Climate change and the human immune system: Ultraviolet radiation & immunity study, assessing the impact of ultraviolet radiation on the immune response to primary vaccination in Australian adults

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Background: Climate change models predict that human populations may be exposed to increased solar ultraviolet radiation (UVR), largely as a result of changing behavioural and clothing patterns, and potentially via an indirect effect of global warming on stratospheric ozone[1]. Numerous studies have demonstrated that UVR is locally and systemically immunosuppressive to animals and humans[2]. Animal models have shown the deleterious effect of UVR on mammalian hosts infected with various pathogens, including Mycobacteria leprae, Leishmania, Plasmodia and fungi [3]. It has been estimated that ~ 90 minutes of mid-latitude, midday, solar UVR exposure would be sufficient to suppress, by 50%, the human immune response to infection by Listeria monocytogenes [4]. The immunosuppressive potential of UVR may be of critical importance in affecting vaccine efficacy, particularly in the developing world. In the context of climate change, UVR-induced impairment of the immune response following vaccination could have major public health implications.

Aims:

- To assess the impact of solar UVR exposure on the human immune response to primary vaccination.
- To assess the association between other climatic variables sensitive to climate change and latitude, and the human immune response to primary vaccination.

Methods: We propose to measure the immune response to primary immunization with Keyhole Limpet Haemocyanin (KLH) antigen - a safe, reliable immunogen - in a population of Australian adults residing over a wide ambient UVR gradient. Participants for this cross-sectional epidemiological study will be recruited from temperate Canberra (35.3S) and sub-tropical Darwin (12.3S) over four seasons for a 12 month period. Participant inclusion criteria are consenting, healthy adults (aged 18-30 years). Exclusion criteria are an allergy to seafood allergy, pregnancy, immunosuppressive medication, chronic illness and inter-current infection.

Experiment 1: Humoral Immune Response Baseline blood tests will be taken for KLH-specific antibody titres, Vitamin D levels, and general biochemistry / haematology. Participants will complete baseline validated questionnaires on demographic information, exercise patterns and fitness, psychosocial parameters, nutrition, past medical history, medication, alcohol intake and smoking history. Examination of skin type and skin sun damage, and spectrophotometry will be performed. Participants will be vaccinated with 100mcg of KLH antigen subcutaneously in a sun-exposed aspect of the forearm. Participants will wear a validated UVR monitor (worn as a wristband), and keep a ‘sun exposure’ diary for 7 days. In addition, ambient UVR monitoring will be undertaken by calibrated outdoor UV detectors in the study cities. At Day 7 participants will return their UV wristband, and have a repeat blood test (10mls) for KLH-specific serology. At day 21, further blood will be collected for serology, lymphocyte proliferation assays and cytokine gene testing.

Experiment 2: Cell Mediated Immune Response A sub-group of the above participant cohort from each site will undergo intra-dermal vaccination with 1ug KLH antigen at day 21 post initial KLH vaccination. Daily measurements of skin induration (in millimetres) will be undertaken for 96 hours by a study researcher, as a measure of delayed type hypersensitivity (DTH) reaction. Outcome Measures: Antigen-specific humoral and cellular immune responses following primary immunisation correlated to UVR exposure, and other climatic variables sensitive to climate change.

Timeline: Project commencement mid- 2009; to be completed in 2010. Significance of Study: UVR-induced impairment of the immune response following immunisation will have broad public health implications, particularly in the developing world and in the context of climate change. Our proposed study is a collaboration of leading Australian epidemiologists, immunologists, environmental and laboratory scientists. The results of this investigation will also help direct lines of future immunological and epidemiological research.