

# Marco Polo of Australian neurology

Matthew C Kiernan,<sup>1</sup> Peter J Goadsby,<sup>2</sup> David Burke<sup>3</sup>

## The neurologist who put migraine on the map, with more than half a century of citation classics

This month's issue of the journal contains a manuscript from Professor James Lance,<sup>1</sup> the final contribution to a partnership with the *Journal of Neurology, Neurosurgery and Psychiatry* (JNNP) that dates back over some 60 years of publications.<sup>2–21</sup> Not only a fine researcher, Lance was an expert clinician and teacher, a true gentleman of neurology.

The body of publications by Lance published in this journal mirrors his development as an academic neurologist, a career path that before Lance, had not been traversed in Australia. Lance started his mission as a postgraduate doctoral student in the fledgling brain research unit at the University of Sydney, with a particular focus on neurophysiology, then an emerging technology with as-yet unrealised potential applications to human disease. Lance's initial studies focused on the pyramidal tract, and then on human movement and movement disorders, particularly relevant to his current publication in JNNP that postulates a contribution of myoclonus to the process of falls in the elderly.

After completing MD by research, Lance moved to London, working at the Hammersmith Hospital and then the National Hospital for Neurology and Neurosurgery, Queen Square. During this period in London, Lance encountered Edward Arnold (EA) Carmichael, who had previously served as Editor-in-Chief of JNNP (1938–1948, having taken over from Kinnier Wilson).<sup>22</sup> The friendship with Carmichael led in turn to a lifelong association for Lance with JNNP. Carmichael's guiding philosophy was that the best way to study neurological disease was to study human physiology, a principle that Lance was keen to adopt for his own career. Carmichael's contributions in this regard were later



**Figure 1** Professor James Waldo Lance AO CBE 29 October 1926–20 February 2019.

recognised through the establishment of the Carmichael Memorial Lecture, first delivered by Pat Merton with the title Neurophysiology on man.<sup>23</sup>

On return to Sydney, Lance became Superintendent of Northcott Neurological Centre, where he developed a lifelong interest in headache. With skills acquired at Queen Square, Lance analysed the case histories of 500 patients suffering from migraine. This research led to his first major opus in JNNP, published in 1960, a paper that has become a citation classic.

There followed a further period of international experience, this time with Raymond D Adams at the neurology department, Massachusetts General Hospital. During this attachment, Lance and Adams described the development of post-hypoxic myoclonus, now known as the Lance-Adams syndrome and, with Robert S Schwab, he defined the action tremor of Parkinson's disease. Lance then returned to Australia to establish the country's first academic department of neurology at the Prince Henry and Prince of Wales Hospitals in Sydney, and was appointed to the first Chair of Neurology in Australia, at the University of New South Wales in 1975.

While developing concepts about motor control, in 1965, Lance demonstrated that reflex irradiation in healthy subjects and patients with spasticity was not due to intraspinal projections of group Ia afferents from the percussed muscle, but was due to the percussion spreading in bone to excite spindles in these muscles, thus setting up multiple homonymous reflex contractions.<sup>13–19</sup> Having shown that the percussion set up a vibration that spread through the limb, he then applied a vibrating tool to his own quadriceps in an attempt to mimic the spread of vibration produced by percussion. To his amazement, he found that this produced a slow tonic contraction of the vibrated muscle. At the same time, the vibration suppressed the tendon jerk (and the H reflex) of the vibrated muscle,<sup>18</sup> a phenomenon that he and his team demonstrated was a presynaptic phenomenon, now attributed to post-activation depression of transmitter release at the Ia-motoneuron synapse. With this tool, he and his students then documented the descending pathways that controlled this tonic contraction (tonic vibration reflex),<sup>24</sup> and this formed the basis of concepts about muscle tone, posture and the control and movement. His group then addressed muscle tone and the disturbed control of movement in spasticity,<sup>15–17</sup> Parkinson's disease,<sup>14</sup> athetosis and cerebral palsy, setting new benchmarks in our understanding of 'why'. This work led him to be recognised internationally as one of the pioneers of an emerging field: neurophysiology studied in humans. The Lance 1980 definition of spasticity became the internationally accepted definition and is still cited whenever its mechanisms are discussed: 'Spasticity is a motor disorder characterised by a velocity-dependent increase in tonic stretch reflexes (muscle tone) with exaggerated tendon jerks, resulting from hyperexcitability of the stretch reflex, as one component of the upper motoneuron syndrome'.

A key development in growth at the rapidly evolving campus was the establishment of a headache clinic. Linked to this clinical service, research prospered. Lance focused his attention on the physiology of migraine, which soon led to work on serotonin, and particularly its effects on blood vessels and brain pathways involved in pain. This research led to the discovery by Pat Humphrey and development by Glaxo Laboratories in London of sumatriptan, the first and still most widely prescribed of the triptans, revolutionising migraine care for decades to follow. The success of this therapy promoted Glaxo to the peak of the European Stock Exchange, and led to the establishment of the James Lance GSK

<sup>1</sup>Department of Neurology, Royal Prince Alfred Hospital, Brain and Mind Centre, University of Sydney, Sydney, New South Wales, Australia

<sup>2</sup>Headache Group, King's College London, London, UK

<sup>3</sup>Department of Neurology, Royal Prince Alfred Hospital and University of Sydney, Sydney, New South Wales, Australia

**Correspondence to** Professor Matthew C Kiernan, Bushell Professor of Neurology, Brain and Mind Centre, University of Sydney, Mallet Street, Sydney, NSW 2040, Australia; matthew.kiernan@sydney.edu.au

Clinical Trials Unit as part of the department of neurology of the Prince of Wales Hospital.

Further analysis of the partnership between Lance and JNNP serves to identify a persistent interest in the development of a physiological underpinning for clinical symptoms and syndromes in neurology, from headache and its various manifestations<sup>6 11 21</sup> through to blip,<sup>5</sup> neck-tongue<sup>12</sup> and brilliantly conceived Harlequin syndromes.<sup>10</sup> Allied to these phenomenological studies were experimental approaches to spasticity,<sup>15–19</sup> driven by an abiding interest in reflexes<sup>13 14</sup> and their mechanisms.<sup>4</sup> Lance's career emphasises the importance of a clinician's curiosity and illustrates how careful clinician-led research into the mechanisms and management of neurological disorders develop our specialty. Like a fine bottle of wine from a grand vintage, these pioneering studies only serve to improve with time, being further layered by the scientific discoveries of the present day.<sup>25–27</sup> And down to the last drop, we acknowledge a brooding career in the clinical neurosciences—vale Jim!

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