National Study of Nephrotic Syndrome - (NephroS)

Information Sheet for Parents/Guardians/Families

Your child is being invited to participate in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve for you and your child.

Please take time to read the following information carefully and discuss it with others if you wish. If appropriate, please encourage your child to read their information sheet and discuss the study with them.

Your child's kidney specialist will explain if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish your child to take part.

Thank you for taking the time to read this.

The purpose of this study

Your child's kidney specialist has made a diagnosis of Nephrotic Syndrome (NS). This can be described as either Steroid Sensitive Nephrotic Syndrome (SSNS), Steroid Resistant Nephrotic Syndrome (SRNS) or Focal Segmental GlomeruloSclerosis (FSGS). SSNS is usually a milder disease and most cases respond to steroids, but occasionally it becomes resistant to steroids and is then termed SRNS. The cause of this is rarely known and SRNS/FSGS can be very difficult to treat. The treatment itself can have side effects and appears to be more effective in some than in others.

For this reason the kidney research unit in Bristol has developed a special interest in NS/FSGS and what happens to the kidney in this disease. They want to find out:

- If some patients are likely to develop the disease because of gene mutations. Our genes sit in all the cells of the body and hold the information to develop and maintain the cells. If the programming of the gene is slightly altered this results in a 'gene mutation' which can result in a disease. We know that there are some gene mutations which cause NS but we don't know how often this occurs in the UK.
- How the disease actually affects the kidney.
- Whether NS causes a pattern of changes in the kidney cells which is the same in every patient.

Why has my child been chosen?

The research team are approaching all children and adults with Nephrotic Syndrome, at hospitals running this study in the United Kingdom.

Does my child have to take part?

It is up to you to decide whether your child takes part. If you do decide for your child to take part, you will be asked to sign a consent form. You are still free to change your mind and withdraw at any time without giving a reason. If you decide not to take part or to withdraw from the study this will not affect the treatment your child receives.

What will happen if my child agrees to take part?

There are several parts to this study:

1) When your child has a blood test, a little extra blood will be taken. The amount of blood to be taken is 1 - 8 teaspoonfuls depending on the age of your child (5-40mls).

2) Your child's medical details will be reviewed from the rare kidney disease database, RaDaR. You may have previously consented to their details being placed onto this, if not, this will be done at the same time as consenting for this study.

3) At times of acute illness, a little extra blood will be taken. If you/your child are willing, we may ask you to visit the hospital to donate samples at times of relapse outside of your routine appointments. These visits are optional and you can choose whether you wish to consider visiting the hospital at these times. Any expense you incur as a result of so doing will not be reimbursed.

4) Urine samples may be collected during routine appointments and at times of acute illness.

5) If your child had/has a kidney biopsy as part of their routine care, we ask your permission to collect any surplus tissue for research purposes. Your child will not be asked to have another kidney biopsy as part of the research. If however, in the future their doctor feels a biopsy is needed for routine clinical care, we will ask your consent to collect an additional sample for research use.

6) In the rare cases where a child has a kidney transplantation and the disease returns in the transplanted kidney, they are likely to undergo a treatment called 'plasma exchange'. During this treatment your child's plasma is exchanged for new plasma

and the original plasma is discarded. In this study samples of the discarded plasma would be sent to the research group.

7) You/Your child may be given a questionnaire to complete about their quality of life at various time points throughout their disease course. This will either be given to you in clinic or sent to you. These will not have their name on it, just their unique study number. There will be help available to complete this form if needed.

Your child's samples will be used in a variety of tests in the lab, which may include looking at your child's genetic material. Cells within some of your child's samples may be used to generate cell lines. This means that the cells can continue to divide in the laboratory indefinitely. Most cells die once they have been removed but by generating these cell lines, researchers can continue to work on the cells for longer.

Your child may also be invited to participate in other medical research studies. This will include the chance for your child to have a comprehensive DNA analysis as part of the BioResource – Rare Diseases study. Your child's DNA will be sequenced and analysed for changes in the DNA code that may be responsible for their NS. You will be provided with full information regarding this study and are free to decide whether or not your child takes part.

What will happen to any information about my child?

The information that has been or will be collected by the RaDaR study is stored on a secure web server. Researchers who are interested in your child's condition can view their anonymized data and that of others will the same condition.

The research group leading this research has signed a confidentiality agreement with the RaDaR group. A restricted number of NephroS researchers can see your child's personal information e.g. to invite them to studies such as the BioResource study. These researchers have been carefully selected and are only given access appropriate to their roles. At the end of the study the research group will no longer have access to this information, and the RaDaR group will continue to store it securely.

What will happen to my child's samples?

[Instruction for sites - Please delete one of the below paragraphs and these instructions depending on whether you are a Site Type A (NephroS) or Site-Type B (NURTuRE-NephroS) centre]

[Site Type A - Your child's samples will be sent to the lab for use in medical research. Some samples may be made available to researchers in other organisations in the public and private sector (e.g. pharmaceutical and biotechnology industry) both in the UK and Overseas. This will help develop discoveries that benefit patients with NS. At the end of the study the samples will continue to be stored pending further study.]

[Site Type B - Your child's samples will be collected for use in medical research both in the UK and Overseas. Their samples will be used in academic research, commercial research and some samples will be stored for future use in a central Biobank where they will be stored anonymously, identified by a barcode linked to their unique study number. Access to these stored samples will be controlled by an Independent Access Committee to make sure your child's samples are used in the best way possible to develop discoveries that benefit patients with NS.

How will I know the outcome of the research?

We expect that about 20% of children with NS/FSGS tested will have a gene mutation identified which may not have been known about previously. Any results on genetic testing will be fed back to your child's kidney specialist (if you consent to this) who will talk to you about the result. The RareRenal website (rarerenal.org) will have information on each of the genes being tested and will be kept up to date as new information is found.

The data and other tests will be collated and published and your specialist will explain the findings to you. Results of studies will be made available to the public through scientific publications, reports, websites or publications but your child will not be identified personally in these.

Will my GP know about this research?

If you would like your child's GP to know about this research, your child's specialist can inform your family doctor of their participation and of any results from the study. Your child's GP will only be contacted if you consent to them being informed.

Can I have more time to decide?

Yes. There is no time limit. You can discuss this research proposal with anyone you choose.

What if I wish to withdraw?

You may withdraw at any stage without having to give an explanation. You can do this in writing to your local kidney doctor or to the research team directly if you wish. At that time you can decide if you are happy for us to use samples collected or if you would like these to be destroyed.

What are the risks/benefits in participating in this study?

The majority of samples collected in this study do not require you to attend hospital more frequently or for your child to undergo extra procedures, only to have more blood taken and to give urine samples at routine appointments. At times of relapse, we may ask your child to visit the hospital to have a blood sample taken. This would be an additional procedure, and carries the small risk of bruising, inflammation or fainting. Biopsy samples would only be requested from procedures that have already taken place, or take place during the routine care of your child. No extra biopsy operations would be performed for research purposes, although we ask your consent to take an extra sample of kidney tissue during these routine procedures.

The benefits are to increase the medical knowledge about this disease and the research group hope that the information obtained will help provide better treatment for NS in the future.

What happens if a discovery is made using my donated samples?

The samples donated are given as a gift i.e. without payment. You will not receive any financial benefit if the research leads to new treatments or tests.

What do I do if I have concerns about the study?

If you have any concerns or further questions about this study or the way it is carried out, you should contact your child's kidney specialist (the Local Investigator) in the first instance. You can also contact the PALS service of the hospital where you are being treated.

Has this research study been approved by an ethics committee?

This study has been approved by the South West Central Bristol Research Ethics Committee, reference number 09/H0106/80.

OPTIONAL –Relative Samples

It is useful to have blood/saliva samples from relatives as this allows us to study the impact of genetic factors on the development of a disease. In particular, if a potential disease-causing mutation is found in your child's samples, samples from relatives can help verify the mutation found.

It is up to you to decide whether to take part.

If you agree to join, we will ask you to sign a consent form. A small amount of blood will be taken, approximately 2 teaspoonfuls (10 ml) by an experienced staff member. Alternatively, a saliva sample can be given. Your sample will be used in research to determine the genetic causes of Nephrotic Syndrome. At the end of the study the samples will continue to be stored pending further study.

If you do take part, you are still free to change your mind and withdraw at any time without giving a reason. If you decide not to take part or to withdraw from the study this will not affect the treatment your child/relative receives.

Chief Investigator: Prof. Moin Saleem, University of Bristol

Local Investigator: