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Experimental human pneumococcal carriage

Submission date
01/08/2016

Recruitment status
No longer recruiting

Registration date
25/08/2016

Overall study status
Completed

Last Edited
12/09/2023

Condition category
Infections and Infestations

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Pneumonia is a serious disease which causes swelling (inflammation) in the lungs and is usually caused by a pneumococcus bacterial infection. It is a major cause of death in children under five around the world. There are more than 90 different strains of pneumococcus and currently vaccines only cover around 13. In addition, strain replacement is also occurring, which means that the strains that used to cause disease that we now vaccinate against are being replaced by other strains for which we have no vaccine. There is therefore an urgent need for new vaccines. In most people pneumococcus can occasionally be found harmlessly inhabiting the nose where it does not cause any problem (pneumococcal carriage). About 10% of adults carry pneumococcus at any one time, and almost all adults experience an episode of carriage at least once per year. Carriage acts as a natural vaccine, boosting immunity against pneumococcal infection in adults and children. In order to develop an effective vaccine against pneumonia, it is important to understand how pneumococcal carriage acts to boost immunity. The aim of this study is to inoculate (place in the nose) people with varied doses of pneumococcal bacteria to determine the optimum dose for carriage (dose-ranging study) and then reproduce these findings in sufficient participants to be sure that we have a reproducible method (reproducibility study).

Who can participate?
Healthy adults who speak English fluently.

What does the study involve?
120 healthy participants (who have no current pneumococcal carriage) receive a small dose of live pneumococcal bacteria into each nostril, at a range of different concentrations. Six groups of participants are inoculated with a strain called serotype 23F and 60 with a strain called serotype 6B. After 48 hours and one week and 4 weeks, participants have samples taken from their nose to monitor the presence or absence of pneumococci. At 48 hours and four weeks, participants also have samples of blood and urine taken, as well as having a throat swab and samples taken from the lungs during a bronchoscopy and lavage (where a camera inserted into the lungs via the nose and the a small segment of the right lung is washed before cells are collected) procedure. If a participant becomes a carrier, they are given a three day course of antibiotics at the end of the study to ensure that the pneumococcus has been cleared.
60 additional participants are later recruited and randomly allocated to receive an inoculation of either serotype 23F or 6B, the concentration to use is determined from the first part of the study. After 48 hours and one week and 4 weeks, participants have samples taken from their

nose to monitor the presence or absence of pneumococci. At 48 hours and four weeks, participants also have samples of blood and urine taken, as well as having a throat swab and samples taken from the lungs during a bronchoscopy and lavage.

What are the possible benefits and risks of participating?
There are no significant benefits to being involved in the study. Risks are related to blood tests, bronchoscopy (camera into the lungs via the nose) and inoculation (live bacteria put into the nose). Blood tests may cause minor pain or bruising. Inoculation carries a risk of infection including meningitis, pneumonia (chest infection, otitis media (ear infection) or sinusitis. Bronchoscopy carries a risk of chest pain, fever, infection, allergic reaction to sedation or anaesthetic throat spray, coughing up a small amount of blood, sore nose, sore throat, nose bleed, aspiration pneumonia (vomit going into your lungs if not starved of food and fluid before the bronchoscopy), cardiac arrhythmia (unusual heart rhythm and rate), and hoarse voice.

Where is the study run from?
1. Royal Liverpool Hospital (UK)
2. Liverpool School of Tropical Medicine (UK)

When is the study starting and how long is it expected to run for?
April 2011 to January 2013

Who is funding the study?
Bill and Melinda Gates Foundation (USA)

Who is the main contact?
Dr Andrea Collins

Contact information

Type(s)
Scientific

Contact name
Dr Andrea Collins

Contact details
Liverpool School of Tropical Medicine
Pembroke Place
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United Kingdom
L3 5QA

Additional identifiers

Protocol serial number
11731

Study information

Scientific Title

Can Experimental Pneumococcal Carriage in healthy volunteers be established – what dose and strain is best?

Study objectives
The aim of this study is to determine an optimum inoculum dose of pneumococcal bacteria to develop experimental carriage.

Ethics approval required
Old ethics approval format

Ethics approval(s)
North West 3 REC - Liverpool East, 11/10/2011, 11/NW/0592

Study design
Non-randomised study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Specialty: Infectious diseases and microbiology, Primary sub-specialty: Antimicrobial therapy

Interventions
Dose ranging study:
120 healthy adult volunteers are allocated into 10 groups of 10, and are inoculated with 0.1ml pneumococci (well-characterised penicillin sensitive) to each nostril, 60 participants will be inoculated with serotype 23F and 60 with 6B.

