A controlled human pneumococcal infection model

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Primary objective: - To establish a controlled human infection model in which healthy Dutch adult volunteers are inoculated with a wild-type Streptococcus pneumoniae bacterium with strict safety reviews.Secondary objectives: - To assess the...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Bacterial infectious disorders
Study type	Interventional

Summary

ID

NL-OMON51807

Source
ToetsingOnline

Brief title
Controlled human pneumococcal infection model (PIM) study

Condition

- Bacterial infectious disorders

Synonym
nasal carriage of Streptococcus pneumoniae; pneumococcal infection

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Carriage, Nasal administration, Nasal Immune response, Streptococcus pneumoniae, systemic immune response

Outcome measures

Primary outcome

Primary endpoints:

- Percentage of volunteers infected with S. pneumoniae

Secondary outcome

Secondary endpoints:

- The number of solicited (S)AEs from baseline visit (day -1 to -6) till the

end of the study (day 28±3)

- Number of colony forming units detected in nasal wash of infected

participants at various samples timepoints

- Concentrations of S. pneumoniae-specific IgM, IgG and IgA in serum and

mucosal lining fluid at the various sampling time points

Study description

Background summary

In most cases infection with Streptococcus pneumoniae (the pneumococcus) occurs in the absence of clinical symptoms. However, infection can also lead to mild disease such as otitis media, or to invasive pneumococcal disease such as pneumonia, bacterial meningitis and sepsis. Invasive pneumococcal disease is a leading global cause of morbidity and mortality, particularly in children and the elderly. Although vaccines exist that protect against invasive pneumococcal disease, these vaccines do not cover all circulating pneumococcal serotypes and are less effective in preventing infection. New strategies to reduce pneumococcal infection are therefore urgently needed. An Experimental Human Pneumococcal Carriage (EHPC) model has previously been developed at the Liverpool School of Tropical Medicine (LSTM). This model has been used to

assess new strategies to treat or prevent pneumococcal infection and to answer questions about host-pathogen interaction and immunity. Investigating these aspects in a different population could provide new insights due to e.g. differences in circulating pneumococcal strains and infection-induced immunity. Moreover, this could increase the capacity of vaccine testing. Therefore, we aim to implement this model at the Radboudumc, combining world leading expertise regarding controlled human infection studies and pneumococcal research. This will assure maximum scientific output in a volunteer safe setting. The current study aims to establish this model in healthy adults living in the Netherlands using the inoculation dose currently used at LSTM.

Study objective

Primary objective:
- To establish a controlled human infection model in which healthy Dutch adult volunteers are inoculated with a wild-type Streptococcus pneumoniae bacterium with strict safety reviews.

Secondary objectives:
- To assess the frequency and nature of (severe) adverse events of a controlled human infection model in which healthy Dutch adult volunteers are inoculated with a wild-type Streptococcus pneumoniae bacterium
- To evaluate the duration and density of S. pneumoniae in volunteers following inoculation with S. pneumoniae
- To investigate the S. pneumoniae-specific IgM, IgA and IgG antibody responses in serum and in nasal lining fluid in healthy adult volunteers who have been inoculated with S. pneumoniae

Study design

Intervention study

Intervention

Participants will be inoculated intranasally with strain BHN418, a penicillin sensitive serotype 6B strain of S. pneumoniae that was previously isolated from a healthy carrier and characterized by Birgitta Henriques-Normark and colleagues. This strain has been used as the challenge agent in >1100 participants at LSTM without safety concerns. Following inoculation, participants will be closely monitored and blood and nasal samples will be collected over a period of 28 days. Participants will receive a course of pheneticillin to eradicate infection on day 28±3, unless no S. pneumoniae is detected on both day 14 and 28±3 post-inoculation.

Study burden and risks

Although the vast majority of cases, nasopharyngeal infection with S. pneumoniae occur in the absence of clinical symptoms, participants remain at risk of developing pneumococcal disease. However, there have been no reported cases of severe pneumococcal disease in the more than 1100 volunteers who have been inoculated with the same challenge strain used in this study at the LSTM. We therefore expect the risk of developing (invasive) pneumococcal disease in participants to be minimal. To further minimize risks, a healthy adult study population is selected and participants will be monitored closely to detect possible adverse events if they occur. Dosage and strain to be tested in this study has previously been tested and proven to be safe at the LSTM. In case participants develop symptoms or disease potentially caused by S. pneumoniae, this can be treated effectively with antibiotics. Participants may experience discomfort during the collection of blood and nasal samples. The study involves 7 visits in the hospital in total, including 1 nasal inoculation, 6 blood drawings, 6 nasal washes, 6 mucosal lining fluid samples and 4 nasal swabs. Additionally, participants are asked to complete a short questionaire at several moments during the study and are asked to collect nasal lining fluid 5 times at home. Depending on the infection outcome, a volunteeer may need to take an antibiotics course to clear infection ±four weeks after inoculation. Potential benefits for participants such as developing protective antibodies are uncertain, and as such, it must be assumed that volunteers will not experience any benefit from their participation in the study.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Participant is:
- Aged >= 18 and < 50 years on the day of screening.
- In good health as confirmed by review of medical history and physical examination.
- Able to arrive within 3h at the Radboudumc at any time during the study participation, and participant is able to arrive within 1h at the Radboudumc from his/her home address.
- Willing to take a curative antibiotic course after inoculation with S. pneumoniae, according to the study protocol.

Exclusion criteria

- Any history, or evidence at screening, of clinically significant symptoms, physical signs or abnormal laboratory values suggestive of systemic conditions which could compromise the health of the volunteer during the study or interfere with the interpretation of the study results.
- Smoking
- Previous pneumococcal vaccination or infection with the pneumococcus at screening or inclusion visit
- Close physical contact with at risk individuals (>15 min within 1.5m distance)
- For female participants: pregnancy, lactation or intention to become pregnant during the study.
- Known hypersensitivity to or contra-indications (including co-medication) for use of penicillin

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	31-05-2022
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO Date:	09-03-2022
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	24-08-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL79171.091.22

Study results

Results posted: 13-02-2024

First publication
05-02-2024