Advances and Insights into Neurological Practice 2016-17

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Papers published by the European Journal of Neurology reflect the broad interest of practicing neurologists in advances in the aetiology, diagnosis and management of neurological disorders. As a general neurology journal, the proportion of papers in the different subject areas reasonably reflects the case load of a practising neurologist.

Stroke represents the largest proportion of papers published, including those on pathophysiology (1-23), acute stroke management (24-47) and the outcome of patients who have suffered stroke (48-72). Stroke is a world-wide problem, but its prevalence varies and may reflect both the genetic and environmental contributions to stroke, both in turn reflecting the known risk factors for stroke. It is of note that vascular risk factors were less prevalent in the Middle East compared to the USA, with the exception of diabetes and smoking (3). Thus targeting this Middle East population with education and lifestyle changes would appear to be particularly relevant. The potential genetic contribution to stroke was highlighted by a study from Sweden of young onset strokes (age<55 years), 47% had a family history (5). An interesting finding from Korea reported that sleep duration >8 hours was significantly associated with an increased risk for intracerebral haemorrhage that was dose dependent: 8h OR 1.57, >9h OR 5.0 (11). The incidence of intracerebral haemorrhage appears to be declining (19), perhaps due to better management of hypertension and other risk factors. Of concern is that there is under anti-coagulation treatment of atrial fibrillation, a recognised risk factor for stroke (45).

The advances in our understanding of the cause, progress, management and treatments available for multiple sclerosis have transformed the outlook for many patients with this disorder (73-104). Recent information on risk factors includes the recognition that low vitamin D increases risk, and that vitamin D may provide a neuroprotective effect (86, 89). An epidemiological study from Canada found a protective effect of low socio-economic status from developing MS, although this was not found in other countries (88).

Parkinson disease (PD) in its early years can be well managed with symptomatic dopaminergic therapy (105-125), while other movement disorders are less satisfactorily treated126-134). The development of motor complications is a significant limitation to the long term use of levodopa. A community based incident cohort in Scotland found that 21.3% developed motor fluctuations and 28.4% dyskinesias after 59 months (108). Cumulative levodopa dose, age at diagnosis and female sex were identified as associated with motor complications, confirming previous studies in this area. As PD progresses, parenteral therapy may be required, and this includes the use of intestinal levodopa infusions to help control motor function and improve dyskinesias. Of a longitudinal study of 33 levodopa infusion patients, at baseline, 3 had developed peripheral neuropathy and 7 had subclinical neuropathy (111). At 2 years following levodopa infusion, four patients with normal neurophysiology at baseline developed subclinical neuropathy, and a

further seven developed a subclinical neuropathy. Peripheral neuropathy in PD is said to have a prevalence of 55% compared to 9% in age-matched controls (110). Alpha-synuclein pathology in the peripheral nerves may contribute, as may levodopa related metabolic disturbances such as low vitamin B12 and B6, and increased methylmalonic acid and homocysteine. The association with levodopa is cumulative dose related.

A significant advance in our understanding of the pathogenesis of PD has come from the observation that mutations of the glucocerebrosidase (GBA) gene are numerically the most important risk factor for development of the disease. Furthermore, PD patients without GBA mutations exhibit low GBA enzyme activity resulting from accumulation of alpha-synuclein. GBA mutations are also strongly associated with the risk for dementia with Lewy bodies, highlighting the link between GBA and the synucleinopathies. However, the prevalence of GBA mutations in multiple system atrophy has not been consistently found to be increased and a recent study from Germany found no increase in progressive supranuclear palsy, primary progressive aphasia or frontotemporal dementia, two of 39 patients with corticobasal syndrome had mutations (116). Another genetic study in PD, focussing on the mitochondrial genome found associations between haplotypes and both increased and reduced risk for PD (117). These findings were supported by functional analyses using cybrids.

The neurodegenerative diseases constitute major economic and social as well as medical challenges (135-162). The association of dementia with income, mortality, morbidity and medication use has been highlighted with a study from Denmark (155), with effects seen years before diagnosis. The additional healthcare costs and lost productivity prior to diagnosis was estimated at 2082 euros per patient more than matched controls. This figure increased to 4544 euros per patient after diagnosis. In the UK, the average annual cost of caring for a patient with Huntington's disease is 24,000 euros, 16,000 euros of which was informal care for inside and outside the home (161). These figures highlight the considerable potential for investing in research to slow, stop or prevent these and other neurodegenerative diseases. Advances in our knowledge on the genetics and environmental associations in amyotrophic lateral sclerosis promise to provide important insights into potential strategies to reduce risk and highlight potential treatments (163-176).

Epilepsy likewise represents another neurological disorder with significant societal and economic consequences, as well as medical (177-190). Treatments for epilepsy have been available for many years; a recent study on the long term prognosis of epilepsy found 59% of patients were seizure free, with a progressive increase in remission over time (184). Thus the long term prognosis of epilepsy is favourable, but poor prognosis for remission can be predicted with reasonable accuracy.

Neuromuscular disorders (191-213), trauma (214-215), neuro-inflammation (216-223), headache (224-231) and more general neurological topics (232-248) complete the 2016 spectrum of the Journal's purview.

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Stroke – Pathophysiology

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