that two other diseases of the nerve-muscle junction, the Lambert-Eaton myasthenic syndrome and acquired neuromyotonia, were due to antibodies to different proteins that control the signalling process. This meant that these conditions too could be successfully treated with immuno-suppressive therapies, and his findings also threw new light on a poorly understood relationship between cancer and neurological diseases.

In each case, Newsom-Davis's research group was able to establish laboratory methods for the detection of the antibodies, ensuring that neurologists in other countries could also diagnose, and thence treat appropriately, their patients. In parallel, they defined several genetic diseases that involve the nerve-muscle junction, but are not caused by the immune system and require different treatments.

(*The Independent*, by Angela Vincent, 18th September 2007)

### TRIBUTE TO JND

A very sad event indeed, for everybody and especially for the Romanian MG patients. We feel like we are cursed....we lost a father... It's awful. (*Nadia Radulescu, Romanian MG Association*)

The *French Muscular Dystrophy Association (AFM)* wishes to express its deep sorrow and to acknowledge Dr. Newsom-Davis' fundamental contributions to the understanding and treatment of Myasthenia gravis. (*AFM, Paris*)

I am deeply shocked about this sudden, unexpected death of John....He was one of the most generous colleagues to my knowledge.....His death came too early; he had had much to give to the MG research. (*Ritva and Georg Matell, Stockholm*)

It's really too sad news that you sent me. My sympathy is with everybody in the big Myasthenia Gravis Family. John was my teacher in myasthenia gravis subject from time when I first met him in 1989 years. He was always ready to help us and support us in our work. .... (*Marija Sostarko, Zagreb*)

John Newsom-Davis was a very energetic, kind and encouraging friend, colleague and gentleman. Since he touched so MANY lives, John will leave many broken hearts and several HUGE vacua, eg, among patients, colleagues, myastheniologists, thymectomists, younger medics, editors, charities/ research councils, friends and family.....(*Nick Willcox, Oxford*)

.....It was always a pleasure to discuss not only his latest work in MG, but also to revisit some of our other mutual interests. He was a major and guiding force in MG during my entire professional career, and I will miss that almost as much as I will miss our personal interactions. (*Don Sanders, Durham, USA*)

What a loss for us all. John was the most excellent researcher, the superb clinician, and a very open-minded, warm and kind colleague and friend. My warm regards...(*Nils Erik Gilhus*)

.....No doubt, John's death leaves us with a most saddening and irreplaceable loss both in personal and scientific respects. John gave MG research an unmistakable and highly appreciated voice in the world, a voice that was British and cosmopolitan alike....No doubt, we shall keep John a deeply grateful memory forever. (*Alex Marx and Philipp Stroebel, Mannheim*)

John Newsom-Davis was the hope of many Greek MG patients and a role-model (and very good friend) for Greek researchers and clinicians involved with MG. We are shocked by his sudden death. He made an unprecedented impact on MG and his absence will be obvious to us for very long time. (*Socrates Tzartos and colleagues from Athens*)

.....He was a wonderful man always listening with kindness. He discussed with authority but courteously and his advices were always positive. When one discussed with John one felt clever and the question became clear. His contributions to MG research are, as everybody knows, outstanding in the immunological field, the clinic and the treatment. (*Philippe Gajdos*)

We are all deeply saddened by the tragic death of John Newsom-Davis. .... He was extremely warm and friendly, a superb researcher and a kind man. We will all miss him. (*Hubert Kwiecinski, Anna Kaminska, Anna Kostera-Pruszczyk, Warsaw*)

JND during the 11th Annual Conference, last May in Chicago



## Newsletter EuroMyasthenia, November 2007

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### Our Partner, University of Maastricht, identifies novel characteristics on some antibodies

In cooperation with blood bank Sanquin and the Genmab company, researchers from the department of Neuroscience of Maastricht University, with prof. Marc de Baets as research coordinator, have discovered a new, unique characteristic of the IgG 4 molecule. This discovery may have a large impact on future treatment of people with a certain autoimmune disease. The findings have been published in an article in the scientific international journal, Science.

The study reveals a basic mechanism of IgG4 antibodies that is defined as 'very remarkable for such a protein' according to prof. Marc de Baets. 'An antibody looks like a four-teeth fork consisting of two symmetrical halves. If you separate the two halves of IgG4, each half will bind to the half of another fork. This is completely new, because antibodies usually break down into building blocks (amino acids) that are used to make new antibodies'.

### **Mestinon crisis in Romania**

Last August our Collaborating Partner from Romania, Asociatia Nationala Miasthenia Gravis Romania, contacted us with a very serious issue: the lack of medication to be made available to MG patients. The situation was a result of two main decisions from the Romanian Ministry of Health: the withdrawal of Mestinon from the list of drugs supplied free of charge to MG patients, and the penury of the drug itself that was no longer imported in Romania because the Ministry of Health has refused to renew the import authorization. While the decision to withdraw such a vital drug as Mestinon from the free-drug list for economical reasons was **intolerable** and had **outraged** the patients and their spokesperson, it was also unclear why the Ministry of Health refused to renew the authorization to import the drug into Romania.

The result was that not only the patients in need could not receive their vital medication free of charge, but also they could not even purchase it with their own funds.

Just then the coordinator asked the partners what they suggest to do in order to help our Romanian friends. Immediately a letter was administered by Dr. Sonia Berrih-Aknin to the Minister of Health of Romania, asking him to try to resolve the problem. This letter was signed by all our project partners.

Finally, after a long period, Mestinon is back for all the Romanian patients.

### **Forthcoming meetings**

- **Nicotinic Acetylcholine Receptors 2008, 23-26 April 2008, Wellcome Trust Conference Centre, Cambridge, UK** (*more info: [www.wtconference.org.uk](http://www.wtconference.org.uk)*)
- **Second Euromyasthenia Meeting, Maastricht 14 December 2007** (*more info: [www.euromyasthenia.org](http://www.euromyasthenia.org)*)

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### **EUROMYASTHENIA WEBSITE**

As you are aware, the **EuroMyasthenia Website**, now available via [www.euromyasthenia.org](http://www.euromyasthenia.org), is one of the most powerful communicating tools of our project. It is waiting for your contributions. Visit it to see its new look and new postings.

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