BROAD-SPECTRUM THERAPEUTICS FOR VIRAL DISEASES: A MEDICAL COUNTERMEASURE PLATFORM FOR EMERGING THREATS

Neurological Sequelae – Assessing The Hazard

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Is an understanding of the long-term consequences of exposure to biological warfare (BW) agents required?
Whilst a body of data exists characterising the potential acute effects of infection, the longer-term impacts (sequelae) remain unknown. Neurological sequelae are medical conditions associated with damaged neurons resulting from a previous disease, injury or other trauma that often result in significant cerebral, sensory, or motor deficits. These can range in severity and impact; including fatigue, headaches, photophobia and breathlessness to more severe presentations such as behavioural / emotional instability, neuromuscular weakness, paralysis and seizures. There are a number of viruses known to cause neurological sequelae after naturally occurring outbreaks (e.g. Ebola virus, Venezuelan equine encephalitis virus (VEEV), Eastern equine encephalitis virus (EEEV), Western equine encephalitis virus (WEEV), Nipah virus), as well as those which circulate endemically (e.g. herpesviruses, cytomegalovirus, Epstein Barr virus). New world encephalitic alphaviruses VEEV, WEEV and EEEV cause disease in people after the bite from by an infected mosquito, often leaving survivors with severe neurological complications. The frequency of these is up to 90% of survivors, who were unable to work, although were expected to have an average life-span. In the event of exposure to a BW agent where neurological sequelae is a recognised consequence, there is potential for a significant loss of service personnel due to illness - likely to require long-term monitoring and healthcare support, as well as significant funding (~$3m required for one individual suffering from residual complications of naturally acquired EEEV in 1995).
How might this impact operational decision making? For example, what could be the potential effects on overall operational success, operational burdens (e.g. need for rapid administration of medical countermeasures), and the levels of health monitoring required, as well as any associated financial burden?
There are a number of approaches in assessing the impact of neurological sequelae, one of which could be to establish a capability to objectively measure the general health and baseline neurological/behavioural functions in a relevant, representative model of disease. This capability could then be exploited to study sequelae in a number of priority BW pathogens. Investment made by UK MoD in establishing an in vivo model of inhalational, non-lethal encephalitic alphavirus disease (VEEV) may provide the means by which to begin to evaluate the hazard posed by virus-induced neurological sequelae.