

A human controlled infection study to establish a safe, reproducible and practical human *Bordetella pertussis* colonisation model for the identification of correlates of protection against colonisation

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Background: Globally *Bordetella pertussis* is one of the leading causes of vaccine preventable death. Over the last 20 years pertussis appears to have become resurgent in a number of countries in the developed world that boast high immunisation coverage (see figure 1). To improve vaccine strategies, a greater understanding of human *B. pertussis* colonisation is required.

Objective: To develop a safe human challenge colonisation model, to inform improved understanding of the natural protective immune response against wild type *B. pertussis* in order to facilitate development of bioassays and next generation pertussis vaccines.

Design: First in human, controlled human infection model

Setting: Single centre study, NIHR Clinical Research Facility Southampton

Participants: Healthy volunteers aged 18-45 years

Methods: A controlled human colonisation model using *Bordetella pertussis* will be developed over two phases. In phase A, a low dose of the inoculum will be given intranasally to healthy participants with a low (≤ 20 U anti-pertussis toxin level). The colonisation period, transmission and exploratory immunology will be assessed during a 17 day inpatient stay and follow-up over one year (see figure 2). The inoculum dose will be escalated or de-escalated until a colonisation rate of approximately 70% is reached without causing disease (see figure 3). The dose of inoculum which achieves 70% colonisation will then be confirmed in phase B, comparing healthy participants exposed to *B. pertussis* with a control group receiving a sham inoculum. Ethics and dissemination: REC reference: 17/SC/0006, 24 February 2017.

Results: Advertisement and media interest stimulated >4000 people to express interest, 790 volunteer information sheets were distributed and 11 participants have been screened. Two volunteers were excluded because of a high anti pertussis toxin level. The first five volunteers have been challenged with a median dose of 1140 colony forming units (cfu), have completed eradication therapy and the admission period.

Figure 1: Increase in *B. pertussis* incidence in the UK over time. Adopted from Public Health England, Enhanced Pertussis Surveillance, 05/05/2016

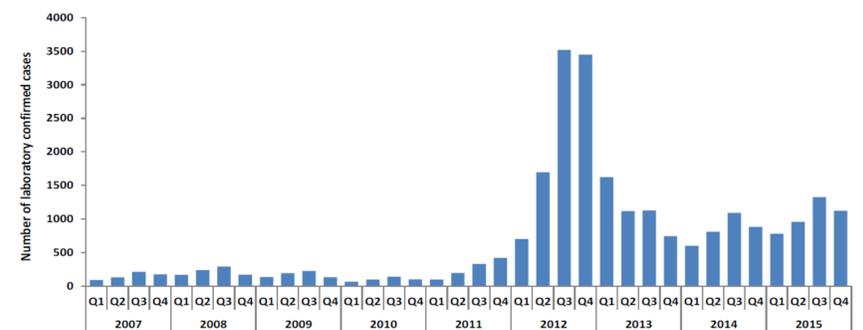


Figure 2: Study schedule including admission period and follow up visits

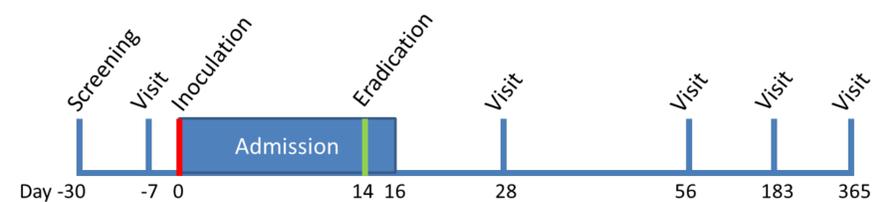
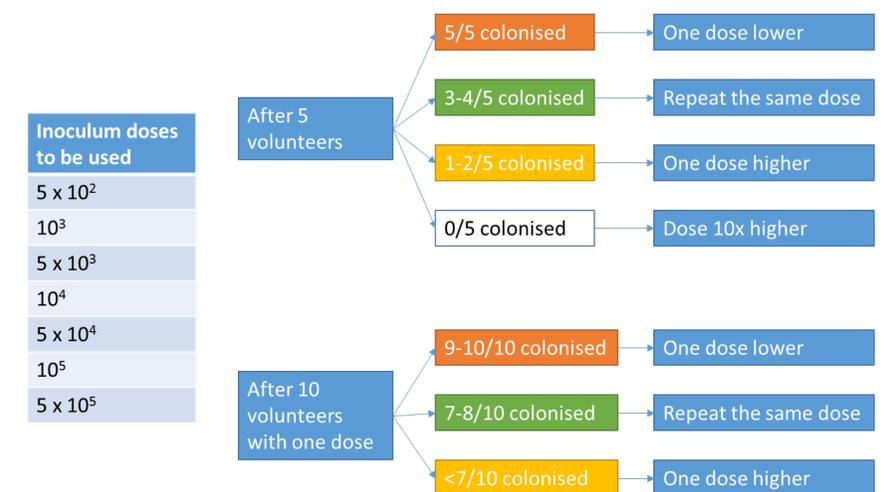


Figure 3: Escalation or de-escalation of the inoculum dose in cfu



To continue until 10 volunteers are colonised with the same dose of inoculum

No safety issues were encountered and no colonisation or shedding was found; all cultures were negative. Further volunteers will now be recruited with escalating doses per protocol.

Future work: Depending on the colonisation rate, phase A will continue until January 2018 – July 2018. After completion of phase A the protocol for phase B will be amended and submitted to the ethical committee and Health Research Authority as a substantial amendment.

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