John Newsom-Davis, MD, FRS, 1932-2007

John Newsom-Davis was a great deal more than a neurologist, of course; he was one of the very few UK clinician scientists of the 1970s and 1980s, and as such had an enormous influence on many who were to come. Here, as well as summarising briefly his achievements, I shall try to draw together some of the aspects of John’s early professional life which helped to shape the person that we all admired. Some of the details (given in quotes below) are taken from a transcript of an interview that John gave to the American Neurological Association in 2003, and I am indebted to them and to Barbara Sommer who interviewed him.

John was born the older of twins by a few minutes (his twin sister and older sister are both alive and well). He had a rather conventional middle-class upbringing, but he often admitted that he did not enjoy boarding school (the inference being that he was bullied – probably because he was slight in build and did not enjoy the more macho sports). A much more positive influence was undoubtedly the time he spent in the RAF as a national serviceman (an obligatory two-year stint in one of HM’s forces) since he was one of a select few who were trained as pilots. As a result he got his wings in 1953 and flew Metors for a short period before he left the RAF. Meanwhile, he became interested in psychiatry and decided to become a doctor (like his maternal grandfather). He had already been offered a place at Pembroke College, Cambridge to read English, but this decision meant that he had to go to a crammer to achieve the necessary higher certificates (A levels) before they would allow him to change to Natural Sciences.

From a relatively undistinguished time in Cambridge he moved to the Middlesex Hospital for his clinical training and it was there that he was particularly influenced by two eminent neurologists: “the first was Dr Michael Kremer, a neurologist who was extraordinarily sharp and who had a remarkable flair for diagnosis, (though it was not always possible – for a medical student – to follow the thought processes by which he reached the right conclusion). But one of his axioms was ‘If you can’t make the diagnosis, take the history again’ advisable advice that is as relevant now as it was then. The other neurologist who taught me at that time was Professor Roger Gilliatt who had a joint appointment between the Middlesex Hospital and Queen Square. He was a very powerful figure, and a pretty daunting one for a medical student” It was these two who he subsequently acknowledged as the most important in determining his future career.

He could never understand why, when it came to housejob applications, he was selected for the Professorial Unit at the Middlesex under Prof Moran Campbell but considered that privilege as another major career influence and deeply valued Moran’s support thereafter. “He himself was passionately interested in research, and a great teacher and I reckon I owe my career to him. He remained immensely supportive through my early career, and I co-authored a monograph with him and Emilio Agostoni, ‘The Respiratory Muscles: Mechanics and Neural Control’ while I was still a junior doctor.”

From that position it was straightforward to be appointed to the Gilliatt and Kramer firm and he was all set for a successful career in Neurology until Gilliatt decided that John was “too old” for neurology and would be more suited to a less demanding specialty! Nevertheless, after a spell at the Brompton where he developed an interest in the neural control of respiration, he started research with Tom Sears at Queen Square looking at the sensation of respiration which he presented as his MD – winning the Queen Square neurology prize. As a result, he was appointed to the Gilliatt and Kramer firm and he

...
ricardo mileti knew tom sears, my ex-supervisor, who put him in touch with me. John started providing Katz and mileti with muscle biopsies for the neuromuscular junction and myasthenia studies but he continued to work on the muscle spindles for another couple of years. However, during this time news from the usa highlighted three seminal findings. First, an experimental form of myasthenia could be induced by immunisation against purified (fish) acetylcholine receptors; second, the acetylcholine receptors were reduced in MG muscle (sadly similar work by mileti was still in progress at this time and was not therefore, published until 1978); and thirdly, there were antibodies to AChRs in MG sera. All of these findings pointed to a pathogenic role for the antibodies but the final proof came from two very simple but elegant experiments. In 1975 Toysk + et al demonstrated the passive transfer of MG to mice by injection of purified MG IgG, and in 1977 John, Tony Pinching and Keith Peters demonstrated that removal of the circulating antibodies by plasma exchange led to marked improvements. These developments and many others relevant to the field are summarised by Peter Rothwell and Paul Matthews in Parkinson’s disease: a comprehensive review (Vincent Nat Reviews Immunology 2002).