Group 1: Participants are inoculated with 0.1ml pneumococci, serotype 23F at a concentration of 1x104 cfu/nostril
Group 2: Participants are inoculated with 0.1ml pneumococci, serotype 23F at a concentration of 2x104 cfu/nostril
Group 3: Participants are inoculated with 0.1ml pneumococci, serotype 23F at a concentration of 4x104 cfu/nostril
Group 4: Participants are inoculated with 0.1ml pneumococci, serotype 23F at a concentration of 8x104 cfu/nostril
Group 5: Participants are inoculated with 0.1ml pneumococci, serotype 23F at a concentration of 1.6x105 cfu/nostril
Group 6: Participants are inoculated with 0.1ml pneumococci, serotype 23F at a concentration of 3.2x105 cfu/nostril
Group 7: Participants are inoculated with 0.1ml pneumococci, serotype 6B at a concentration of 1x104 cfu/nostril
Group 8: Participants are inoculated with 0.1ml pneumococci, serotype 6B at a concentration of 2x104 cfu/nostril
Group 9: Participants are inoculated with 0.1ml pneumococci, serotype 6B at a concentration of 4x104 cfu/nostril
Group 10: Participants are inoculated with 0.1ml pneumococci, serotype 6B at a concentration of 5x104 cfu/nostril

Group 11: Participants are inoculated with 0.1ml pneumococci, serotype 6B at a concentration of 1.6x105 cfu/nostril
Group 12: Participants are inoculated with 0.1ml pneumococci, serotype 6B at a concentration of 3.2x105 cfu/nostril

An additional 20 participants are inoculated with 0.1ml 0.9% saline solution (control)

Saliva, blood, urine, nasal wash, throat swabs are taken at screening. Urine, nasal wash, throat swab are taken at day 2 post inoculation. Nasal wash is taken 7 days after inoculation. Saliva, blood, urine, nasal wash are taken in week 4.
Volunteers will have a total duration of observation and follow up of up to 20 weeks.

Reproducibility study:
60 additional volunteers are recruited and randomly allocated to be inoculated with one of the 2 serotypes (serotype 23F and 6B, 30 in each group). The concentration will be determined by the results of the dose ranging study.

Saliva, blood, urine, nasal wash, throat swabs are taken at screening. Urine, nasal wash, throat swab are taken at day 2 post inoculation. Nasal wash, blood, urine is taken 7 days after inoculation and again at week 4, 5 and 6. At week 7-9 Saliva, blood, urine, nasal wash are taken. Bronchoscopy (and BAL) is optional are performed after week 7-9 after antibiotics have been completed. A final blood sample is taken at week 10-20.
Volunteers will have a total duration of observation and follow up of up to 20 weeks.

Intervention Type
Other

Primary outcome(s)
Presence of pneumococci is measured using classical culture methods in nasal wash at 48 hours and/or 7 days following inoculation.

Key secondary outcome(s))
No secondary outcome measures

Completion date
04/01/2013

Eligibility

Key inclusion criteria
1. Adults aged 18-60 years old
2. Fluent English spoken

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
60 years

Sex
All

Key exclusion criteria
1. Close contact with young children, elderly or immunocompromised individuals (either at work or home)
2. Asthma or pre-existing lung disease
3. Cigarette smoking of greater than 20 pack years
4. Chronic illness
5. Pregnancy
6. Penicillin allergy

Date of first enrolment
21/10/2011

Date of final enrolment
08/12/2012

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Royal Liverpool Hospital
Prescot Street
Liverpool
United Kingdom
L7 8XP

Study participating centre
Liverpool School of Tropical Medicine
Pembroke Place
Liverpool
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L3 5QA

Sponsor information

Organisation
Royal Liverpool Hospital

ROR
https://ror.org/01ycr6b80

Funder(s)

Funder type
Charity

Funder Name
Bill and Melinda Gates Foundation

Alternative Name(s)
Bill & Melinda Gates Foundation, Gates Foundation, Gates Learning Foundation, William H. Gates Foundation, BMGF, B&MGF, GF

Funding Body Type
Government organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	15/02/2013		Yes	No
Results article	results	01/03/2013		Yes	No
Results article	results	15/04/2013		Yes	No

Results article	results	01/12/2014		Yes	No
Results article	results	15/12/2014		Yes	No
Results article	results	15/12/2016		Yes	No
Results article		10/03/2020	12/09/2023	Yes	No
Results article		05/06/2018	12/09/2023	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes