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Cytomegalovirus (CMV) and health care costs

Dr Rod Jones (ACMA)
Statistical Advisor
Healthcare Analysis & Forecasting, Camberley, UK
hcaf_rod@yahoo.co.uk
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A recent series of articles has highlighted a curious repeating pattern in emergency medical admissions, bed occupancy, A&E attendance, total health care costs and a resulting cycle of surplus/deficit in health care. The step-like increase in activity and costs at the commencement of each cycle occurs at an interval of 3 to 8 years; is age, gender and diagnosis specific and international in scope. Repeating outbreaks of a persistent viral-illness have been proposed to account for this behaviour (see Jones 2010a-e, 2011a-c and references therein).

The near simultaneous international outbreaks suggest that a fairly ubiquitous virus must be involved; however, to account for the cluster of immune-related diagnoses this virus would need to possess powerful immune modulating behaviour (Miller-Kittrell et al 2009). One candidate does indeed exist, but up until recent years has been largely regarded as only posing a risk to the developing foetus (where it is responsible for 40% of all congenital malformations) and the severely immune compromised (HIV/AIDS and transplant recipients). Interestingly an increase in costs associated with neonates was observed in England following the proposed 2007 outbreak (Jones 2010d).

Cytomegalovirus (CMV) is a member of the herpes group of DNA viruses and causes a persistent infection with reactivation (via a range of mechanisms) to cause observable clinical symptoms which include a lupus- or influenza-like illness with fatigue, headache, fever and occasional respiratory infection – all of which match some of the more non-specific diagnoses that accompany each outbreak. Indeed an increase in influenza-like symptoms was noted in primary care during the 1993 outbreak. More severe symptoms can occur in almost any body organ or tissue which often resolves with specific anti-viral therapy (Soderberger-Naucler 2006, Varani et al 2009, 2010). Infection of the nervous system or brain can lead to a range of mental health issues. Recent research has also suggested that a range of sub-clinical effects also occur which lead to the virus being a risk factor in a diverse range of inflammatory and autoimmune diseases (Varani et al 2009, 2010) and survival in the intensive care unit (Andre et al 2009). All of these more specific symptoms also match the range of diagnoses that appear to be associated with each outbreak.

A range of studies have shown that the healthy elderly are either not infected with CMV or have very low levels of antibody titre suggesting that the virus is maintained in a latent state. The frail or unwell elderly are characterised by increasingly high antibody titres (Vescovini et al 2010, Wang et al

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2010) and what is known as the immune risk profile (IRP) appears to be associated with CMV infection (Derhovanessian et al 2009, Pawelec et al 2009). CMV also leads to the equivalent to premature aging in T cells which is linked to diseases such as atherosclerosis (van de Berg et al 2010).

Hence while we seem to have a reasonably good match with the range of symptoms how could epidemic-like international outbreaks occur? CMV is curious in that it has no recognised serotypes (for example Influenza A & B) but instead shows a wide range of strains with high genetic diversity (Stanton et al 2010). Different strains appear to prefer different organs/tissue and individuals can be simultaneously or sequentially infected with different strains (Ver braak et al 1998, Stanton et al 2010). Transmission is via body fluids (blood, saliva, semen, urine) and requires a degree of direct contact and this mode of transmission concurs with the rather slow further spread after the initial outbreak(s). The virus can cross the species boundary with primates (Swinkels et al 1984).

Fairly rapid mutation is observed when the virus is subject to serial culture in vitro (Stanton et al 2010). Hence a significant in vivo mutation (which is slower than in vitro) in a particular strain could be rapidly carried by high volume air, rail, road and sea transport from the initial locus to create an international 'epidemic' of poor health. There is indeed some evidence that seroprevalence is higher in particular years (deOry et al 2004, Vyse et al 2009). The curious higher incidence of the 'new immune disease' in women also concurs with general higher incidence of CMV in women along with a tendency to higher antibody levels (Matos et al 2010). The higher costs associated with breast cancer following the 2007 outbreak in England (Jones 2010d) appear to be consistent with research indicating that elevated antibodies to CMV appear to precede breast cancer in some women (Cox et al 2010) and that CMV appears to be present in 97% of cases of breast ductal carcinoma (Harkins et al 2010).

In conclusion, while there is an excellent match regarding the range of symptoms we will still require clinical confirmation of elevated serum antibody levels to confirm that CMV is the actual causative agent in the proposed outbreaks of the 'new' disease and it also remains to be confirmed as to how the near simultaneous international outbreaks occur and how the curious collective switch to dormancy also occurs after around 3½ years. It would seem that we are getting closer to solving one of the more intriguing aspects of health care and associated trends in activity and cost. Whatever the outcome, this disease/syndrome represents one of the most powerful influences on the international cost behaviour in health care and therefore demands an explanation.

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