Progress Report

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Title of Project: Neuroinflammation in the Peripheral and Central Nervous System: Epidemiological Factors, Vitamin D Status and Functional Relevance

Summary: (approximately 1,000 words)

Vitamin D has been demonstrated to be important in modulating the immune system response. Reduced vitamin D levels are associated with autoimmune conditions such as multiple sclerosis and type I diabetes. Sunlight and the distance from the equator (latitude) are important in determining vitamin D levels as sun exposure is required to produce vitamin D. Accordingly, the prevalence of autoimmune disorders is also associated with latitude. In Australia, multiple sclerosis (MS) is seven times more common in Tasmania (higher latitude) than in Queensland (lower latitude) in association with this latitude gradient. Importantly, in patients with MS, vitamin D levels are also associated with disease activity and disability, suggesting that they may provide markers of disease burden. However these factors have never been investigated in patients with chronic inflammatory demyelinating polyneuropathy (CIDP), a related autoimmune neuroinflammatory disorder which affects the peripheral nervous system – leading to progressive difficulties with walking and sensation.

This project is designed to examine the rates of CIDP at different latitudes in Australia – in New South Wales, Queensland and Tasmania – to determine if CIDP prevalence is associated with latitude. In order to determine if vitamin D levels are associated with disability in CIDP, we will measure vitamin D levels in CIDP patients and compare with their functional ability. We have developed and implemented a comprehensive series of tests to examine function in patients with CIDP, including novel tests of nerve function. We will also compare with a group of MS patients to determine the differences in vitamin D levels across the spectrum. The overall aim is to develop a marker of disease activity and to examine the potential for a trial of vitamin D supplementation in these patients.

We have made progress with all aspects of the study but data collection is still ongoing. In particular, the ethics and governance requirements to undertake a prevalence study are complex and have required considerable time. However we have now obtained ethics approval for all sites, with governance approvals complete in Tasmania and ongoing in Queensland and New South Wales sites. We anticipate that these processes should be complete within the next few months. We have

collected 45 patients with inflammatory neuropathy for the study and will continue data collection in order to maximise patient numbers.

Hypothesis vs Findings

Aims

1. To establish the prevalence of peripheral neuroinflammatory disorders at different latitudes

Hypothesis: The prevalence of peripheral neuroinflammatory disorders will be greater at higher latitudes

Update: We have several methods underway to correctly ascertain the number of cases of peripheral neuroinflammatory disorders at different latitudes. Prevalence estimates will be undertaken in conjunction with the date of the national census. The census data is anticipated to be released mid next year. Ethics approval has been obtained for Tasmania from the University of Tasmania ethics committee and case ascertainment is underway in conjunction with Professor Bruce Taylor. Ethics approval has also been obtained from the University of Sydney human research ethics committee and the Sydney local health district (RPAH zone) human research ethics committee for the project. Approval has been obtained for the collection of health information under the Public Health Act from the Director General of Queensland Health. Governance approval is underway at the Townsville Hospital and Health Service and the Cairns and Hinterland Hospital and Health Service. Governance is also underway at the Hunter New England Health district. In addition, we have submitted a proposal to the National Blood Authority to obtain latitude-specific information regarding usage of intravenous immunoglobulin for inflammatory neuropathies.

2. To identify the functional significance of Vitamin D level on chronic inflammatory demyelinating polyneuropathy (CIDP) severity

Hypothesis: Vitamin D levels will be correlated with functional status and disease severity in CIDP

Update: We have developed a questionnaire to ascertain sun exposure and dietary exposure to vitamin D within the past 3 months in conjunction with Dr Vasant Hirani and Professor Rebecca Mason. 45 patients with inflammatory neuropathy have been recruited to the study. A blood sample has been collected from patients and serum stored for Vitamin D analysis. In addition functional outcome measures have been undertaken in all patients which will enable us to compare vitamin D levels with disease severity. The vitamin D analysis will be conducted by South Eastern Area Laboratory Services in a single run – using liquid chromatography tandem mass spectrometry rather than immunoassay methods which are less sensitive.

3. To compare Vitamin D status between central and peripheral neuroinflammatory disorders longitudinally

Hypothesis: Vitamin D levels will be reduced in both central and peripheral neuroinflammatory disorders compared to healthy controls

Update: Patients returning for clinical follow-up will be re-tested – typically at one year follow-up. In addition, 28 healthy control participants have been recruited to the study and have provided a blood sample for vitamin D analysis as well as undertaking a nerve function assessment. We have formed a collaboration with a local MS clinic to recruit patients with MS.