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Understanding how two common respiratory infections interact in the nose of healthy adults: Respiratory Syncytial Virus and Streptococcus pneumoniae

Submission date
11/10/2023

Recruitment status
No longer recruiting

Registration date
19/10/2023

Overall study status
Completed

Last Edited
02/07/2025

Condition category
Infections and Infestations

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

Plain English summary of protocol

Background and study aims
This study is looking at two different germs: a bacterium called Streptococcus pneumoniae ('pneumococcus', Spn) and a virus called Respiratory syncytial virus (RSV). These germs can cause a variety of symptoms from cold-like illnesses to chest infections or sepsis. When someone is exposed to both, which is very common in winter, it might affect how likely they are to develop an infection or how serious their symptoms are. It is important to understand this relationship better so that future studies on treatments or vaccines can be performed.

The study aims to understand how RSV and pneumococcus interact in the nose of healthy adult volunteers. The knowledge generated in this project could be used to help develop new interventions such as anti-virus agents and drugs targeting the host body response.

Who can participate?
Healthy volunteers aged 18 - 55 years.

What does the study involve?
If you are eligible and decide to take part, you would be deliberately exposed in safe and controlled conditions to either RSV or pneumococcus first through drops in the nose. After this, participants will receive the other infection seven days later. Participants will be asked to self-isolate at home or remain in a medical facility after RSV exposure for up to 10 days to reduce the risk of transmission to others. You would also have samples taken during clinical visits to assess immune response to the germs and you would be required to complete a short online diary for 21 days after exposure.

What are the possible benefits and risks of participating?
You will be a valuable part of a research study that we hope will eventually lead to the development of new methods to prevent or treat respiratory infections. The risks from sample collection are limited to localised discomfort at the site of nasal sampling and discomfort and

bruising at the site of blood sampling. Because you will be exposed to live RSV or pneumococcal bacteria there is a small risk of infection to you or your close contacts. Both germs have been used in previous studies in healthy adults with no serious side effects. You may however get cold-like symptoms, headaches, earaches, a cough or a fever. We will provide a safety pack as described above and you will have 24-hour access to the research team by phone.

Where is the study run from?
University of Oxford (UK)

When is the study starting and how long is it expected to run for?
October 2023 to December 2025

Who is funding the study?
Pfizer Inc. (USA)

Who is the main contact?
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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
327739

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 56008, 70999117

Study information

Scientific Title
Understanding how two common respiratory infections interact in the nose of healthy adults: Respiratory Syncytial Virus and Streptococcus pneumoniae

Acronym
RESPECCT

Study objectives
In this study we propose to evaluate pathogen interaction dynamics and immune responses in a combined pneumococcal (Spn) and RSV controlled human infection model. Better understanding of respiratory infections synergy, transmission and associated nasal immunity can unlock the potential for indirect protection by vaccination to reduce mortality, morbidity and costs associated with pneumonia in at-risk groups in the UK and globally.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 19/10/2023, East of England – Cambridge South REC (Equinox House, City Link, Nottingham, NG2 4LA, United Kingdom; +44 207 104 8194; cambridgesouth.rec@hra.nhs.uk), ref: 23/EE/0219

Study design
Interventional randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Other

Participant information sheet
Available from trial website

Health condition(s) or problem(s) studied
Respiratory infections, respiratory syncytial virus and pneumococcus

Interventions
The study has a follow-up duration of 60 days and up to 9 clinical visits during that period.

In Phase A: Up to 10 Healthy volunteers will be challenged with either Spn6B or RSV-A at day 0 followed by a reciprocal challenge (RSV-A or Spn6B) at day 7. Participants will be subject to confinement for 7-10 days after either primary or secondary RSV-A inoculation within a dedicated clinical research facility. This is to facilitate monitoring by a resident clinically trained member of the research team. During this phase we will assess safety of the co-infection model and confirm the self-isolation protocols.

