Participant Information Sheet: Nose and Throat Study (Group 2)

Early and late nasal and tonsil cell responses during human pneumococcal colonisation

Research working towards developing new vaccination in the prevention of pneumonia

This information leaflet tells you why this research is being done and what it will involve. 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 this study?

We are researching a bacteria called pneumococcus. We think that small numbers of bacteria present in the nose ("nasal carriage") may protect people against disease. Small numbers of these bacteria are often found in the nose of healthy adults (at least once per year) and more often in children. Usually, the carrier does not know the bacteria are there but in some people it can cause illness. Mild infections with pneumococcus are very common, such as ear infections in children. Pneumococcus can also infect the lung (causing pneumonia); more severe infections of the brain (causing meningitis) or the blood (causing sepsis) are very uncommon in healthy adults: about 50 cases in Liverpool per year. Very young children and adults who are elderly or those who have other illnesses are more likely to become ill.

For the purpose of this study we will put small number of the bacteria in the nose of volunteers similar to the amount commonly carried by healthy adults. This will allow us to learn about the protective mechanism that occur in the nasal lining and use this later in the development of new vaccine against pneumonia.

More than 700 volunteers have already been studied safely using this method of putting bacteria in the nose.

Do I have to take part?

No. Taking part in this study is voluntary.

Why have I been asked to take part?

If you have consented to have surgery and general anaesthesia for nasal procedure, we would like to invite you to take part in research. We are looking for volunteers who are fit and healthy that are undergoing nasal surgery planned by their doctor who would be happy to have additional tissue samples taken from the nose and the tonsil. 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. We will also check for natural carrier of the pneumococcus bacteria in the nose at the initial screening visit. Participants that are natural carriers at screening (approximately 10-15%) will be excluded from taking part in the study.

You will not be eligible if:

- You are younger than 18 or older than 50
- you are a regular smoker or have a significant history of daily smoking
- you have taken part in pneumococcal carriage studies in the last three years or other research that may be relevant
- you are allergic to penicillin or amoxicillin
- you are in close contact with those who have lower immune levels (such as immunosuppressed adults, young children and the elderly)
- the study doctor thinks that a health condition, or medication means that you are at increased risk of infection or that the medication may affect study results for example steroids or long term antibiotics
- Asthma or respiratory disease
- If you are pregnant or not using appropriate birth control
- Previous tonsillectomy

To prevent the risk of infection women are required to have a negative pregnancy test before taking part. Either adequate contraception or abstinence from sexual activity during the study is advised. If you do become pregnant then please advise the study doctor.

What happens if I choose to take part?

Consent – you will be invited to discuss the study with a member of the research team. When you have read this information and if you then decide to take part we will ask you to sign a consent form when you are sure you want to take part.

Health check – for safety, we check that you are well. This includes a clinical assessment (listening to your heart and lungs) and ask questions to check the list above. We will request some information from your GP relevant to the study to ensure it is safe for you to take part. We will send a sample of blood to check your immunity. If the GP summary care records are available electronically in the hospital, we will ask you permission to access the data.

Bacteria in the nose – a small amount of live pneumococcus bacteria is dropped into the nose to mimic the amount commonly found in healthy adults. We will ask you to contact us daily to make sure you are well for a week. And ask you to let us know of any other symptoms during the follow up period.

Monitoring visits – We take samples from the nose and throat to see whether the bacteria is present, also blood samples as below. We provide a plan of the schedule.

What kind of samples do you take?

We collect nasal and blood samples to look at the immune response and bacteria in the nose.

Nasal Wash: we gently 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.

Blood samples: We take blood samples from a vein in your arm (using a needle). We will take up to 50 mL (about the same as 10 teaspoons) over a four-week period this will be up to five occasions.

Nasal mucosal lining sample:

We collect two types of nasal lining samples.

1) Nasal cells- we insert a very small plastic spoon (similar to a tooth pick) into the inner surface of the nose that is withdrawn in a sweeping motion to collect small cells. We will do this on up to three occasions.

2) Nasal tissue sampling - up to two small tissue samples approximately 2-4 mm (about the width of one matches) are taken by the doctor from the nasal lining. To make this more comfortable we will numb the area explained below.

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

Tonsillar tissue sample:

This will be done at the time of your planned nasal surgery while you are asleep (anesthetised). Small tissue sample 2-4 mm (about the width of one matches) will be obtained from one of your tonsil while you are having your nasal surgery.

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 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 ask that you "gift" your samples to LSTM. We will store them so that in the future, we can 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.

