This was a one-day conference organised by the Royal College of Physicians and British Society of Rehabilitation Medicine held at the Royal College of Physicians, London. The main theme of the meeting was to enable professionals involved in the care of patients with brain injury to have a clear understanding of the scope as well as the complexities involved in rehabilitation of this patient group.

Professor Carol Black, President of the Royal College of Physicians gave the welcome address and was pleased that so many people involved in brain injury rehabilitation, not only from the statutory services but also from the voluntary and charitable sectors, had come to this meeting. She went on to say that the meeting covered a topic that has not received the attention it deserves in the past. The meeting was conducted in four sessions.

1. Morning sessions
   Chair: Dr Vera Neumann, President of the British Society of Rehabilitation Medicine

1.1. The patient journey
   Title: National Service Framework (NSF) for long term conditions: Guidance and evidence for traumatic brain injury (TBI) rehabilitation
   Speaker: Professor Lynne Turner-Stokes, Vice-Chair – External Reference Group of the NSF for long term conditions

   Take home messages:
   1. There is an urgent need for further research in traumatic brain injury (TBI) rehabilitation
   2. Users’ and carers’ views must be fully taken into account in further development of TBI rehabilitation
   3. A new research typology has been developed with information on classification of design, quality rating and grades of evidence and recommendations

   Title: Robin’s story – one family’s experience of brain injury
   Speakers: Steve and Ann Harris, Robin’s parents

   Take home messages:
   1. Good practice in post brain injury rehabilitation has been rather patchy
   2. There needs to be better co-operation and co-ordination of services for those with brain injury in the community

1.2. Clinical conundrums
   Title: Management of agitation and challenging behaviour
   Speaker: Dr Simon Fleminger, Consultant Neuropsychiatrist

   Take home messages:
   1. Managing restless, agitated and aggressive patients following brain injury requires a team approach
   2. The medication to control these problems must be used judiciously in conjunction with psychological and behavioural management programmes

   Title: Profound brain damage: locked in or vegetative state
   Speaker: Dr Keith Andrews, Director – Institute of Complex Neuro-disability

   Take home messages:
   1. There is still much confusion among the clinicians between locked in, minimally conscious and vegetative states
   2. It is important to be aware of potential pitfalls in diagnosis as well as problematic presentations

2. Afternoon sessions
   Chair: Dr Kyaw Nyein, Consultant in Rehabilitation Medicine

2.1. Brain injury rehabilitation services
   Title: Acute care and the interface with rehabilitation
   Speaker: Professor John Pickard, Consultant Neurosurgeon

   Take home messages:
   1. The interface between acute care and rehabilitation services are far from ideal
   2. Head injury co-ordinators are essential in ensuring smooth movement of patients through acute care, rehabilitation and support in the community

   Title: Specialist rehabilitation service networks – a model of care
   Speaker: Dr Kyaw Nyein, Consultant in Rehabilitation Medicine

   Take home messages:
   1. Network of specialist rehabilitation services are essential to ensure appropriate and timely care for patients with brain injury
   2. There needs to be an ever closer collaboration between the specialist rehabilitation services and the district and community services in delivering a seamless service to patients with severe complex disability in the community

2.2. Living with brain injury
   Title: Longer term community support and case management
   Speaker: Dr Andy Tyerman, Consultant Clinical Neuropsychologist

   Take home message:
   1. Need to promote an interdisciplinary client centred approach in practical service delivery
   2. Professionals should work in collaboration with service users to achieve realistic personalised goals

   Title: Back to work following brain injury
   Speaker: Dr Andy Tyerman, Consultant Clinical Neuropsychologist

   Take home message:
   1. Supported work re-entry programmes are effective in reintegrating the brain injury population to their workplace
   2. Need to develop local inter-agency protocols
   He then launched the inter-agency guidelines on vocational assessment and rehabilitation after acquired brain injury, which was well received.

There was widespread agreement among those who attended the one-day conference that the highlight of the meeting was Steve and Ann Harris’s powerful presentation of their son Robin’s journey following his brain injury. The trials and tribulations that they encountered as well as the triumphs that they achieved with able support from many of the professionals involved in Robin’s care left a powerful and indelible impression on those who attended the meeting as to the importance of patient centred care.