In Phase B/C: Up to 103 healthy volunteers will be challenged with either Spn6B or RSV-A at day 0 followed by a reciprocal challenge (RSV-A or Spn6B) at day 7. Participants will self-isolate at

home for 7-10 days after either primary or secondary RSV-A challenge, following self-isolation protocols validated within Phase A.

Phase A will also determine if it is feasible to proceed to Phase B without pre-screening for pre-existent levels of IgG to RSV. If fewer than 2 volunteers are infected with the challenge virus in Phase A, then Phase C will be conducted instead of Phase B. Phase C will be identical to Phase B, but the study population will be pre-screened for RSV neutralizing antibody titres.

In both phases longitudinal testing for pathogen detection will occur at 2, 7 and 14 days after challenge (final samples 60 days after primary challenge). Participants will be asked to visit our outpatient facility (wearing FFP2 masks and avoiding public transport) for sampling. The following samples will be collecting during the visits: nasal cells (small scrapes taken inside the nose); nasal washes (whereby the nose is irrigated with normal saline and the liquid that is produced is collected and analysed); blood samples (for immunological testing); shedding samples (participants will be asked to cough onto a culture plate and rub their nose onto their hand, to see how the bacteria/Virus is shed from the nose); viral throat swab; nasosorption (participants will have small pieces of filter paper inserted into nostrils for maximum of 2-3 minutes); exhaled detection facemask (participants wear a facemask so that it covers their nose and mouth for 15-60 minutes during which time they can talk freely); saliva samples (participants will spit into a tube).

For both phases volunteers will be challenged with either Spn6B or RSV-A at day 0 followed by a reciprocal challenge (RSV-A or Spn6B) at day 7. After inoculation participants will be given a safety pack containing Thermometer, Safety Informaton leaflet, Study ID card and antibiotics. Participants will be asked to contact members of the team every day for 5 days with their temperature and how they are feeling. Throughout the study, participants will have access to a 24/7 on-call telephone service which they can contact.
Vital signs assessment and Clinical review of symptoms will occur at each visit. Sera and PBMcs samples for immunology will be collected at screening and days 6, 14 and 60 after primary inoculation. Blood for genomics will be collected at Day 0 and days 2, 7 and 9 after primary inoculation. Nasosorption samples will be collected at day 0 and days 2, 6, 7, 9 14 and 21 after primary inoculation. Nasal swab will be collected at screening, day 0 and days 2, 6, 7, 9 14 and 21 after primary inoculation. Nasal wash, Nasal cells, throat swab and saliva will be collected at screening and days 2, 6, 9, 14, 21 and 60 after primary inoculation. Shedding samples will be collected at days 2, 6, 9 and 14 after primary inoculation. Finally breath samples will be obtained at day 6 and 14 after primary inoculation.
At visit 0, participants will be trained in self-sampling. The samples will be conducted at the participant place of residence during their confinement/self-isolation phase. To ensure samples are collected within 15 minutes of the planned time participants will be asked to photograph the sample and send with a text. Samples will be stored at home in a biohazard-appropriate packaging (supplied by the research team) in a freezer. Self test will include: nasal swab, nasosorption and symptom diary.
For both phases of the study, at the end of day 21, if a participant has been colonised with Spn6B at any time point and have not had two subsequent, consecutive negative samples, they will be asked to take 3 day course of amoxicillin.

Intervention Type
Biological/Vaccine

Pharmaceutical study type(s)
Not Applicable

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Respiratory syncytial virus, pneumococcus

Primary outcome measure
Presence of Spn6B detected by classical microbiology in at least one nasal wash sample at any timepoint following Spn6B challenge: e.g Day 2, Day 6, Day 9, Day 14, Day 21 and Day 60

Secondary outcome measures
1. Absence of SAEs measured in Phase A before progression to Phase B: Timepoints: Day 2, Day 6, Day 9, Day 14, Day 21 and Day 60
2. Presence of Spn6B detected by RT-qPCR in at least one nasal wash sample at any timepoint following Spn6B challenge: e.g Day 2, Day 6, Day 9, Day 14, Day 21 and Day 60
3. Presence of Spn6B detected by combined RT-qPCR and classical microbiology in at least one nasal wash sample at any timepoint following Spn6B challenge: e.g Day 2, Day 6, Day 9, Day 14, Day 21 and Day 60
4. Spn6B density detected by combined RT-qPCR and classical microbiology in nasal wash sample at any timepoint following Spn6B challenge: e.g Day 2, Day 6, Day 9, Day 14, Day 21 and Day 60
5. Spn6B presence and density detected by combined RT-qPCR and classical microbiology in nasal wash sample at any timepoint following Spn6B challenge: e.g Day 2, Day 6, Day 9, Day 14, Day 21 and Day 60
6. Presence of RSV-A detected by RT-qPCR in at least one nasal wash sample at any timepoint following RSV-A challenge: e.g Day 2, Day 6, Day 9, Day 14, Day 21 and Day 60
7. RSV-A presence and viral load detected by RT-qPCR in nasal wash sample at any timepoint following RSV-A challenge: e.g Day 2, Day 6, Day 9, Day 14, Day 21 and Day 60
8. Number of URTI and LRTI symptoms per participant after secondary challenge. Timepoints: Day 9, Day 14, day 21 and Day 60
9. Shedding of pathogens from the nose and throat will be assessed by:
9.1.Coughing plate (Spn6B colonies detected by classical microbiology after Spn6B challenge: timepoints D2, D6, D9 and D14).
9.2. Hand swab after nose touching (Spn6B colonies/DNA copies detected by classical microbiology and RT-qPCR after Spn6B challenge: timepoints D2, D6, D9 and D14).
9.3. Facemasks assessments (RSV viral load quantification by RT-qPCR Spn6B colonies/DNA copies quantification by classical microbiology and RT-qPCR; timepoints: D6 and D14)
10. Self-collected home samples (nasopharyngeal swabs) collected once per week for 2 weeks from household contacts will be analysed for RSV-A presence using RT-qPCR.

Overall study start date
11/10/2023

Completion date
31/03/2025

Eligibility

Key inclusion criteria
1. Healthy adults aged 18-55 years (inclusive, at the time of consent)
2. Fluent spoken English – to ensure a comprehensive understanding of the research project

3. Capacity to provide written informed consent in English
4. Females of childbearing potential with a negative urine pregnancy test at screening and willing to practice adequate contraceptive measures as per UK Clinical Trial Facilitation Group during the study.
5. Willing to provide their household contacts with the Close Contact Screening Information Letter
6. For Phase C, RSV neutralising antibody titre in the lowest 10th percentile of screened participants

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
55 Years

Sex
Both

Target number of participants
Planned Sample Size: 113; UK Sample Size: 113

Total final enrolment
111

Key exclusion criteria
1. Research participant:
1.1. Currently involved in another study unless observational or non-interventional. Exceptions may be applied at the discretion of the Chief Investigator to ensure no harm comes to the participants (e.g. excessive blood sampling or nasal sampling)
1.2. Participated in a previous Spn6B EHPC study < = 3 years or an Spn3 EHPC study < = 1 year before screening
2. Unable to travel to outpatient clinic for visits without using public transport
3. Unable to wear an FFP2 mask
4. Nasal carriage: Participants who have natural pneumococcal or RSV-A nasal carriage identified at visit 1 will be excluded before randomisation (see table 2A).
5. Vaccination:
5.1. No live vaccination within four weeks prior to enrolment (defined as time of first inoculation)
5.2. Previous pneumococcal or (investigational) RSV vaccination (including in a research study)
6. Allergy to beta-lactam antibiotics (including penicillin and amoxicillin)
7. Medical history leading to increased risk of severe infection, illness including but not limited to:
7.1. Asplenia or dysfunction of the spleen
7.2. Chronic respiratory disease (e.g. asthma [requiring medication (including salbutamol inhaler) within last 12 months], COPD, bronchiectasis and sleep apnoea)
7.3. Chronic heart disease (e.g. angina, ischaemic heart disease, chronic heart failure) –

controlled and stable hypertension may be included
7.4. Chronic kidney disease (e.g. nephrotic syndrome, kidney transplant, requires dialysis)
7.5. Chronic liver disease (e.g. cirrhosis, biliary atresia, hepatitis)
7.6. Chronic neurological disease that limits mobility, bulbar or respiratory function (including stroke, Parkinson's disease, dementia and multiple sclerosis)
7.7. Diabetes mellitus (including diet controlled)
7.8. Receipt of immunosuppressive therapy such as anti-cancer chemotherapy or radiation therapy within the preceding 12 months or long-term systemic corticosteroid, Roaccutane, or disease modifying anti-rheumatoid drugs therapy (for more than 7 consecutive days within the 3 months prior to enrolment).
7.9. Individuals with cochlear ear implants
7.10. Individuals with major cerebrospinal fluid leaks (e.g. following traumatic, major skull surgery, or requiring CSF shunts)
7.11. Subjects with known or suspected immune deficiency (e.g. known IgA deficiency, immotile cilia syndrome, or Kartagener's syndrome)
7.12. History of frequent nose bleeds
7.13. Bleeding disorders
8. Current medical issues
8.1. Acute upper respiratory tract infection in the four weeks preceding recruitment (as per definition in Annex 1)
8.2. Any uncontrolled medical or surgical condition (e.g. mental health conditions, epilepsy, narcolepsy or chronic pain) at the discretion of the study doctor
9. Any major pneumococcal illness or pneumonia requiring hospitalisation in the last 10 years
10. Medication
10.1 Any medication that may affect the immune system in the last 3 months (e.g. systemic steroids [IM/IV], Roaccutane, disease modifying anti-rheumatoid drugs)
10.2 Long-term antibiotic use
10.3 Recipient of monoclonal antibodies for any indication
10.4 Recipient of blood transfusion products within the last year
10.5 Any medication that may affect the coagulation system in the last 3 months (excluding aspirin)
10.6 Use of any medication or other product (prescription or over-the-counter) for symptoms of rhinitis or nasal congestion within the last 1 month
11. Maternal
11.1. Female participants who are pregnant
11.2. Female participants who are lactating
11.3. Female participants who intend to become pregnant during the study
11.4. Female participants unable to take contraception measures during the study (from consent to final study visit at day 60)
12. Direct caring role or share living accommodation with individuals at higher-risk from infection
12.1. Children < = 3 years of age
12.2. Adults > 65 years old
12.3. Adults with chronic ill health or immunosuppression
12.4. Adults classified as clinically extremely vulnerable by the NHS
13. Health-care worker
14. Smoking
14.1. Current or ex-smoker (regular cigarettes/cigars/e-cigarette/vaping/smoking of recreational drugs) in the last 6 months
14.2. Previous significant smoking history (more than 5 cigarettes per day for 20 years or the equivalent [i.e. > 5 pack years]).
15. Current alcohol and recreational drug use
15.1. Regularly drinks > = 3units/day (male) or > = 2units/day (female)

15.2. Regularly uses recreational drugs
15.3. Participants may be excluded at the discretion of the research clinician
16. Significant mental health disorders: Uncontrolled condition or previous admission to a psychiatric unit (at the discretion of the research clinician) which would impair the participants ability to safely participate in the study
17. Overseas travel planned within the study period (60 days after primary challenge)
18. Participants FBC results do not meet the required criteria on screening bloods

Date of first enrolment
23/10/2023

Date of final enrolment
05/11/2024

Locations

Countries of recruitment
United Kingdom

Study participating centre
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ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Industry

Funder Name
Pfizer

Alternative Name(s)
Pfizer Inc., Pfizer Consumer Healthcare, Davis, Charles Pfizer & Company, Warner-Lambert, King Pharmaceuticals, Wyeth Pharmaceuticals, Seagen

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal

Intention to publish date
30/09/2025

Individual participant data (IPD) sharing plan
The current data sharing plans for this study are unknown and will be available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		01/07/2025	02/07/2025	Yes	No