# Inhibition of *Neisseria gonorrhoeae* complement-mediated killing during acute gonorrhoea infection is dependent upon antibody ratio

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**Background:** Control of gonorrhoea within the population is difficult due to increasing levels of antibiotic resistance and the lack of an effective vaccine. High rates of re-infection are caused by the failure to produce immune memory. The reason for this remains poorly understood, in part because there are very few reports of large-scale studies of the human immune response to the gonococcus.

**Aim/Methods:** The current project is an extension of the G-ToG clinical trial reported by Ross, *et al*. (2019; The Lancet: 93: 2511-2520), where the effectiveness of the study drug, gentamicin, was compared with ceftriaxone for the treatment of acute gonorrhoea. Serum samples were obtained from 720 infected participants upon trial enrolment, and cultured gonococcal isolates were also taken from a variety of anatomical sites for a subset of 307 participants. These samples provided a unique opportunity for large-scale analysis of humoral immunity, specifically focussing on concentrations of different antibodies and complement activation.

**Results:** Serum bactericidal assays were used to show that serum from nine participants demonstrated inhibition of complement mediated-killing of their infecting gonococcal strain. These isolates were killed by a pool of human sera from healthy individuals, but resistant when incubated with serum from the host from which they had been isolated. Antibody isotypes IgG, IgM and IgA were purified from these inhibitory participant sera. Purified IgG and IgM from these sera protected all matched bacteria from killing by pooled healthy serum. Only three of these isolates were protected by the purified matched IgA. Quantitative analysis revealed a strong correlation between the ratio of IgG subclasses binding and the ability to protect against complement mediated killing.

**Conclusions:** Our data revealed a mechanism that is distinct from previous literature on the inhibition of serum killing against *Neisseria gonorrhoeae* and other Gram-negative bacteria. Further analysis of the mechanism would be invaluable for informing gonococcal vaccine development.