Session 1 Stroke – the quiet revolution

This session began with Dr Matthew Giles (Consultant Physician, John Radcliffe Hospital, Oxford) addressing the importance of transient ischaemic attack (TIA) triage. Almost one quarter of all patients with ischaemic strokes report a preceding TIA (most within the previous week).1 Conversely, the risk of stroke after TIA is 5% at seven days and 10–15% at 90 days.2 Much work has gone into predicting the high-risk TIAs, culminating in the six-point ABCD predictive score based on Age, Blood pressure, Clinical features and TIA Duration,3 since refined to include presence or absence of Diabetes (ABCD2).4 While not perfect, it is a helpful tool over the phone and in the clinic. Other techniques to predict stroke risk post-TIA include defining TIA aetiology (with risk reducing in the order large vessel > cardioembolic > small vessel)5 and early magnetic resonance imaging (MRI) scanning, although how practical this is on a large scale is questionable. Of course, predicting high-risk TIAs is only useful if this risk can be modified. Studies of secondary prevention after stroke have demonstrated benefit with aspirin, statins and blood pressure lowering in most patients, and from warfarin, carotid endarterectomy and possibly dual antiplatelet therapy in a select group.6 The EXPRESS (Early use of eXisting PREventative Strategies for Stroke) study, a prospective, population-based comparison of faxed advice versus immediate initiation of secondary prevention, found that early intervention significantly reduced the subsequent stroke risk.7 Which aspect of early secondary prevention provides the benefit is unclear, and this question is still being addressed.

Professor Peter Sandercock (Professor of Medical Neurology, University of Edinburgh) reviewed thrombolysis in acute stroke. He stressed the importance of recognising acute stroke as an emergency (‘time is brain’) as the benefit of thrombolysis diminishes with time. Up to three hours, the number needed to treat for net benefit from intravenous (IV) thrombolysis is 10, whereas after three hours the benefit is unclear.8 Currently the IV recombinant tissue plasminogen activator (r-tPA) licence is fairly restrictive, and only 0.2% of all UK strokes are thrombolysed. It permits the treatment of patients with clinical features of an acute stroke aged less than 80 years presenting up to three hours after stroke onset with no contraindications. In this group the risk of fatal haemorrhage is 3%. Computed tomography (CT) is invaluable in excluding haemorrhage but also in providing positive radiological evidence of early ischaemia, for example loss of grey/white differentiation, loss of the insula or basal ganglia, or a hyperdense artery. Infarcts that are clearly defined should ring alarm bells that the stroke is older than three hours prompting a review of the history. The recently published European Cooperative Acute Stroke Study (ECASS) trial provides some evidence for extending the time window to 4.5 hours,9 and the ongoing Third International Stroke Trial (www.ist3.com) endeavour to determine if a wider group of patients might benefit from IV r-tPA, including those over 80 years of age and those with stroke onset between three and six hours previously. It is a multicentre, prospective, randomised open-label trial comparing r-tPA with best medical management of acute ischaemic stroke, and is due to complete recruitment by mid-2011.10
Dr Keith Muir (Senior Lecturer in Neurology, University of Glasgow) discussed when stroke should be referred to an expert. Any stroke may present a diagnostic or management challenge and in the GP/paramedic/A&E setting the diagnostic accuracy for stroke is only approximately 80%, and lower still with TIAs.11 There is clear evidence that patients benefit from care in designated stroke units with interested staff, but selected patients may benefit further from referral to a regional neuroscience centre.12 These centres provide specific opportunities for diagnosis in acute and/or unusual stroke situations, for example, venous sinus thrombosis, cerebral vasculitis, carotid/vertebral artery dissection and stroke in the context of other disease, such as systemic lupus erythematosus (SLE), cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) and congenital cardiac defects.

Neuroscience centres also offer different stroke treatments because of the availability of neurosurgeons, interventional neuroradiologists and vascular neurologists. For instance, combined results from the HAMLET (Hemicraniectomy After MCA Infarction with Life-threatening Edema Trial), DESTINY (DEcompressive Surgery for the Treatment of Malignant INfarction of the middle cerebral arterY) and DECIMAL (DEcompressive Cranietomy In MALignant middle cerebral artery infarcts) trials favour decompressive hemicraniectomy over conservative management of acute ischaemic stroke complicated by cerebral oedema.13 Interventional radiologists have a role in promoting early vascular recanalisation (e.g. with intra-arterial thrombolysis, clot retrieval/embolectomy and mechanical clot disruption plus stenting), which is important in ischaemic stroke setting the diagnostic accuracy for stroke is only approximately 80%, and lower still with TIAs.11 There is clear evidence that patients benefit from care in designated stroke units with interested staff, but selected patients may benefit further from referral to a regional neuroscience centre.12 These centres provide specific opportunities for diagnosis in acute and/or unusual stroke situations, for example, venous sinus thrombosis, cerebral vasculitis, carotid/vertebral artery dissection and stroke in the context of other disease, such as systemic lupus erythematosus (SLE), cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) and congenital cardiac defects.

