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Development of a gonorrhoea pharyngeal controlled human infection model for the assessment of novel prevention and therapeutic strategies

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Background

Infection with Neisseria gonorrhoeae is a major public health problem characterised by increasing global incidence and antimicrobial resistance. Accordingly, novel and innovative gonorrhoea prevention and therapeutic strategies are urgently required. As N. gonorrhoeae is a human-restricted pathogen, preclinical animal infection models for assessment of novel interventions have important limitations. A gonorrhoea urethritis controlled human infection model (CHIM) has led to significant progress in understanding gonorrrhoea urethritis pathogenesis. Increasing evidence suggests that pharyngeal infection plays a key role in gonorrhoea transmission and antimicrobial resistance, however there is a paucity of data describing N. gonorrhoeae pathogenesis and host responses to infection of the pharynx. Here, we describe progress towards establishing a first-in-field pharyngeal gonorrhoea CHIM.

Aim/Methods

First, genomic analysis will be used to select a panel of contemporary, globally-relevant N. gonorrhoeae strains optimised for patient safety and vaccine antigen coverage from a panel of 5,911 N. gonorrhoeae isolates. This panel will undergo detailed phenotypic characterisation including antimicrobial susceptibility testing and in vitro infection assays using human pharyngeal epithelial cell lines. In parallel, development and validation of standard operating procedures for preparation and storage of the challenge strains will be performed in accordance with good manufacturing practice (GMP), aimed at obtaining regulatory approval for challenge strain production. An ethical and locally-appropriate study design for a pharyngeal gonorrhoea CHIM will be then be developed, informed by a program of community engagement and consultation with key stakeholders. Finally, an observational, dose-escalation inpatient pharyngeal gonorrhoea CHIM trial will be undertaken in carefully-screened healthy adult male volunteers.

Results

The requirements for a contemporary pharyngeal gonorrhoea CHIM will be described, including i) the rational selection of a contemporary, globally-relevant N. gonorrhoeae strain; ii) development of a GMP-grade cell bank that produces well-characterised single-dose vials of the challenge strain and iii) design of an ethical and locally-appropriate clinical trial protocol.

Conclusions

Development of a contemporary gonorrhoea pharyngeal CHIM may potentially serve as a powerful platform for assessment of novel gonorrhoea prevention and therapeutic strategies.