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Experimental Human Pneumococcal Carriage: Asthma and immune function

Submission date
21/11/2016

Recruitment status
No longer recruiting

Registration date
15/12/2016

Overall study status
Completed

Last Edited
31/10/2017

Condition category
Respiratory

[ ] 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 meningitis, 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. Studies have shown that people with asthma have a higher chance of developing pneumonia due to this bacteria. The aim of this study is to find out if experimental human pneumococcal carriage is possible in people with asthma and to see if it effects their immune systems.

Who can participate?
Adults aged 18-50 years with mild, well controlled asthma,

What does the study involve?
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 (inoculation), and then secretions are collected and blood samples taken. Those who carry the bacteria will be invited to repeat this after 6-12 months to see if they have developed natural immunity. Participants are asked to report any early signs of infection, we provide a thermometer and antibiotics to identify and treat infection early. The research team is available 7 days a week and provides access to healthcare if needed. In the second part of the study, a sub-set of participants from the first part are invited back to be inoculated again. They then have samples taken on days 2, 7, 9, 14, 22 and 29 to assess their immune response

What are the possible benefits and risks of participating?
There are no direct benefits involved with participating. There is a small risk that asthma could be made worse or participants may experience an infection.

Where is the study run from?
Liverpool School of Tropical Medicine (UK)

When is the study starting and how long is it expected to run for?
September 2015 to April 2019

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

Who is the main contact?
Dr Seher Zaidi
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Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
20857

Study information

Scientific Title
Experimental Human Pneumococcal Carriage Model (Programme Grant):The effect of asthma on immune response to pneumococcus

Study objectives
In adults with asthma nasal inoculation with Streptococcus pneumoniae leads to lower rates of acquisition and lower density of nasopharyngeal carriage compared with healthy adults.

The aim of this study is to:
1. Determine the rate of experimental human pneumococcal carriage acquisition in people with asthma
2. Study the systemic and mucosal immune responses over time following experimental human pneumococcal challenge and carriage in people with asthma and compare with previous results seen in healthy adults. Immunological measurements will include antibody levels and function (opsonophagocytic killing assays) from serum and nasal washes, inflammatory cell populations and cytokine profiles at the nasal mucosal surface.
3. Determine the protective effect of carriage against reacquisition of carriage following re-inoculation with pneumococcus in people with asthma

Ethics approval required
Old ethics approval format

Ethics approval(s)
Liverpool East Ethics Committee, 18/03/2016, ref: 16/NW/0124

Study design
Randomised; Interventional; Design type: Prevention, Vaccine, Cellular

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Specialty: Respiratory disorders, Primary sub-specialty: Respiratory disorders; UKCRC code/ Disease: Respiratory/ Acute upper respiratory infections

Interventions
In the first part of the study, adults aged 18-50 years with asthma who are non-smokers will be inoculated with pure culture of one well-characterised, fully sequenced penicillin-sensitive pneumococcal serotype (6B). Nasal and serum samples will be collected at different time points (days 2, 7, 9, 14, 22 and 29) to assess the immune response. Participants will keep a record of their peak expiratory flow rate as well.

In the second part of the study, a subset of volunteers will be invited for a re-challenge with the 6B strain at 80,000CFU/naris. Nasal and serum samples will be collected at different time points (days 2, 7, 9, 14, 22 and 29) to assess the immune response.

Intervention Type
Other

Primary outcome(s)
Detection of S. pneumoniae by classical bacteria culture methods from one or more nasal wash samples collected following initial pneumococcal challenge at days 2, 7, 9, 14, 22 and 29.

Key secondary outcome(s))
1. Duration and density of pneumococcal carriage in people with asthma is measured using microbial culture at days 2, 7, 9, 14, 22 and 29.
2. Rates of experimental human pneumococcal carriage among people with asthma at BTS treatment step 2 and 3 is measured using microbial culture at days 2, 7, 9, 14, 22 and 29.
3. Protective effect of initial carriage on the reacquisition of carriage after a second inoculation is measured using microbial culture at days 2, 7, 9, 14, 22 and 29

Completion date
20/04/2019

Eligibility

Key inclusion criteria
1. 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)
2. Fluent spoken English - to ensure a comprehensive understanding of the research project and their proposed involvement
3. Access to their own mobile telephone (safety and timely communication)
4. Capacity to give informed consent
5. Adults aged 18-50 years, with a physician diagnosis of asthma; BTS treatment step 2 and 3 (see Appendix 1)
6. No exacerbations requiring antibiotics or oral steroids within the last 28 days
7. Spirometry: Forced Expiratory Volume in one second >70% predicted

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
50 years

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 more than 14 units of alcohol per week. – 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 (For loose tobacco: ounces per week × 2/7 × number of years smoked = pack years(22))
5. Taking regular daily medications that may affect the immune system e.g. oral steroids, steroid nasal spray, antibiotics, and disease-modifying anti-rheumatoid drugs.
6. Any acute illness (new symptoms within preceding 14 days which are unexplained by the known past medical history)
7. Having received any antibiotics, oral steroids or nasal steroid spray in the preceding 28 days
8. More than 1 asthma exacerbation in the last twelve months (Asthma exacerbation defined as an acute episode of progressive worsening of symptoms of asthma, including shortness of breath, wheezing, cough, and chest tightness, or a decline in objective measure such as peak expiratory flow rates of more than 30 percent requiring treatment with oral corticosteroids for a period of 3 days or more)
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. Currently 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, and asthma at treatment step 2 and 3)
15. Disease associated with altered immunity, including diabetes, alcohol abuse, malignancy, rheumatological conditions
16. Pregnancy
17. Taking any medications except those on the “allowed list”. The “allowed medications” list encompasses mediations which will not cause significant alteration to our measures of immune function, and which are used in the treatment of co-morbidities. These are: statins; anti hypertensives 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), inhaled steroids upto 800 micrograms BDP equivalent per day, inhaled beta 2 agonists and leukotriene receptor antagonist.

Date of first enrolment
01/06/2016

Date of final enrolment
30/09/2018

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Royal Liverpool University Hospital
Prescot Street
Liverpool
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Sponsor information

Organisation
Liverpool School of Tropical Medicine

ROR
https://ror.org/03svjbs84

Funder(s)

Funder type
Research council

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
The datasets generated during and/or analysed during the current study will be stored in a publically available repository, this will be completed at the end of the study.

IPD sharing plan summary
Stored in repository

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