Participant information sheet

Research: working towards a nasal vaccine for pneumonia

Exploring the effect of age on immunity against pneumonia

Would you like to take part in our research? This information leaflet tells you how you could take part. A member of our team will also discuss it with you: please ask us if you have questions. You may want to talk to other people about the study: please do so. Take your time to decide if you want to be involved.

What is the purpose of the study?

We are developing a new vaccine to protect against bacteria called **Pneumococcus.**

Small numbers of these bacteria are often found in the nose. Usually, the carrier does not know the bacteria are there. In most adults this is present at least once per year and more often in children. We think that small numbers of bacteria present in the nose ("nasal carriage") can help to protect people against disease.

Mild infections with pneumococcus are very common, such as ear infections in children. But pneumococcus can also infect the lung (causing pneumonia) or the brain (causing meningitis) or the blood (causing sepsis). These severe infections are very uncommon in healthy adults: about 50 cases in Liverpool per year. Very young children and adults who are elderly (mainly those who have other illnesses) are more likely to become ill.

We may be able to protect people against severe disease from pneumococcus using a vaccine which could be sprayed into the nose. We don't yet know if this will work.

To test the idea, our research team want to study what happens when small numbers of the bacteria are put up the nose of healthy volunteers. We have already studied this using more than 400 volunteers, and have found this type of study to be safe.

All of the volunteers we have studied so far have been less than fifty years of age. In order to develop a vaccine that will protect older people, we need to understand the immune responses to bacteria in adults aged over fifty.

Do I have to take part?

No. Taking part in this study is voluntary.

Why have I been asked to take part?

We are looking for volunteers who are fit and healthy. We check for reasons which may put you at higher risk from the study. We also make sure that your participation will provide helpful information to us. If we find any reason you may be at higher risk of infection, then we will not invite you to take part.

You will not be eligible if:

- You are aged less than 50 years
- You are a regular smoker or have a significant history of daily smoking
- You are in close contact with those who have lower immune levels (such as young children and people with chronic ill health)
- You have taken part in similar research before
- You are allergic to penicillin
- You have heart or lung disease
- The study doctor thinks that a health condition, or medication means that you are at increased risk of infection

What happens if I choose to take part?

1. **Health check** – for safety, we check that you are healthy. This includes a clinical assessment and checklist (as above).
2. **Consent** –We ask you to sign a consent form when you are sure you want to take part.
3. **Taking samples** – We take samples from the nose, throat and blood *(see below)*. We also do a heart tracing (ECG) and breathing test (spirometry)—again this is to check that you are healthy
4. **Being given drops of pneumococcus in the nose** - We put a few drops with a small numbers of bacteria up your nose
5. **Monitoring**– we will ask you to contact us daily (by phone or text) to make sure you are well
6. **Monitoring visits** – We take samples from your nose to see whether the bacteria is present.

Part one takes less than four weeks then after three to six months we will invite some participants to repeat this for part two.

A small number of participants may be allocated at random to receive drops of water in their nose rather than pneumococcus bacteria. This is called a **placebo**, and will help us determine if people develop symptoms (e.g. runny nose) *because* of the pneumococcus bacteria, or simply as a reaction to our other study procedures. You will not know if you have received pneumococcus or a placebo until the end of the study, and all participants will follow the same study protocol.

What kind of samples do you take?

Samples from the nose: To collect cells from your nose we place a small piece of blotting paper inside your nostril for a few minutes ("nasosorption"), and also run a small plastic rod along the inside of each nostril ("nasal probe"). We also perform a "nasal wash", where we squirt a little salty water into your nose. After a few seconds the water runs out into a sample bowl. This will tell us about the bacteria in your nose and your immunity.

Throat swab: we wipe the back of your mouth with a sterile swab (like a cotton bud). The laboratory can use this to find out if there are any bacteria or viruses.

Saliva samples: we will ask you to chew on a small sponge for two minutes. We can then test the saliva in the sponge for bacteria.

Blood samples: We take blood samples from a vein in your arm (using a needle). We will never take more than 50 mL (about the same as 10 teaspoons).