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A vascular neurologist also has a treatment role, for example, in aggressive immunosuppression of stroke associated with central nervous system (CNS) vasculitis. Dr Muir concluded that all stroke patients require expert diagnosticians, radiologists, nurses and therapists irrespective of where they are seen, but a selected group also benefits from the expertise available at regional centres.

SESSION 2
THE MANAGEMENT OF CHRONIC CONDITIONS

Dr Monty Silverdale (Consultant Neurologist, Hope Hospital, Manchester) opened the second session with a discussion of the management of Parkinsonian syndromes. He reviewed the cardinal features of Parkinson’s disease (PD), namely asymmetrical onset of tremor, rigidity, bradykinesia and the typical gait disturbance with early loss of arm swing. Initial treatment usually consists of either levodopa or a dopamine agonist, with the former being the most effective and best tolerated drug but with the long-term risk of motor complications. Dopamine agonists are less potent and have more side effects (nausea, dizziness, confusion), particularly in the elderly, but have the advantage of a lower risk of long-term motor problems.15 Common practice is to reserve dopamine agonists for younger PD patients and otherwise use levodopa first, but young patients should not be denied levodopa early on if their functional limitations warrant it. Other drugs such as catechol-O-methyltransferase (COMT) inhibitors and monoamine oxidase type B inhibitors can increase ‘on’ time by a small amount but tend not to be used in early PD. Anticholinergics are now rarely used due to their cognitive side effects.

Treatment of advanced PD poses a major challenge. Motor complications such as dyskinesias and on-off fluctuations can be managed by smoothing the dopaminergic stimulation, for example by rationalising levodopa dosing, increasing the dose of the dopamine agonist as it has a longer half life or introducing duodopa via percutaneous endoscopic gastrostomy (PEG) or subcutaneous apomorphine. Axial symptoms, including postural instability and speech/swallow disturbances, are possibly due to neurodegeneration in areas not influenced by dopamine and therefore tend not to respond to dopaminergic therapy. Frequently, management is limited to physiotherapy, occupational therapy and speech and language therapy. The management of PD dementia and psychiatric complications is often a balance between continuing to treat motor symptoms with dopaminergic drugs while cutting back these same drugs to minimise cognitive problems. Levodopa is generally the ‘least bad’ of the dopaminergic drugs in this respect. Other options are atypical antipsychotics (quetiapine, olanzepine) or cholinesterase inhibitors such as rivastigmine. Often it is the non-motor problems that are the most disabling and the hardest to treat in advanced PD.

Prof. Scott Murray (St Columba’s Hospice Professor of Primary Palliative Care, University of Edinburgh) and Dr Deirdra Sives (Medical Research Fellow, Strathcarron Hospice, Stirlingshire) discussed decision-making at the end of life. They identified three different illness trajectories: ‘prolonged dwindling’ as seen in dementia and the frail elderly, ‘long-term limitations with intermittent severe episodes’ as in organ failure, and ‘relatively good function followed by a short period of decline’ as is often seen in cancer.16 Each model is associated with different palliative care needs so identification of the trajectory can be useful for end-of-life planning purposes. Prof. Murray and Dr Sives also discussed where terminally ill neurology patients might fit into this framework. Advanced care planning aims to facilitate discussion between health professionals, patients and carers about end-of-life wishes, and this was addressed in the context of the Gold Standard Framework for Scotland, a GP-based programme to improve cancer and palliative care needs in the community.17
SESSIONS 3 AND 4
DEVELOPING PATIENT-CENTRED SERVICES IN NEUROLOGY AND AN UPDATE ON SEIZURES

The Sydney Watson Smith endowed lecture was given by Dr Aileen Keel, Deputy Chief Medical Officer for the Scottish Government, and was an interesting overview of patient-centred services for people with neurological impairments. Recent practical developments, such as establishment of the Long Term Conditions Alliance Scotland (LTCAS) and its patient-orientated self-management strategy, were highlighted. Future plans were discussed, including the expansion of Managed Clinical Networks, addressing the variation in neurological services across Scotland and expanding the role of neurology nurse specialists and the development of NHS Quality Improvement Scotland (QIS) Standards that aim to improve patient care for all neurology patients but highlight specific neurological diseases (headache, epilepsy, motor neuron disease, multiple sclerosis and Parkinson’s disease).

