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Case study: Influenza; impact of pre-existing immunity on study end points

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Adults have experienced a number of influenza infections and may have been immunised with influenza vaccine which will result in heterogeneous immunity. In 1972 Hobson et al. showed that a haemagglutination inhibition (HI) serum antibody titres between 1:18 to 1:36 provided 50% protection against influenza challenge in adult volunteers. Subsequently, an HI titre of 40 has been adopted as a surrogate correlate of protection in adults. The haemagglutination inhibition assay is a good assay for screening research subjects and indicating susceptibility to a given influenza challenge virus. However, the multifaceted immune response to influenza may require further testing of subjects to improve the challenge model. Recent challenge and cohort studies have shown neuraminidase inhibiting antibodies, nasal wash IgA and stalk specific antibodies can also provide protection from challenge. Furthermore, cellular immune responses including CD4, CD8 and IFN-γ secreting cells have been shown to correlate with protection from infection. This talk will review the impact of pre-existing immunity on study endpoints and examine how the baseline tests can be used to ensure acceptable homogeneity in the responses to challenge.