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Experimental human Pneumococcal carriage: Aging and immunity

Submission date
08/11/2016

Recruitment status
No longer recruiting

Registration date
08/11/2016

Overall study status
Completed

Last Edited
08/11/2016

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 are a type of bacteria which can cause severe infections such as pneumonia, sepsis (blood poisoning) and meningitia, particularly in those with weaker immune systems, such as the very young and the very old (especially if other long-term illnesses are present). This bacteria is commonly present in the nose of healthy adults without any sign of illness (carriage), which may help develop a natural immunity to the infection. Carriage is rarely detected in older people. Vaccines protect against a few of the many sub-types of the pneumococcal bacteria. To develop new vaccines the research team has established an Experimental Pneumococcal Carriage Model (EHPC) that allows healthy volunteers to carry these bacteria in their nose safely. This study aims to find out if EHPC is possible in older people and to measure their immune response to EHPC.

Who can participate?
Healthy adults aged over 50 years, starting with people aged 50-64, then 65-74, and finally 75-85.

What does the study involve?
The study is conducted at the clinical research facility in Royal Liverpool University Hospital. The first part of the study takes around 4-5 weeks. All participants have a few drops of the live bacteria put into their nose, and then secretions are collected and blood samples taken. Part two of the study lasts for 2-3 weeks, and involves those who carry the bacteria being invited to repeat the procedures from part one after 6-12 months to see if they have developed natural immunity. Participants are asked to report any early signs of infection, and are provided with a thermometer and antibiotics to identify and treat infection early. The research team are available any time day or night and provide access to healthcare if needed.

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 cell scrapes) 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 are available any time day or night and provide access to healthcare if required.

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

When is the study starting and how long is it expected to run for?
December 2015 to March 2018

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

Who is the main contact?
Mr Hugh Adler
Hugh.Adler@lstmed.ac.uk

Contact information

Type(s)
Public

Contact name
Mr Hugh Adler

ORCID ID
https://orcid.org/0000-0003-4437-2298

Contact details
Dept of Clinical Sciences
Liverpool School of Tropical Medicine
Pembroke Place
Liverpool
United Kingdom
L3 5QA
+44 7490 392 877
Hugh.Adler@lstmed.ac.uk

Additional identifiers

Protocol serial number
20792

Study information

Scientific Title
Experimental Human Pneumococcal Carriage (Programme Grant) Research: working towards a nasal vaccine for pneumonia. The effect of age on immune function

Study objectives

The aim of this study is to determine the rate of experimental human pneumococcal carriage acquisition in an aging population

Ethics approval required
Old ethics approval format

Ethics approval(s)
NHS REC, Liverpool East, 04/02/2016, ref: 16/NW/0031

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

Primary study design
Observational

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Specialty: Ageing, Primary sub-specialty: Ageing; UKCRC code/ Disease: Respiratory/ Influenza and pneumonia

Interventions
Initial safety pre-screening will comprise a clinical assessment and examination by a physician, spirometry, electrocardiography and basic blood tests (blood count and kidney function).

If no issue is picked up at pre-screening, participants proceed to baseline study screening, where the following tests are performed:
1. Nasal wash (rinsing out the nasal cavity to detect bacteria)
2. Nasal cell sampling (scraping away some of superficial cell lining inside the nose)
3. Nasosorption (placing a small piece of filter paper inside the nostril to measure the immune response)
4. Throat swab
5. Saliva sampling
6. Blood tests

Up to one week following screening, participants undergo pneumococcal inoculation. For pneumococcal inoculation, participants will be placed in a semi-reclined position, and 100 microlitres of saline (containing pneumococcal bacteria) will be 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 return for follow-up visits at two, seven, nine, 14, 22 and 29 days after inoculation.

The nasal wash, nasosorption, throat swab and saliva will be repeated on days two, seven, nine, 14, 22 and 29 after inoculation.
Nasal cells will be repeated on days two, seven, nine and 29.
Blood tests will be repeated on days two, seven 14 and 29.
Only participants who have been colonised will attend on day 22, and participants who remain colonised will be advised to take antibiotics at the end of the study.

The total duration of the study (observation and follow-up) is five weeks, with a subset invited for a repeat study within one year.
For the repeat study, participants undergo the same screening and inoculation as in part one of the study. They return for follow-up at 2, seven and 14 days after inoculation, and participants who remain colonised will be advised to take antibiotics at the end of the repeat study.
Nasal wash, nasosorption, throat swab and saliva will be repeated on days two, seven, and 14.
Nasal cells will be repeated on days two and seven.
Blood tests will be repeated on day 14.

