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Using scrapings from the inside lining of the nose to investigate carriage of pneumococcal bacteria

Submission date
15/03/2018

Recruitment status
No longer recruiting

Registration date
14/05/2018

Overall study status
Completed

Last Edited
08/11/2019

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
Pneumococcal bacteria can cause pneumonia, meningitis, sepsis and otitis media. These diseases combined are the largest killers of children under 5 years old globally. Better vaccines are needed to help prevent these diseases. Pneumococcal bacteria are carried in the nose of one in ten of the healthy adult population and in higher amounts of children, up to nine in ten, this is referred to as colonisation.
We have developed a model to investigate the human immune response to pneumococcal bacteria present in the nose. This model involves putting the bacteria (inoculation) into the nose of healthy volunteers and monitoring if the bacteria remain in the nose through follow up visits by performing nasal washes. This model has been successfully used for 6 years in Liverpool and we can now achieve a reproducible rate of colonisation (40-50% post inoculation). We would like to obtain cellular samples from the nose by taking small scrapes from inside the nose. We do not know if taking these samples will provide enough cells to carry out analysis, reduce the rate of experimental colonisation and if they will result in any bacteria in the blood stream. We aim to investigate if adequate tissue can be sampled from the nose of healthy volunteers using a small probe. The samples will be analysed in the laboratory to determine if the cell numbers and types are enough to perform immune system tests on.We also aim to determine if the repeated sampling of the nose will affect the number of volunteers that become colonised with the bacteria following inoculation. We also want to investigate if the sampling method will cause any bacteria to move into the blood stream, this will be achieved by taking a blood sample before and 15 minutes after each nasal sample.

Who can participate?
Adults aged 18-50

What does the study involve?
Healthy volunteers will have small amounts of live bacteria put in their noses. They will be followed up in clinic for 2 weeks when samples will be taken to see if the bacteria are still

present in their nose. We expect that 40-50% of volunteers will "carry" the bacteria from previous studies therefore we want to see if this rate of carriage remains the same in this study whilst we are taking repeated samples from their nose.

What are the potential risks and benefits of participating?
There are no direct benefits to the participants however they will be part of vaccine development for future generations. Healthy volunteers will be compensated for their time and inconvenience.

Where is the study run from?
Royal Liverpool University Hospital (UK)

How long is the trial expected to run for?
June 2015 to November 2015

Who is funding the study?
UK Medical Research Council

Who is the main contact?
Dr Andrea Collins
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

Protocol serial number
15/NW/0146

Study information

Scientific Title

Pilot study of repeated mucosal sampling on experimental human pneumococcal colonisation (EHPC) model

Study objectives
The principle objective is to evaluate if repeated mucosal sampling will obtain sufficient tissue for immunological assessment.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Research Ethics Committee North West: Liverpool East, 05/05/2015, ref: 15/NW/0146

Study design
Healthy volunteers will be nasally inoculated with Pneumococcal bacteria. Repeated mucosal samples will be taken during follow up visits to determine if adequate tissue can be obtained for immunological assessment. We will determine if repeated mucosal samples affect the rates of colonisation following inoculation.

Primary study design
Observational

Study type(s)
Other

Health condition(s) or problem(s) studied
Nasal colonisation with pneumococcal bacteria

Interventions
All volunteers will have screening samples taken including nasal wash, nasal cell samples, nasosorption and blood samples. A clinical examination will be performed during the screen visit and a pregnancy test for females will be completed. Volunteers that pass screening will attend the clinic a few days later for the inoculation. This will involve putting a small amount of liquid containing pneumococcal bacteria inside each nostril. Full safety instructions including a course of antibiotics and 24 hour access to medical assistance will be provided.
Volunteers are followed up in clinic at day 2, 7, 9 and 14 post inoculation to review their symptoms and collect samples. Volunteers are invited to undergo a bronchoscopy at the end of the study, they do not have to take part in the bronchosocopy part of the study to participate in the study.

Intervention Type
Other

Primary outcome(s)
The principle objective is to evaluate if repeated mucosal sampling will obtain sufficient tissue for immunological assessment. Nasal cell yield will be measured using the flow cytometer to count the cell populations from the nasal cell samples taken at baseline, day 2, 7, 9 and 14 post-inoculation.