Thereafter John turned most of his attention to myasthenia, recognising the emerging field of neuroimmunology and taking an evening course in immunology at the Middlesex Hospital in order to be better prepared for the future. He started a research group at the Royal Free Hospital recruiting myself (from UCL where I had done much of the myasthenia muscle work) and then Bethan Lang, Nick Wilcox and David Beeson over the next eight years, which grew into a very active and multidisciplinary team. It was at this point that he began to apply his investigative bent towards clinical immunology, recognising that Lambert Eaton myasthenic syndrome (LEMS), which had already been investigated physiologically and morphologically by Ed Lambert and Andrew Engel at the Mayo Clinic – was likely also to be antibody mediated. Plasma exchange was effective and Bethan Lang spent months injecting purified IgG into mice in which Dennis Bray (recently retired as Professor of Physiology in Leeds) showed had neuromuscular junction defects. Similarly we showed that seronegative MG was also antibody-mediated even though at that stage we had no idea about the nature of the target antigen which took another 15 years and is still ongoing!

When John was appointed in 1987 to the Action Research Chair of Neurology 16 of us moved from the Royal Free Hospital to the Institute of Molecular Medicine (now Weatherall Institute) in oxford, as well as neurophysiologist kerry Mills and anaesthetist Laurie Lob to the Radcliffe Infirmary. there he attracted some excellent clinical fellows from the commonwealth as well as the uk and continued to lead the research group in myasthenia, concentrating mainly on the more tricky areas of thymic pathology. T cell specificity and potential therapies with Nick Wilcox and the team. David beeson started cloning the acetylcholine receptor genes, mutations in which he subsequently discovered in genetic forms of myasthenia. During this period John spent much of his time in the USA highlighting three seminal findings. First, acetylcholine receptors were reduced in MG muscle; second, the acetylcholine receptors in the nodes of Ranvier were labeled and used to provide a radioimmunoprecipitation assay for the antibodies. What was not clear at the time is that the antibodies are not necessarily against the VGKCs themselves but can be against other proteins that are part of the membrane complexes that hold the VGKCs in place at the nodes of Ranvier (see my update). If we hadn’t used a rather crude brain preparation of VGKCs and, instead, as one would now, expressed the VGKCs in a cell line using molecular techniques, we would probably not have detected the antibodies in many of the patients! But as a result of the use of simple unsophisticated techniques, one of the legacies of John’s career is the major interest in antibody-mediated CNS disease that has followed the work on the VGKCs in a cell line using molecular techniques, as one now would, expressed the VGKCs in a cell line using molecular techniques, we would probably not have detected the antibodies in many of the patients! But as a result of the use of simple unsophisticated techniques, one of the legacies of John’s career is the major interest in antibody-mediated CNS disease that has followed the work on the VGKCs.

Quite rightly John was noted for his modesty, lack of pretentiousness, his carefully conceived but effortlessly given lectures, his ability to enthuse individual doctors at early stages of their careers, and to act as a mentor and role model thereafter. Much of this continued when he retired formally from oxford in 1998, took over the editorship of Brain, and began to plan the thymectomy trial that NIH, eventually, funded and which is now led by Gil Wolfe in Dallas. In this phase of his very productive life, perhaps more than in any other, he was able to influence younger colleagues and, in particular, patients worldwide. A remarkable conversationist with an excellent (and highly enviable) memory for faces, names and facts, he was loved by far more people than most of us can remember even knowing. When he died so tragically in a RTA in August 2007 literally hundreds of emails reached us from all over the world – almost everyone said “John was such a good friend”. There aren’t so many eminent men or women of whom that can be said.  

Selected publications as Davis-JN


Boek


Selected publications as Newcom-Davis J