Dr Andrew Thu, Dr Charlie Nyein, Regional Rehabilitation Unit, Northwick Park Hospital, London.
Doctors, nurses and professionals allied to medicine (PAM’s) gathering in a nor-
ern city in a temperate weather zone in early winter? – it must be the ALS/MND sympos-
um. All those with a significant interest in motor neurone disease (MND) or amyotrophic lateral sclerosis (ALS), gathered in Philadelphia. For a relatively uncommon condition, MND generates disproportionate interest, probably because most health care workers recognise the awful truth of this disease.

This year more that 750 delegates gathered to present, discuss, debate and exchange the most recent advances in the fields of MND basic science research and clinical care. Each year the size of this meeting increases, reflecting the impact that MND has upon patients, their families and professional carers alike. The symposium proper was preceded by several days of satellite sessions and an allied professionals meeting for the day immediately preceding the opening plenary ses-
sion. The format of opening and closing joint plenary sessions, separated by parallel sessions covering basic science research and clinical care is well established. Most clinical academics are forced to make difficult choices between key ses-
sions covering important areas of scientific advance and those concentrating on important issues of care provision.

One of the major themes highlighted this year was the similarity of MND to many other neurodegenerative conditions. Several keynote speakers emphasised this point with reference to Parkinson’s disease, Alzheimer’s disease and some of the tri-nucleotide repeat disorders. It is now more that ten years since the first report that mutations in Cu/Zn superoxide dismutase (SOD1) are causal in approximately 20% of familial MND cases. Finally, mutated SOD1 is starting to give up its aetiological secrets. Several elegant scientific presentations put forward evi-
dence that, in common with other neurodegenerative conditions, mutant SOD1 associated familial MND appears to be a disorder caused by protean mis-folding, failed degradation and ulti-
mate pathological aggregation. These problems appear fundamental to motor neurone cell loss in mutant SOD1 associated MND, and may well be of great importance in sporadic MND, where protein aggregation was first reported and serves as gastrostomy and ventilation for MND patients. Increasing evidence supports the use of some form of pressure measurement as the most accurate monitor of respiratory function (maxi-
mum inspiratory or expiratory pressure, nasal sniff pressure, peak cough flow), with overnight oxygen saturation and forced vital capacity being relatively insensitive indicators of the need for some form of ventilatory intervention.

A clinical session was devoted to non-invasive ventilation (NIV). Several groups reported the results of their experience in the use of NIV for their MND patients, and factors which influ-
enced successful and compliant use of NIV. The Newcastle (UK) group reported the results of the only positive therapeutic trial presented at the symposium. More than 40 MND patients fulfill-
ing predetermined criteria for NIV were randomly allocated to receive NIV or “standard” conservative management of their respiratory insufficiency. A significant overall survival bene-
fit, but more importantly a highly significant and sustained improvement in quality of life was detected in patients receiving NIV.

The symposium closed with two excellent present-
sations on differing epidemiological studies of MND. Dr Chio (Italy) reported on the high inci-
dence of MND amongst professional footballers in Italy, supporting the widely held but largely anec
dotal view that MND is over represented in high performing sports men and women. The mechanisms behind this apparent finding remain elusive. Dr Cox (USA) presented what appears to be the answer to a near 100-year-old conundrum – the very high incidence ALS / Parkinsonism / dementia complex (ALS/PDC) affecting the Chamorro peoples of Guam. Nearly 20 years ago this disorder was linked to an environmental toxin β-methyl-alanine-L-alanine (BMAA), found in cycad seeds, a staple of the Chamorro diet. However, the level of BMAA appeared to low in the flour derived from these seeds. It now appears that BMAA is concentrated in flying foxes (fruit bats), a delicacy highly sought after by the Chamorro peoples, the ingestion of which led to their toxic exposure to BMAA and the develop-
ment of ALS/PDC. Intriguingly, Dr Cox pre-
sented preliminary data indicating the presence of BMAA in the brain tissue of Alzheimer’s dis-
ease patients in Canada (who had no association with Guam) raising the possibility that such tox-
ins are present in other parts of the world and may even contribute to neurodegeneration.

Suitably enthused, and having had ample opportunity to reinforce old collaborations and forge new ones, delegates left with plenty of new scientific and clinical information to digest, and thoughts of a temperate Dublin next December in their minds.

Dr Timothy Williams,
Consultant Neurologist & MND Care Centre
Medical Director, Newcastle,
Following the heavy snow in Boston last year, balmy New Orleans was a welcome change. Genetics was the topic for the annual course. The number of single gene epilepsies identified continues to increase. As in other clinical areas, there is a "many-to-many relationship"; the same clinical syndrome may be associated with different genes and abnormalities of the same gene may be associated with different clinical syndromes. For example, SCN1A truncating mutations cause severe myoclonic epilepsy of infancy and missense mutations cause generalised epilepsy with febrile seizures plus (GEFS+), which may also be associated with mutations of the SCN1B, SCN2A and GABA receptor gene mutations. Lennox and Lennox demonstrated a concordance of 80% in MZ twins for IGE syndromes half a century ago and this has been almost exactly replicated by Berkovic and colleagues. In rare IGE families with a dominant pedigree, abnormalities of the GABA receptor have been identified. However, the genetic bases of common idiopathic epilepsies remain elusive. A late onset form of idiopathic generalised absence epilepsy has been recognised for some years but recent studies have shown that up to a quarter of IGE has onset over the age of 20. If your patient has tonic clonic seizures with no aura, triggered by fatigue or alcohol, and a familial history, think IGE.

Another major session was devoted to neuronal development. Since the 1970’s it has been known that the cortical neurons arise from the ependymal zone and then migrate along radial glial fibres. Arnold Kriegstein from San Francisco, used labelling methods to show how glial cells at the ventricular zone start to produce their radial fibre then divide asymmetrically to produce another glial cell and a neuron which then migrates up the glial fibre. Some of the molecules that help to determine the fate of either cell, are being identified. By contrast divisions of cells slightly further along their route, in the subventricular zone, are symmetric, giving two neurons. Some radial cells have GABAA receptors and studies show that GABAA active drugs can influence neurogenesis of significance as we consider antiepileptic drugs in pregnancy. When radial glial cells reach the cortex they change into astrocytes, which may retain some stem cell activity. Pat Levitt from Vanderbilt University pointed out that interneurons are only 10% of neurons and so changes in pathologic states may be difficult to detect. He described how in the rat they arise from the ventral telencephalon and then migrate into the cortex by a mechanism dependent on hepatocyte growth factor (HGF). A knockout mouse with reduced HGF has fewer interneurons and increased susceptibility to seizures. They are also less social and more sensitive to diazepam. He speculated that altered functional anatomy of cortical columns may cause these changes and that they may be a model for autistic spectrum disorders. Amy Brooks from Pennsylvania addressed the question of why young animals are particularly susceptible to seizures. In immature neurons there is a higher intracellular chloride concentration than in mature neurons. Consequently, chloride fluxes controlled by GABA receptors move in the opposite direction and are depolarising rather than hyperpolarising. She also described how A and B type GABA subunits switch during development to alter their functional properties such that young mice are particularly prone to seizures in the postnatal period. Glutamate receptor function is also enhanced from postnatal day 5-15 in the mouse. In addition the response of the brain to seizures appears to be different at different ages. After status in neonatal mice there is an upregulation of GABAA with an increased sensitivity to benzodiazepines, which is not seen after status in adults. All adults in these studies developed spontaneous seizures within 4 days of status whereas neonates did not. If similar factors operate in humans, they may clearly be significant in designing and using drugs in young children rather than in adults.

In the annual Lennox lecture, Dr Pitkänen from Denmark emphasised an increasing theme that current therapies treat seizures and we should be looking at factors that underly the development of epilepsy. She argued that current models may not be representative of human epilepsy and suggested different models and the use of surrogate markers in assessing the severity of acute brain injury such as 14-3-3 protein levels in the CSF. She showed how the adrenergic blocker atipamezole may make established seizures worse but is anti-epileptogenic; if given early after injury may reduce the severity of subsequent epilepsy by 90%.

One session was devoted to evidence-based guidelines in the drug treatment of epilepsy. The background was set with a talk that described the evolution over 20-30 years from expert opinion through consensus statements to evidence-based medicine, a process driven partly by cost considerations. Dr Ben Menachem chaired an ILAE team which analysed all the existing drug trials in different forms of epilepsy, used to inform the current guidelines of the ILAE. In monotherapy studies of focal epilepsy, only 1 trial (from 1985) was considered to be of class 1a quality and only 10 of 33 studies were in the top tier. The panel adopted the view that only where a good quality trial had been conducted could firm conclusions be drawn. So if you conduct a good study on a mediocre drug it gets in the guidelines and if you conduct a bad study on a good drug it doesn’t. Recommended first line treatment for focal epilepsy in adults is carbamazepine, oxcarbazepine, topiramate and valproate (men) with alternative treatments gabapentin, lamotrigine, phenytoin (downgraded by toxicity) and valproate (women). There are no ILAE recommended drugs for childhood absence epilepsy because there are no good trials and sulphamide (not available for decades in the UK) is the only recommended drug for benign rolandic epilepsy as it is the only one subjected to a decent clinical trial. This approach emphasises the need for more carefully conducted trials. But where none is available, taking the evidence-based principle to extremes denies a wealth of clinical experience, implies that opinion and consensus are worthless and results in guidelines that are frankly bizarre – better no guidelines at all. As the leading international epilepsy organisation the view of the ILAE has an authority which it risks losing if it generates guidelines to which nobody will adhere.

The issues around pregnancy and epilepsy continue to figure largely. Whether maternal seizures contribute to major foetal malformations remains uncertain but the various registries give useful and sometimes disturbing information about AED’s, with valproate remaining the villain of the piece. Carbamazepine and lamotrigine data are more reassuring. A recent Cochrane review concluded that
there is insufficient evidence of the benefit of specialist nurse intervention. Insufficient evidence of efficacy does not imply absence of efficacy and a US study using the QOLIE-89 demonstrated that nurses do provide significant quality of life improvements for their patients.

It is always somewhat mind-numbing to work round 1000 posters in two sessions. There was of course basic science that we didn’t understand and the usual posters telling how different new drugs really do work quite well in this or that form of epilepsy in which they haven’t been tried before. Here is a baker’s dozen highlights that struck us: 1) Intravenous furosemide or mannitol suppressed interictal spike activity as measured by intraoperative EEG spike recording during epilepsy surgery. 2) Over 90% of 75 patients with JME identified lifestyle as seizure triggers (sleep deprivation 77%, stress 83%, menstruation 33%, alcohol 11% - an underestimate I think – and various cognitive tasks in a small number each), important factors to consider in your patients. 3) Late-onset non-tumoral temporal lobe epilepsy in 20 patients was associated with very high antithyroid antibodies, 18 of whom did not fulfil criteria for diagnosis of Hashimoto’s encephalopathy. This may need to be added to the list of autoimmune causes including paraneoplastic and voltage-gated-potassium channel antibodies. 4) Pre-ictal headache affected 11 of 100 consecutive patients and lasted more than 30 minutes in 4. In 9 patients it was ipsilateral to the seizure focus (nb headache is often a prodrome of psychogenic non-epileptic seizures. 5) There is always a little hesitancy in using baclofen in patients with epilepsy but in one study of 42 children with cerebral palsy, intrathecal baclofen at least, did not increase seizures. 6) When do you decide when to abandon trial of a new drug in your patient? A study from Alabama suggests that the strategy varies from drug to drug; they found topiramate has a ceiling response at around 400mg and gabapentin at 2400mg per day. Higher doses yielded few new responders. By contrast, oscarbazepine had a more linear dose-response, all the way to the maximum recommended 2400mg. 7) Lamotrigine levels start to fall only 3 days after withdrawing concomitant valproate. In women with catamenial epilepsy lamotrigine levels peak at ovulatory day 10-13, with up to 31% reduction premenstrually. 8) One study reported good efficacy but poor tolerability of bromides in 17 patients with refractory epilepsy. Plus ça change! 9) Beware stopping AED in seizure-free patients; in an analysis of 12 studies where treatment was reinstituted, it took up to 1 year for half of patients to become seizure free and 10% never regained seizure-freedom. 10) Confusion is such a common presentation in the elderly that it is easy to forget the occasional patient presenting with non-convulsive status. Even those who had previously suffered a bout were not diagnosed for 29 hours on average. 11) Of 10 patients in one study with unexplained syncope, 9 had psychogenic pseudosyncope; “swoons” are rarely organic. 12) Rapidly titrated levetiracetam has been used successfully in the treatment of refractory focal status. MRAM also has found it valuable in this indication and would be interested to hear from others with similar experience. 13) Depression in TLE patients was associated with inferior frontal hypometabolism on FDG-PET. Hypometabolism developed in similar areas in those who developed depression after temporal lobectomy; an organic cause is implied.

Dr Mark Manford,
Consultant Neurologist,
Cambridge.