The next three speakers focused on seizures and their mimics. Dr Margaret Jackson (Consultant Neurologist, Newcastle General Hospital) discussed neurological conditions that mimic seizures, reminding us that 25% of patients labelled with medically refractive epilepsy do not have epilepsy at all. She illustrated her talk with videos reinforcing how useful it is to actually see an attack, but often this is impossible and, as ever in neurology, the history is key. The differential diagnosis of generalised shaking episodes includes the common seizure mimics, syncope and psychogenic nonepileptic attacks, whereas focal jerking can be due to rarer conditions like dystonic tremor, limb-jerking TIAs and hemifacial spasm. Drop attacks can be mistaken for atomic seizures, but the differential includes cataplexy, syncope again, myopathies and idiopathic drop attacks. Abnormal movements in sleep raise the possibility of rapid eye movement and non-rapid eye movement parasomnias as well as frontal lobe seizures. In summary, the diagnosis of epilepsy is primarily clinical, can be difficult and, if unsure, it is better to watch and wait rather than hastily label something as epilepsy and then try and retract the diagnosis at a later date.

Dr Derek Connelly (Consultant Cardiologist, Glasgow Royal Infirmary) reviewed cardiac conditions that may mimic epilepsy, introducing a scoring system based on features of the history to aid differentiation between syncope and seizure. He stressed the importance of distinguishing between simple, reflex syncope and cardiac syncope (due to structural heart disease or arrhythmias) as the latter has a worse prognosis, including risk of sudden death. Causes of cardiac syncope include aortic stenosis, hypertrophic cardiomyopathy, Brugada syndrome, long QT syndrome, arrhythmogenic right ventricular dysplasia and left ventricular dysfunction. Most can be identified with a careful history including family history and an eyewitness account, examination and appropriate investigations, and many are amenable to treatment (drugs, ablation, pacing, surgery). An electrocardiogram (ECG) is mandatory but will often miss the diagnosis so one should consider 24-hour ambulatory ECG (assuming episodes are near daily), patient-activated event recorders, wearable or implantable loop recorders, induced events (by exercise or tilt table) and echocardiography for structural disease.

Lastly, Dr Susan Duncan (Consultant Epileptologist, Edinburgh) reviewed epilepsy management. A helpful approach is to classify the epilepsy type broadly into generalised versus localisation-related (partial/focal) epilepsy and let this guide antiepileptic drug (AED) choice. Standard And New Antiepileptic Drugs (SANAD) was a UK-based, randomised, unblinded pragmatic trial comparing various AEDs, published in 2007. Arm A compared carbamazepine, lamotrigine, gabapentin, topiramate and oxcarbazepine in partial epilepsy. It found lamotrigine was better than the standard first-line treatment carbamazepine with respect to time to treatment failure, and was not significantly different regarding time to 12-month remission, and therefore concluded lamotrigine was a reasonable alternative to carbamazepine for first-line treatment of partial epilepsy.

Arm B compared valproate, lamotrigine and topiramate in generalised or unclassifiable epilepsy. It concluded that valproate was more efficacious than lamotrigine and better tolerated than topiramate so should remain the AED of first choice in these patients, with the caveat that the known teratogenic effects of valproate might influence this decision in women of child-bearing age. Despite being generally well received, SANAD has its critics and one unavoidable shortcoming was its failure to include the newer AEDs (levetiracetam, pregabalin, zonisamide and lacosamide), which also need to be considered when selecting an AED.

Surprisingly, despite an exponential growth in the number of AEDs, the prognosis for seizure control does not seem to have improved dramatically since the 1940s. When encountering apparently drug resistant epilepsy, the first step is to confirm the diagnosis of epilepsy (often with video electroencephalography [EEG]) and then potentially consider other treatment options such as neurosurgery and neurostimulation. Surgery can be appropriate for epilepsy secondary to tumours, cavernous haemangiomas, cortical dysplasia, dysplasplastic neuroepithelial tumours (DNETs) and hippocampal sclerosis. The key is careful patient selection, including psychological assessment and demonstration of congruence between seizure semiology, magnetic resonance imaging (MRI) appearances and EEG. Neurostimulation includes vagal nerve stimulation and the newer NeuroPace systems, incorporating a sensor that detects seizure onset and a stimulator that aims to abort the
subarachnoid haemorrhages (the bottom line – it depends on the size, treatment and if they are benign/malignant/have bled). Common sense told us that in chronic neurological diseases, such as multiple sclerosis and Parkinson’s disease, safety depends on functional limitations and a driving assessment is always an option. However, the revelation that alcohol dependency indicates a driving ban until a year free from alcohol problems was a surprise to many. Ultimately, our responsibility is to inform the patient to contact the Driver and Vehicle Licensing Agency (DVLA), and the pragmatic take-home message was to download the DVLA ‘at a glance’ guidelines so they are always to hand.21

REFERENCES