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Experimental Human Pneumococcal Carriage Model Testing New Strains

Submission date
03/07/2017

Recruitment status
No longer recruiting

Registration date
15/08/2017

Overall study status
Completed

Last Edited
07/08/2019

Condition category
Infections and Infestations

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Mild infections with pneumococcus are very common, such as ear infections in children. But pneumococcus can also infect the lung (causing pneumonia) or the brain (causing meningitis) or the blood (causing sepsis). These severe infections are very uncommon in healthy adults: about 50 cases in Liverpool per year. Very young children and adults who are elderly or those who have other illnesses are more likely to become ill. A new vaccine could protect people against severe disease from pneumococcus. It is thought that small numbers of bacteria present in the nose ("nasal carriage") can help to protect people against disease. The aim of this study is to find out what happens when small numbers of the bacteria are put up the nose of healthy volunteers.

Who can participate?
Healthy adults 18-50 years of age.

What does the study involve?
Participants are seen to discuss potential study involvement. Consent is obtained following time for participants to make a fully informed decision about volunteering. Once consent is received, during the week prior to the start of the study participants are for screened for eligibility. The first official visit participants are given a sample of the bacteria which is placed in each nostril. They are given a safety pack of antibiotics and a thermometer, and advised to check their temperature daily for seven days.
Participants come back to the clinic two, seven and 14 days following this inoculation where they undergo nasal wash, nasosorption and nasal cells at days two and seven and undergo nasal wash, nasal cells and blood collection on day 14. Some participants are invited for a repeat study between three to six months later and participants who remain colonised by the end of the study are advised to take antibiotics.

What are the possible benefits and risks of participating?
Participants benefit from receiving financial compensation for their time and inconvenience. The risk from the tests performed in the study (such as blood tests and nasal/throat samples) is very low, as these tests are not expected to cause more than mild temporary discomfort. The study involves live bacteria, which can cause severe infection (such as pneumonia or meningitis) in people who are at high risk of infection. To minimize this risk, volunteers who are healthy and

low-risk are carefully selected, and a detailed medical assessment is carried out on all potential volunteers before they start the study. In addition, a thermometer and antibiotics are provided to identify and treat infection early. The research team is available any time day or night and provide access to healthcare if required.

Where is the study run from?
Clinical Research Unit at Royal Liverpool and Broadgreen University Hospitals (UK)

When is the study starting and how long is it expected to run for?
November 2016 to July 2018

Who is funding the study?
Medical Research Council (UK)

Who is the main contact?
Dr Victoria Connor

Contact information

Type(s)
Public

Contact name
Dr Victoria Connor

Contact details
Respiratory Research Fellow RLBUHT/LSTM
Respiratory Infection Group,
Department of Clinical Sciences,
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L3 5QA

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
20815

Study information

Scientific Title

Experimental Human Pneumococcal Carriage model: Research working towards a nasal vaccine for pneumonia: The effect of new strains (types) of bacteria in healthy participants.

Study objectives
The aim of this study is to find out if two more types of this bacteria (strains) can be carried in the nose, how much remains and how long it is carried for then used to develop new vaccines.

Ethics approval required
Old ethics approval format

Ethics approval(s)
North West - Liverpool East Research Ethics Committee, 20/01/2016, ref: 15/NW/0931

Study design
Non-randomised; Observational; Design type: Cohort study

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Specialty: Infectious diseases and microbiology, Primary sub-specialty: Antimicrobial Research; UKCRC code/ Disease: Infection/ Bacterial, viral and other infectious agents

Interventions
Healthy non-smoking adult participant’s are exposed with well-characterised, fully sequenced penicillin-sensitive pneumococci and observe them for the development of pneumococcal carriage.

Initially participants are seen to discuss potential study involvement. Consent is obtained following time for participants to make a fully informed decision about volunteering. Once consent is received, during the week prior to the start of the study participants are for screened for baseline samples. This will involve clinical examination and medical history, nasal wash sample collection, nasal cells, urine sample (pregnancy test for females), viral throat swab and blood test.

If participants are still eligible following screening they are seen the week later to start the study. The first official visit is pneumococcal inoculation, where a nasosorption sample is taken

initially then participants are placed in a semi-reclined position, and 100 microlitres of saline (containing pneumococcal bacteria) is placed in each nostril. They are given a safety pack of antibiotics and a thermometer, and advised to check their temperature daily for seven days.

Participants come back to the clinic two, seven and 14 days following this inoculation where they undergo nasal wash, nasosorption and nasal cells at days two and seven and will undergo nasal wash, nasal cells and blood collection on day 14.

The total duration of the study (observation and follow-up) is four weeks, with a maximum of six visits (including consent visit) with a subset of participants being invited for a repeat study between three to six months later and participants who remain colonised by the end of the study are advised to take antibiotics.

For the repeat study, participants undergo the same screening and inoculation as in part one of the study but with a different strain of pneumococcus. They return for follow-up at day two and day seven after inoculation, and participants who remain colonised are advised to take antibiotics at the end of the repeat study. Nasal wash and nasosorption,are repeated on day two. Nasal wash and blood test are repeated on day 14.

Intervention Type
Other

Primary outcome measure
Inoculated pneumococci is assessed using classical culture methods at any time point from nasal wash recovered from the participants at days 2, 7 and 14 following first pneumococcal challenge.

Secondary outcome measures
1. Factors local to the nasal mucosa which determine the probability or intensity of colonisation (levels of inflammation as measure by cytokines and cellular infiltration measure by flow cytometry) are measured using the nasal cells at days two, seven and 14 following first pneumococcal challenge.
2. Protective effect of carriage against the reacquisition of carriage following inoculation with a different pneumococcal strain to be evaluated after the repeat study on days two and seven following second pneumococcal inoculation.

Overall study start date
01/11/2016

Completion date
31/07/2018

Eligibility

Key inclusion criteria
1. Adults aged 18-50 years ages (chosen to minimise the risk of pneumococcal infection, and to allow comparison with previously published experimental work done by our group)
2. Fluent spoken English (to ensure a comprehensive understanding of the research project and their proposed involvement)

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
50 Years

Sex
Both

Target number of participants
Planned Sample Size: 134; UK Sample Size: 134

Key exclusion criteria
1. Previous pneumococcal vaccination
2. History of pneumococcal illness
3. Close physical contact with at risk individuals (children under 5yrs, immunosuppressed adults, elderly, chronic ill health) -to minimise risk of pneumococcal transmission
4. Any current treatment for asthma – confounding effect of medications such as corticosteroids, and propensity to infection
5. Allergy to penicillin/amoxicillin
6. Taking daily medications that may affect the immune system e.g. steroids, steroid nasal spray, antibiotics. Also medication that may reduce immunity eg. Roacutanne
7. Current illness, acute illness within 3 days prior to inoculation or antibiotic treatment within 2 weeks of inoculation
8. Pregnancy - minimise risk of pneumococcal disease
9. Diagnosed as diabetic
10. Involved in another clinical trial unless observational or in follow-up (non-interventional) phase.
11. Have been involved in a clinical trial involving EHPC and bacterial inoculation
12. History of drug or alcohol abuse
13. Current regular smoker (smokes daily/ smokes > 5 cigarettes per week) - minimise risk of pneumococcal disease
14. Recent smoker i.e. within the last 6 months - minimise risk of pneumococcal disease
15. Ex-smoker with a significant smoking history (>10 pack years) – minimise risk of pneumococcal disease
16. Unable to give fully informed consent

Date of first enrolment
25/08/2016

Date of final enrolment
01/06/2018

Locations

Countries of recruitment

England

United Kingdom

Study participating centre
Clinical Research Unit at Royal Liverpool and Broadgreen University Hospitals
Royal Liverpool and Broadgreen University Hospitals
Prescott Street
Liverpool
United Kingdom
L7 8XP

Sponsor information

Organisation
Royal Liverpool and Broadgreen University Hospitals

Sponsor details
Research and Development
Royal Liverpool and Broadgreen University Hospitals
Prescot Street
Liverpool
England
United Kingdom
L7 8XP

Sponsor type
Hospital/treatment centre

Organisation
Liverpool School of Tropical Medicine

Sponsor details
Research and Development
Pembroke Place
Liverpool
England
United Kingdom
L3 5QA

Sponsor type
University/education

Organisation
Royal Liverpool and Broadgreen University Hospital NHS Trust

Sponsor details

Sponsor type
Not defined

Website
http://www.rlbuht.nhs.uk/Pages/RoyalHome.aspx

ROR
https://ror.org/009sa0g06

Funder(s)

Funder type
Government

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
The findings from this study will be disseminated amongst the scientific community. We intend to publish our findings in a high-impact peer reviewed scientific journal and present data at appropriate local, national and international conferences by December 2019. In addition, we will produce a lay report of our findings which will be made available to all participants.

Intention to publish date
31/12/2019

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are/will be available upon request from the EHPC coordinator (Catherine.Molloy@lstmed.ac.uk); these are considered by the program leads, and will be subject to data transfer agreements and ethical review if necessary.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No