Key secondary outcome(s))

1. To evaluate the effect of repeated sampling of the nasal mucosa (lining of the nose) on the acquisition of pneumococcal colonisation. Pneumococcal colonisation is measured using microbiological techniques. The nasal wash pellet is plated onto agar plates and incubated for 48 hours using our previous published methods. Our previous studies have shown experimental colonisation rates of 40-60% following inoculation. The results of this study will be compared to previous healthy volunteer studies involving inoculation with 6B pneumococcus.
2. To evaluate if repeated mucosal sampling affects colonisation density and duration compared to previous EHPC studies. Pneumococcal colonies are counted from diluted nasal wash by plating the pellet using a Miles and Mizra technique. This is performed at baseline and day 2, 7, 9 and 14 post inoculation. The duration of colonisation is classed as the final timepoint at which pneumococcal bacteria is identified using classical microbiolgical techniques. The density and duration from this study will be compared to results from previous EHPC studies following inoculation of healthy volunteers to determine if the repeated nasal sampling technique has reduced the acquisition rates.
3. To evaluate participant comfort level following repeated mucosal sampling. Participants were asked to complete a Likert-type questionnaire to rate the level of comfort experienced with each mucosal sampling technique.
4. To evaluate the kinetics of nasal inflammatory response during pneumococcal colonisation. Cytokine levels are measured from the nasosorption sample using the Luminex machine. The levels measured on day 2, 7, 9 and 14 will be compared with the levels measured at baseline.
5. To evaluate if nasal sampling of cells causes a transient bacteraemia – patient safety issue. Paired blood cultures will be taken during each visit where nasal cell samples are taken. The first blood culture will be taken prior to nasal sampling and the 2nd blood culture will be taken 15 minutes post nasal cell sampling. These paired blood cultures will be taken at baseline, day 2, 7, 9 and 14 post inoculation. Aerobic and anaerobic blood cultures will be incubated for 48 hours and reported as per hospital guidelines. Presence of any bacteria in the blood culture post sampling will be classed as a possible transient bacteraemia.
6. To evaluate if pneumococcal killing by alveolar macrophages is increased following nasal colonisation. Bronchial alveolar lavage samples will be used to isolate alveolar macrophages. These cells will be incubated with pneumococcal bacteria overnight. The pneumococcal killing will be measured by counting the recovered pneumococcal bacteria following incubation with the macrophages compared to bacteria that were not incubated with macrophages. This demonstrates the number of bacteria killed by the alveolar macrophages. Healthy volunteers that have been colonised with SPN following inoculation will be compared with negative controls.

Completion date
24/11/2015

Eligibility

Key inclusion criteria
1. Has capacity to give informed consent
2. Aged 18-50 years (ages chosen to minimise the risk of pneumococcal infection)
3. Speaks fluent English

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
50 years

Sex
All

Key exclusion criteria
1. Currently involved in another study unless observational or in follow-up phase (non-interventional)
2. Are in close contact with at risk individuals (children under 5 years, immunosuppressed adults, elderly, chronic ill health) – to minimise risk of pneumococcal transmission
3. Current regular smoker (smokes daily) - to minimise risk of pneumococcal disease
4. Significant smoking history [defined as someone who has previously smoked more than 20 cigarettes per day for 10 years or the equivalent (>10 pack-years)] – to minimise risk of pneumococcal disease
5. Asthma (on regular medication) or respiratory disease – to minimise risk of pneumococcal disease
6. Pregnant - to minimise the risk of pneumococcal disease
7. On medication that may affect the immune system in any way e.g. steroids, steroid nasal spray
8. On medication that affects inflammation e.g. aspirin
9. On medication that affects clotting of blood e.g. dipyridamole or warfarin
10. Been involved in a clinical trial involving EHPC and bacterial inoculation over the last 3 years
11. Unable to give fully informed consent
12. Current acute severe febrile illness - to avoid inoculation in participants that may have current infection.

Date of first enrolment
27/06/2015

Date of final enrolment
01/11/2015

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Royal Liverpool University Hospital
Prescot Street

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Sponsor information

Organisation
Royal Liverpool and Broadgreen University Hospital Trust

ROR
https://ror.org/009sa0g06

Funder(s)

Funder type
Not defined

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

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes