PARTICIPANT INFORMATION SHEET

Microbiome and Immune profiling in infants with Non-IgE-Mediated Cow's Milk Protein Allergy

Invitation to take part in the study

We would like to invite you and your baby to participate in a study. To help you understand what this study is about, we are providing you with the following information. We want to be sure you understand the study before you decide if you would like to enrol your baby. This study is collaboration between the University of Glasgow and the Royal Hospital for Children, Glasgow. Please feel free to ask any questions you have about the information you receive, and we will do our best to answer these and provide any further information you require. Take time to decide whether or not you wish to consent for your baby to take part in this study.

What is the purpose of the study?

Cow's Milk Protein Allergy (CMPA) is a condition that can present in the first few months of life. Though it can be managed with a restrictive diet that excludes cow's milk, studies are needed to understand the disease cause better. This absence of knowledge also explains the difficulties that doctors encounter to diagnose and treat this condition as soon as possible.

In this study, we wish to find out more about the effect of CMPA on babies' gut in a non-invasive way. The aim of this study is to identify possible markers in stool or urine samples from babies with this condition and especially those who present mainly with gut symptoms. These markers will then be used as a new non-invasive diagnostic tool for babies with this condition.

This study is also part of a 3-year postgraduate degree (PhD) undertaken by student Caroline Kerbiriou at the University of Glasgow.

Why has my baby been chosen?

You and your baby have been invited to take part in this study as your baby has been showing clinical signs of CMPA or is a healthy baby. In total, we hope to recruit 90 babies with cow's milk allergy and 60 healthy babies to take part in this study. Your baby's results will be compared to those of babies with a different type of milk allergy or healthy babies. In no way this study will affect your baby's food allergy management (applicable to all CMPA participants). We will just be collecting dirty and wet nappies (stool and urine samples) while your baby is on treatment according to the local treatment protocol, in order to observe the changes on the gut bacteria and other markers of gut health.

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Do we have to take part?

No, it is your decision to choose whether or not to take part in this study. If you choose not to participate in this study, we will respect this decision. If you are happy to take part, you will be asked to sign a consent form on behalf of your baby. A copy of this information sheet and consent form will be given to you to keep. If, at any time, you change your mind, you are free to withdraw from this study without having to give a reason for your decision. Your decision to withdraw from this study will not affect the standard of care your baby receives now or in the future. Should you decide to withdraw your consent, samples already acquired will be kept for the study unless you tell us not to do so, in which case the samples will be destroyed. Should you lose capacity to consent during the study, your baby's participation to the study will be withdrawn and identifiable data or samples collected with consent will be retained and used for the study. No further data or samples will be collected or any other research procedures carried out on or in relation to the participant.

What do I need to do if I decide to take part?

If you agree to take part in this study, we will perform the following: (some information might not be applicable to your baby)

1. Record information about your baby such as your baby's gender, age, type of feeding, family history (allergy, household characteristics). Record pregnancy information relevant to the study i.e. antibiotics, substances/alcohol use, duration of the pregnancy and mode of birth. Record information about you (participant's parents/carers) such as demographics, height and weight. Your baby's length, weight and head circumference will also be measured on a maximum of 4 different occasions over a period of 6 weeks by the team's clinician or PhD student during visits at the clinics or at your own home (applicable to all participants).
2. Collect dirty and wet nappies (for stool and urine samples). We will ask you up to 6 times during the study to collect samples. Two samples will be collected on the day of the diagnosis, one sample at week 1, one sample at week 4, two samples on the Oral Food Challenge week (if cow's milk is offered/reintroduced again by your baby's clinician/dietician, according to the local cow's milk allergy protein management guideline), one on week 5 and one sample at week 6. For samples collection, we will give you gauze pads to place in the nappy. Once full, we ask for you to remove the nappy and leave the gauze pad inside.

   Samples should be collected during the scheduled visits at the clinics or at your home. However, if no samples are available at that time, we will ask you to call a member of the research team to organise collection, when a dirty and wet nappy is available. Samples will be collected by a member of the

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research team or a pre-paid taxi at the hospital ward, at the clinic or your home. Contact details of the research team members will be given to you (applicable to all participants).

3. If your baby requires hospital admission and undergoes blood testing for clinical tests, we ask your permission to keep what is left of the blood sample to use for this study. There will not be any needle insertion as part of this study (Not applicable to healthy participants).
4. Make assessment visits at your home at weeks 1, 4, Oral Food Challenge week (on the ward if supervised challenge is required), week 5 and 6. We will look measure your baby's weight, length and head circumference and collect a dirty and wet nappy (Not applicable to participants with IgE-mediated CMPA and healthy participants).
5. Ask you to complete a symptom dairy (i.e. vomiting, diarrhoea, blood in the poo) daily for your baby during the 6 weeks of the study. The diary will be looked at by the research team during the follow up visits (Not applicable to participants with IgE-mediated CMPA and healthy participants).
6. The clinician/dietitian, who is treating your baby, will decide based on the local CMPA management guideline if your baby requires an Oral Food Challenge (supervised or at home) to confirm the diagnosis. If the challenge takes place, we will also ask for two samples from two consecutive bowel motions along with two urine samples after the challenge (Not applicable to participants with IgE-mediated CMPA and healthy participants).
7. If your baby's clinician/dietitian concludes that the symptoms are not due to CMPA (e.g. gastroenteritis), we will keep your baby in the study and the samples will be kept as controls (Not applicable to participants with IgE-mediated CMPA and healthy participants).

Taking part does not mean a change in the clinical management of your baby. We will only be collecting dirty and wet nappies (stool and urine samples) and blood samples if available (left over blood samples after the doctors do their tests).

The stool and urine samples will be processed and analysed in our labs at the University of Glasgow at Glasgow Royal Infirmary, where we will look at the presence of markers involved in milk allergy and gut bacteria. Your baby's anonymised samples will be stored in Human Nutrition and institute of inflammation, immunology and infection, University of Glasgow freezers for a maximum of 15 years. We may use these samples for research purposes in the future, as new techniques become available. A follow up study may also be set up to follow your baby during his/her development at 3 and 5 years of age and may contact you in the future and ask you for more samples, if you agree only. Your personal contact details will be stored for 6 years in a log book within a locked filing cabinet within the premises of the University of Glasgow.

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Are there any risks if my baby participates in this study?

We do not anticipate any risks associated with participation in this study, for both your baby and yourself. The management and treatment of your baby's condition will not be altered by taking part.

Are there any benefits if we take part?

No there are no benefits from participating in this study, but the results of this study are likely to help us to understand the cause of milk allergy and improve early diagnosis and management. At the end of the study, we will give you a £20 Amazon voucher for the nappies provided to say thank you and partially compensate for your time. Alternatively, we can donate this money on your behalf to a charity of your choice.

Will my baby's participation in this study be kept confidential?

Yes. Once you consent to take part in the study, your baby will be allocated an anonymous code which will be used to label all samples and data. We do this to protect your baby's identity during all lab work, data analysis and results presentation. Relevant medical history will be collected by the researchers from medical notes in line with the NHS Code of Practice and current data protection laws.

Other than the direct research team, your baby's data may also be monitored by authorised representatives of NHS GG&C to ensure compliance with regulations. We will also let your baby's GP know that he/she is taking part in the study.

The results of the study will be published in a medical journal, but no personal details about any person taking part in the study will be revealed. There will be no way you or your baby to be identified by them. The NHS GG&C is the sponsor for this study based in the United Kingdom. We will be using information from you, your baby and your baby's medical records in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. The NHS GG&C will keep identifiable information about you for a minimum of 6 years after the study has finished.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

You can find out more about how we use your information at https://www.nhsinform.scot/care-support-and-rights/health-rights#confidentiality-and-data-protection

Who is organising the research, and who has reviewed it?

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This study is funded by the University of Glasgow, the Food Protein Induced Enterocolitis Syndrome (FPIES) foundation and Nutricia, an infant formula manufacturer. All proposals for research using human subjects are reviewed by an Ethics Committee before they can proceed. This proposal was reviewed and approved by the North of Scotland Research Ethics Committee (1) on 25/09/2018.

What if I have a complaint about any aspect of the study?

If you are not happy about any aspect of the study and wish to make a complaint, please contact the team consultant in paediatric allergy, Dr George Raptis, in the first instance. If you remain unhappy and wish to complain formally, the normal NHS complaint mechanism is also available to you via email: complaints@ggc.scot.nhs.uk or phone: 0141 201 4500.

What if I have questions or concerns?

If you have any concerns or questions about this study, please get in touch with Dr George Raptis and the research team on telephone number: 07380 842444, email address: mvls-melinastudy@glasgow.ac.uk or Dr Russell on telephone number 0141 451 6543

Independent advice on clinical trials and research studies can be obtained from Professor Edwards on telephone number 0141 201 8685

Thank you for taking the time to read this leaflet.

Dr George Raptis
Consultant in Paediatric Allergy
Royal Hospital for Children

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PhD Student
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