Visit 1:	**Health check and samples:** 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. We do the nasal wash and scrapes and a blood test. For women, we check that you are not pregnant using a urine test. *We book your next appointments. If you have problems and can't come on a specific date, we can be flexible to accommodate you.*
	⇩ *between 1 to 7 days later*
Visit 2:	**Being given pneumococcus in the nose:** we use a dropper to put a small amount of water containing a small number of bacteria into each nostril. **Safety:** 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. Each day for **the next week** we will ask you to **contact the research team by phone or text** to ensure that all is well and to check your temperature (a thermometer is provided).
	⇩ *Daily phone call or text. Then 2 days later…*
Visit 3:	**Monitoring:** nasal wash and scrapes and blood sample
	⇩ *Continue with a daily text. Then 5 days later*
Visit 4:	**Monitoring*:*** nasal wash and bloods
	⇩ *One week later*
Visit 5:	Monitoring: nasal wash and scrapes and bloods *You will receive phone call to let you know if you need to and when to start taking the oral antibiotics Amoxicillin 500 mg three times per day for three days*
	⇩ *9 days later (+/-7)*
Visit 6:	**Day of your surgery: small tissue samples from your nose lining and tonsil will be taken and blood sample**

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. Pneumococcus is a bacterium that can cause serious diseases such as pneumonia, sepsis and meningitis. It is important that you are aware of this risk.

We give you a separate leaflet which explains the safety precautions, and what to do if you feel unwell. We provide a thermometer and antibiotics that can treat these bacteria if needed. If the pneumococcus bacterium has not been cleared from your nose by your own immunity at the end of the study, we will ask you to take the antibiotics to kill the bacteria.

As a precaution we advise participants not to become pregnant during the study and to advise the research team if they do become pregnant.

Risk of taking blood: Very small risks are associated with blood sampling. Some people can feel light-headed or may have a bruise.

Risk of taking nasal mucosal lining samples: As explained by your surgeon the planned nasal surgery has some risk that may also occur when taking these tissue samples for research. This includes small risk of nose bleed, infection, pain and crusting (dry secretions). Some people may need nasal dissolvable pack placing in the nose to stop the bleeding if cannot be controlled with standard method of electrical cautery. The pack dissolves within two days.

Risk of taking tonsillar biopsy

Very small risk of bleeding, pain and infection in the first 5-7 days after the surgery.

What does Nasal and tonsillar tissue samples involve?

We will ask participants to consent for a nasal lining and tonsillar tissue sampling. This is to allows us to take small amount of nasal lining and tonsillar tissue cells for detailed microscopic examination.

Nasal tissue biopsy: We will two small tissue samples from your nose approximately 2-4 mm (about the width of one matches). The tissue is taken from the same place where we normally perform the surgery for your nose. We will use special surgical forceps (like tweezers) to do that. This sample will be collected whilst you are asleep (anesthetised) for you planned surgery.

Tonsillar tissue biopsy: While you are asleep the surgeon will use an instrument to keep your mouth open. Whilst this is in place we will take couple tissue samples from your tonsils with a special forcep.

The procedure is carried out in the University Hospital Aintree or The Royal Liverpool and Broadgreen Hospital under general anaesthesia (fully asleep) while you are having your planed surgery. You need to be starved for the procedure. Please follow the instruction that you have been given regarding this from the pre-operative assessment team from University Hospital Aintree.

What are the risks of nasal and tonsillar tissue sampling?

Nasal tissue sampling is a safe procedure and commonly performed in the outpatients department in the Ear, Nose and Throat department. As mention above there is a very small risk of pain, bleeding, infection and

nasal crusting (dry secretions) after the biopsy is taken. In rare occasions when the bleeding is present immediately after the biopsy is taken and not controlled with the usual way of cautery (electrical or chemical) we will insert dissolvable nasal pack called Nasopore. This pack will dissolve within 2 days and therefore doesn't require removal or additional trip to the hospital.

Tonsillar tissue samples are usually carried out under general anaesthesia (fully asleep) as it is easier for us to see the tonsil and take the biopsy. Participants in this research will have consented to a general anaesthesia as part of their planned surgery.

There is a small risk of bleeding and infection and soreness in your throat in the first 5-7 days after the sampling. This can be treated with simple painkillers. We recommend Paracetamol.

To minimise the risk of bleeding we will advise you to avoid strenuous physical exertion in the first 2-3 days after the tissue sampling has been done. And to minimise the risk of infection we will advise you to avoid contact with anyone that has cold or flu in the first two weeks after the biopsy.

What will happen after the procedure?

After the procedure you will be observe for approximately 2-4 hours (as per the standard post-operative care) so that any medication can wear off before you leave. You will be offered something to eat and drink. You will be asked to contact us or the Ear, Nose and Throat (ENT) team at University Hospital Aintree or the Royal Liverpool and Broadgreen Hospital the next day if you have any side effects of the procedure. If so you may be asked to come to the hospital for a follow up assessment.

How my nose and throat will feel after the procedure?

After the numbness wears off the nose will not feel any different than what is expected for the surgical procedure that you are having.

Your throat might be slightly sore. And you may have blood stained sputum. If the bleeding continuous please contact the ENT surgical team at University Hospital Aintree or The Royal Liverpool and Broadgreen Hospital immediately or attend the nearest medical emergency department.

Taking part in this study will not require additional follow up visits after the surgery. We do not expect this additional sampling to increase the time for you to recover from your originally planned surgical procedure.

What if there is a problem?

You can contact the research team 24 hours-a-day by phone. They will answer any questions. Any medical care you need will be provided as usual by the NHS. If you are very unwell we always advise you to contact your usual route of health care for example GP or hospital. Please note you may be unwell due to other reasons not related to this bacterium. This team would like you to contact them if you are unwell even for other reasons and are available to advise you day and night.

What if I wish to complain?

If you wish to complain about any aspect of the study, you can contact the study doctor or nurse. 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 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. If at the time of leaving the study you have become carrier of the bacteria in your nose we will advise you take three-day course of oral antibiotics to clear the bacteria. Antibiotics will be prescribed for you by our research medical team.

We would ask you to stop taking part in the study if you are subsequently not eligible or able to comply with the procedure.

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 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 will ask your permission to inform your GP that you are taking part in the trial as this may be relevant to your medical care outside the study. We do not expect to find anything which would affect your health care. If we do, we will let you and your GP know.

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 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.

The Over-Volunteering Prevention Service (TOPS)

We and other units keep a TOPS database of healthy volunteers who take part in studies. This is to ensure participants do not take part in too many studies that may have an impact on their health (such as too much blood sampling) or on the study results.

We will enter these details into the database:

- Your National Insurance (NI) Number
- If you are not a UK citizen and not eligible for a NI number then your passport number may be used)
- The date of your last study medicine.
- Your contact details

These details will be kept for at least 2 years and if we may use these details to contact you if needed. Research staff at the Royal Liverpool Hospital and other Medicines research units may access this data.

There is a small risk of bleeding after the surgery, pain and infection. This will not add recovery time to your original surgery.

How much will I get paid?

The money you are paid is compensation for inconvenience, loss of income and time taking part.

Payment is made at the end of the study, if you withdraw during the study you will be paid for your study involvement to that date.

Visits (more details of sample in the main text)	Appointment time (minutes)	Visit payment
Visit 1: Screening and samples	30 min	£30 + £20 additional travel expenses
Visit 2: Having pneumococcus put up your nose plus £5 per day daily email/SMS/telephone contact for the first 7 days. (We will withhold £5 per day if you do not contact us)	20 min	£50 + £20 additional travel expenses
Visit 3: Nasal samples (wash and scrapes) and blood	20 min	£20 +£20 additional travel expenses
Visit 4: Nasal wash and bloods	10 min	£10 + £20 additional travel expenses
Visit 5: Nasal samples (wash and scrapes) and blood	20	£20 + £20 additional travel expenses
Visit 6: Nasal and tonsillar tissue biopsy and blood Duration as per the planned surgical procedure	45-60 min	£50
Total	£280	

Further Questions – you may speak to a research doctor or nurse

Contact details during working hours:

For booking appointments: Mobile: ********** 0151 706 3381

Out of hours: if you have consented and need to contact us day or night:

Royal Liverpool Hospital Switchboard: 0151 706 2000 (ask for Respiratory Research Team*)

Mobile:

**The Principal Investigator is Dr Jamie Rylance who may be contacted via the Royal Liverpool Hospital or the by contacting the Respiratory Research Team as above.*

This research is sponsored by the Liverpool School of Tropical Medicine. The research has been reviewed for scientific content by an external panel. The National Research Ethics Service Committee (XXXX) has reviewed the study and given approval for it to take place.

Research Consent form for The Nose and Throat Study (Group 2)

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Research working towards developing new vaccination in the prevention of

Participant Study number

Please initial the box if you agree with each statement. Then, print and sign and date below.

I have read and understand the information sheet version * for the above study. I have been able to consider the information and to ask questions.	Initial
I understand that this study is voluntary and that I am free to withdraw without giving any reason without my medical care or legal rights being affected.	Initial
I understand that the section of my medical notes relevant to my taking part in this research and data collected may be seen by the regulatory authorities or NHS Hospital.	Initial
I agree to my GP to be informed of my participation, and to provide information or for the researcher to access my electronic GP summary care record relevant to the study.	Initial
I agree to provide details of a contact who, in the event of an emergency, could be contacted on my behalf.	Initial
I understand that the samples collected will be used and stored for the research described above, and that samples may be sent to national and international collaborating laboratories as part of the study.	Initial
I will gift these samples so that they may be used for future ethically approved research.	Initial
I give permission for the DNA to be extracted from these samples and gifted for use in future studies and may be sent to research collaborators national/international.	Initial
I agree to my details being entered in The Over-Volunteering Prevention Service Database.	Initial
I confirm that I am not planning to conceive and I will use effective contraception if required during the study.	Initial
I agree to take part in this study.	Initial

……	…….	_ _/_ _ _/_ _ _ _
Name of patient (print)	Signature	Date
……	…….	_ _/_ _ _/ _ _ _ _
Name of person taking consent	Signature	Date

Copies: 1 for participant, original for site file and one scanned or filed in hospital medical notes