You may choose to allow the researchers to study the DNA from your blood sample. If you choose not to donate your DNA you may still take part in the study.

What will happen to my samples?

We will process your samples in laboratories at the Liverpool School of Tropical Medicine (LSTM) and at the Royal Liverpool University Hospital. We will measure the levels of bacteria and viruses in your nose, and we will look in detail at how your immune system responds to the pneumococcus bacteria.

To make full use of your samples, we will store the remainder. In the future, we can then go back to them with new tests to answer new questions. For some specialist tests, we may send samples to laboratories in the UK and abroad.

What will happen at each visit of Stage 1?

Visits 1 - 3:

Consent and screening check (spread over about two weeks)

First we will explain the study in detail, obtain your signed consent if you are happy to take part in the study, and ask some basic questions to ensure that you are eligible. We will also write to your GP to confirm some aspects of your medical history (e.g. what medications you are taking, and which vaccinations you have had before).

At the next visit, we make sure you are fit to take part in the study. We ask routine questions about your medical health, check your blood pressure, temperature and listen to your heart and lungs, perform a heart tracing (ECG), breathing test (spirometry) and blood test.

If you are well enough to take part in the study, we do the throat swab, saliva collection, nasal swab, the nasal wash, nasal probe and another blood test.

We then book your next appointments. If you have problems and can't come at a specific time, we can be flexible to accommodate you.

⇩ *Between one to seven days after Visit 3:*

Visit 4:

Being given pneumococcus up the nose

We collect a sample from your nose using blotting paper. We then use a dropper to put a small amount of water containing a small number of bacteria into each nostril. Usually, volunteers have no symptoms afterwards. There will be a doctor or nurse available by telephone 24 hours a day to answer questions. We will give you a course of antibiotics to keep with you, in case you are unwell, as well as a thermometer to check your temperature at home. ***Every day for the next week, we will need to be in contact with you by phone or text to check that all is well.***

⇩ *Up to six visits over the next five weeks*

Visits 5 - 10: Monitoring

At each visit, a number of samples will be taken, which may include throat swab, saliva collection, nasal swab, nasal wash, nasal probe and blood tests

⇩

End of Part 1 of the study

If our laboratory test finds that the pneumococcus bacteria stays in your nose, at this stage we will ask you to take a course of antibiotics to clear it, and we may ask you to be in part 2 of our study.

What about Part 2?

We think that having small number of bacteria in your nose—even for a short time—might protect you against illness from this bacteria, possibly for a long time. But we cannot be certain. To test this, we may ask you to have the pneumococcus put into your nose a second time, after 3 to 6 months. Y*ou do not have to take part in Part 2 if you do not want to*. In total, Part 2 visits will take about 2 to 3 weeks.

What will happen at each visit of Part 2?

Visit 1:

Screening check, consent, and taking samples

We make sure you are still fit to take part in the study, by repeating the questions and examination done at Part 1.

We do the throat swab, saliva collection, nasal wash, nasal probe and blood test.

⇩ *1-7 days later*

Visit 2: *Being given pneumococcus up the nose*	We use a dropper to put a small amount of water containing a small number of bacteria into each nostril, just like before. Each day for the next week we will ask you to contact the research team by phone or text for seven days to ensure that all is well and to check your temperature reading (again, antibiotics and a thermometer are provided in the study).
	⇩ *Daily phone call or text message. 2 days later:*
Visit 3: Monitoring	Throat swab, saliva collection, nasal wash and nasal probe
	⇩ *Daily phone call or text message. 5 days later:*
Visit 4: Monitoring	Throat swab, saliva collection, nasal wash and nasal probe
	⇩ *Up to 7 days later*
Visit 5: End of the study	At the end of Part 2, after a final throat swab, saliva collection, nasal wash and blood test, if our laboratory confirm that you have had pneumococcus in your nose, we will ask you to take the antibiotic course to clear it.

What are the risks of being in the study?

Risks of being given live bacteria

Because the bacteria are alive, there is a very small risk of infection to you or your close contacts. We do not expect anyone to develop an infection but this is why we choose participants carefully, and why we monitor them closely. We provide a thermometer and antibiotics that treat these bacteria. We give you a separate leaflet which explains the safety precautions, and what to do if you feel unwell. If you carry the pneumococcus bacteria in your nose at the end of the study, we will ask you to take the antibiotics to kill the bacteria.

Risks of medical tests during the study

The only side effect of nasal sampling is a little discomfort. Some people experience a runny nose. Some people can feel light-headed after blood tests, and sometimes may have a bruise.

What if there is a problem?

You can contact the research team 24 hours-a-day by phone. They will answer any questions, and an emergency service will be available day and night, including visits to your home if you are unwell and unable to come in to see us. Any medical care you need will be provided by the NHS.

What if I wish to complain?

If you wish to complain about any aspect of the study, you can contact the study doctor. The NHS complaints procedures are also available to you. Complaining will not affect the medical care you receive now or in the future.

What if I change my mind, or want to stop?

Even if you do start in the study, you are free to stop at any time and without giving a reason. If you decide not to take part, or to withdraw from the study, this will have no effect on your future health care.

If you decide to stop, we will continue to use the samples and information that we have already collected unless you tell us not to. You will be paid for the visits completed up to that point.

Will my details be kept confidential?

Yes. For safety, we collect information about your medical history and contact details before you take part. The clinical research team use this information to check you are healthy, and to contact you when needed. We will ask your permission to ask your GP to share some of your medical history with us.

We will also collect information which allows us to understand more about the samples, for example, you age or sex. However, those outside of the clinical team are never given information that can identify you. Your samples are given a unique number, and your name is not used.

We do not expect to find anything which would affect your health care. If we do, we will let you and your GP know about it.

All data will be collected and stored at the Royal Liverpool University Hospital and the Liverpool School of Tropical Medicine. It will be stored for a minimum period of 10 years. Your medical notes and research data are may be looked at by those who monitor the research.

What are the benefits of taking part?

There are no direct benefits to you. You will be a part of what we believe is a valuable research study that may help us to improve medical care for others.

How much will I get paid?

The money you are paid is compensation for inconvenience, loss of income, and possible discomfort of taking part. The first payment will be made at the end of part one. If you are eligible and choose to take part in the second study you will receive a second payment at the end of part two. If you receive a placebo instead of pneumococcus, the payment is unchanged. Our payments are listed below:

Part 1	Visit length	
Visit 1: Study information, signing consent	45 min	-
Visit 2: Health check, screening and samples	60 min	£40
Visit 3: Screening and samples	30 min	£30
Visit 4: Having pneumococcus put up your nose. This includes you making daily telephone/text message contact for the first 7 days. (We will withhold £5 per day if you do not contact us)	30 min	£50
Visits 5 and 6: Nasal samples, throat swab and blood samples	30 min	£20
Visit 7: Nasal samples and throat swab	20 min	£15
Visits 8 and 9: Nasal wash and throat swab (*not all participants will be called for visit 9)*	15 min	£10
Visit 10: Nasal samples, throat swab and blood samples	25 min	£20
Part 2		
Visit 1: Screening and samples from the nose and blood	45 min	£30
Visit 2: Having pneumococcus put up your nose, and follow-up, as above	60 min	£50
Visits 3, 4 and 5: Nasal samples, saliva collection and throat swab	15 min	£15

Contact details

General questions: please contact the research team on 0151 706 3381

The Chief Investigator for this study is Dr Jamie Rylance. You may contact him at the Liverpool School of Tropical Medicine, Pembroke Place, Liverpool, L3 5QA, UK. Telephone: 0151 705 3775.
This research is sponsored by the Liverpool School of Tropical Medicine and the Royal Liverpool and Broadgreen University Hospitals. It is funded by the Medical Research Council. The research has been reviewed for scientific content by an external panel.
The National Research Ethics Service Committee has reviewed the study and given approval for it to take place.