Intervention Type
Biological/Vaccine

Primary outcome(s)
Rate of colonisation of S. pneumoniae by classical bacterial culture methods from one or more nasal wash sample in the first 14 days following initial pneumococcal challenge.

Key secondary outcome(s))
1. Duration and density of pneumococcal carriage in elderly patients is assessed using classical bacterial culture methods during 29 days following initial pneumococcal challenge
2. Rates of EHPC among different age-groups within the older population are assessed using classical bacterial culture methods during 29 days following initial pneumococcal challenge
3. The protective effect of prior carriage against colonisation following rechallenge is assessed using classical bacterial culture methods up to one year following initial pneumococcal challenge
4. Whether nasopharyngeal sampling is more sensitive than oropharyngeal sampling is assessed using classical bacterial culture methods and molecular testing in the first 14 days following initial pneumococcal challenge
5. Population of immune/inflammatory cells in response to challenge and/or colonisation is assessed by flow cytometric analysis during 29 days following initial pneumococcal challenge
6. Presence of a systemic humoral immune response to nasopharyngeal carriage is assessed by measuring specific antibody levels in serum by ELISA during 29 days following initial pneumococcal challenge
7. Presence of a local humoral immune response to nasopharyngeal carriage is assessed by measuring specific antibody levels in nasal washings by ELISA during 29 days following initial pneumococcal challenge
8. Functional activity of antibodies is measured by opsonophagocytic killing assays during 29 days following initial pneumococcal challenge
9. Symptoms following pneumococcal challenge is measured in a study-specific symptom log during the first seven days following initial pneumococcal challenge
10. Changes in the nasopharyngeal microbiome of elderly subjects following EHPC are measured using a multiplex analysis during 29 days following initial pneumococcal challenge

Completion date
04/03/2018

Eligibility

Key inclusion criteria
1. Adults (male or female) aged 50-84 years
2. Fluent spoken English - to ensure a comprehensive understanding of the research project and their proposed involvement
3. World Health Organisation performance status 0 (able to carry out all normal activity without

restriction) or 1 (restricted in strenuous activity but ambulatory and able to carry out light work)
4. Access to telephone (safety and timely communication)
5. Capacity to give informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
1. Close physical contact with at risk individuals (children under 5yrs, immunosuppressed adults) - minimise risk of pneumococcal transmission
2. History of drug or alcohol abuse (frequently drinking over the recommended alcohol intake limit: men and women should not regularly drink > 3-4 units/day and >2-3 units/day respectively) – minimise risk of pneumococcal disease
3. Smoking any cigarettes currently or within the last six months - minimise risk of pneumococcal disease
4. Ex-smoker with a significant smoking history (>10 pack years) – minimise risk of pneumococcal disease
5. Any current treatment for asthma – confounding effect of medications such as corticosteroids, and propensity to infection
6. Taking daily medications that may affect the immune system e.g. steroids, steroid nasal spray, antibiotics, disease modifying anti-rheumatoid drugs
7. Any acute illness (new symptoms within preceding 14 days which are unexplained by the known past medical history)
8. Having received any antibiotics in the preceding 28 days
9. Taking medication that affects blood clotting e.g. aspirin, clopidogrel, warfarin or other oral or injectable anticoagulants
10. History of culture-proven pneumococcal disease
11. Allergy to penicillin/amoxicillin
12. Involved in another clinical trial unless observational or in follow-up (non-interventional) phase.
13. Have been involved in a clinical trial involving EHPC and bacterial inoculation in the past three years
14. Significant cardiorespiratory disease (excluding stable hypertension)
15. Disease associated with altered immunity, including diabetes, alcohol abuse, malignancy, rheumatological conditions
16. Taking any medications except those on the “allowed list”:statins; antihypertensives in stable hypertension; antidepressants; bisphosphonates; treatment for benign prostatic hyperplasia; hormone replacement therapy; vitamin supplements (including multivitamins, iron); anti-acid medications; nicotine replacement therapy (NRT)

Date of first enrolment
06/06/2016

Date of final enrolment
01/09/2017

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Royal Liverpool University Hospital
Prescot Street
Liverpool
United Kingdom
L3 5QA

Sponsor information

Organisation
Liverpool School of Tropical Medicine

Organisation
Royal Liverpool & Broadgreen University Hospitals Trust

Organisation
Liverpool School of Tropical Medicine

ROR
https://ror.org/03svjbs84

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
Data requests should be submitted to the EHPC co-ordinator (Catherine.Molloy@lstmed.ac.uk); these are considered by the programme 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
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes