Information sheet: for participation of child and mother in NOGBS study

Prevention of bacterial infections in newborn babies

Prospective multi-centre observational cohort study on perinatal bacterial infections

Dear Sir/Madam,

We are sending you this letter because your baby has been diagnosed with meningitis or sepsis caused by Group B Streptococcus (GBS) or Escherichia coli (E. coli) bacteria. Although a lot of babies come in contact with these bacteria only a few develop severe illness. It is not generally known why this happens. This study, designed by the Academic Medical Center (AMC) of Amsterdam, investigates bacterial infections in newborns. Here we look at which characteristics of pregnancy and labour are determining for a baby becoming ill or not. We collect data of the bacteria, mother and child, with the aim of preventing sepsis and meningitis in newborns in the future. We would like to ask you if mother and child may take part in this medical-scientific study. Participation is voluntary and requires your written consent. The study takes place in the hospital of admission.

The Medical Research Ethics Committee (METC) AMC has approved this study. General information about the assessment of research can be found in the general brochure on medical research.

Before you decide whether you wish to participate in this study, you will be given an explanation about what the study involves. Please read this information carefully. If you do not wish to participate in one of the parts of the study, as described below, you and your baby may still take part. If you have any questions please ask the investigator for further explanation. You can find the contact details in the appendix to this letter (Appendix A).

1. Purpose of the study

GBS and E.coli bacteria are the most common causes of meningitis and sepsis in newborns. During pregnancy some women are checked to see whether they carry this bacteria. If the bacteria is found in the vagina, rectum or urine, the mother can receive antibiotics during labour in order to prevent illness in the baby. Unfortunately, there seems to be an increase in the number of infected babies, despite this preventive treatment. It is not clear why some babies develop severe illness and others do not. With this study we would like to ascertain why this happens. We look at clinical characteristics of the baby who is ill, genetic characteristics of the bacteria and protective antibodies in the blood of the mother and child. We compare this data with the data of mothers and babies who did not become ill. As a result of this, we hope to get a better understanding of which babies are more prone to becoming ill and to prevent this severe illness, for example, by increasing the number of protective antibodies against these bacteria by vaccination.

2. What participation involves

Participating in this medical-scientific study will not alter the treatment of your child.

What participation involves for you child

- **Data collection:** For this study we use data that doctors have collected about the illness of your child (documentation, results of examinations, discharge letter).
- **Blood collection:** If blood needs to be collected from your baby, we will collect once only a little extra blood (maximum of 2ml) for this study. Your child will receive no extra prick to carry out this study.
- **Residual blood, cerebrospinal fluid and heelprick:** If blood and cerebrospinal fluid is collected in the first days of illness and stored in the laboratories, we will collect this and save this for the study. We also retain any residual blood from the dried blood spots (heel puncture).

What participation involves for the mother

- **Blood collection**: We will collect 10 ml blood to investigate whether there are antibodies present which offer protection against the GBS bacteria.
- **GBS carriage: Urine, breastmilk and genital swab**: To investigate whether you (still) carry the GBS bacteria, we would kindly ask you to provide a small amount of urine and breastmilk. In addition, we need you to collect from you a genital swab (from vagina and anus). You can do this yourself. It is not difficult or painful. This can be collected by inserting the tip of the swab (a cotton swab) first 1cm into the vagina and then 1 cm into the anus, rotating the swab gently on both occasions for 20 seconds. If you wish, a physician is also permitted to collect the swab. We would also ask your permission for us to request results from your GP or midwife if, during pregnancy, carriage cultures/tests were carried out.
- **Residual blood:** We would also ask your permission for us to collect residual blood from your routine pregnancy checks. This is to investigate whether there was an immune response against the GBS bacteria during pregnancy.

3. Possible advantages and disadvantages

It is important that you weigh up properly the possible benefits and disadvantages before you decide to participate. You and your baby will not personally benefit from participation in this study. Participation involves minimal disadvantages. Drawing blood may be painful or cause some bruising, your baby will receive no extra prick for this study. The self-collection of a genital swab is not difficult or painful, but some woman can experience some discomfort

4. If you do not wish to participate or you wish to stop participating in the study

It is up to you to decide whether you and your baby participate or not in this study. Participation is voluntary. If you do participate in the study, you may always change your mind and decide to stop, at any time during the study. You do not have to say why you do not wish to participate or are stopping.
The data collected up till that time will be destroyed.

5. End of the study

Participation stops when your child is discharged from the hospital or you choose to stop. We ask for separate permission to contact you in the future for follow-up studies, for example, to investigate if children experience any residual symptoms after GBS or E.coli disease.

6. Use of data and bodily material

For this study it is necessary to collect and use your baby’s bodily material and medical data. We also register the date of birth of your child to answer important questions posed in this study, for example, after how many days after birth did your child become ill? We will perform genetical analyses with the blood of your child. This will take place anonymously, excluding the possibility to trace the patient through a code or personal information. You are asked to decide separately on the permission form if you do or do not wish your child to participate in this part of the study.

Privacy

To protect your own and your child´s privacy each study subject receives a code. Name and other personal data that could directly identify a person will then be deleted. Only with the key to this code can you be traced. The key to this code will be safely stored at the local research institute. Some people may access your medical and personal data at the research institute, even the data without a code. This is to check whether the study has been conducted in a proper and reliable manner. People who may access the data are representatives of the AMC as initiator of the study, a monitor who works for the initiator and the Healthcare Inspectorate. They will keep the data secret. We ask your consent for this access. The investigator will store the data for 15 years.

Findings of importance

It cannot be ruled out that, during future scientific research with blood, DNA or bodily material of you or your child, findings of importance for the health of you, your child or your family members will be discovered. If this indicates a serious health problem or health risk for which treatment is available, we will notify you. We will always consider carefully if it is necessary to inform you of such findings. In the context of this decision we will also ask advice from the hospital committee.

7. Storage data and bodily material in the MeninGene Biobank

The collected data and/or blood samples/tissue samples may be important for additional and future research to severe bacterial infectious diseases. Therefor the data and bodily material of you and your child will be stored for 50 years in the MeninGene Biobank. If you sign the Biobank consent form (C2 and C4) you give your permission for this storage. Participation is voluntary. If you decline consent for the MeninGene Biobank you can still participate in the NOGBS study. You do not have to say why you do not wish to participate. The AMC has drafted a Biobank Code “Reglement MeninGene”. This contains the rules for the confidential handling of data and the material and the purposes for which this may be used. You can ask the researchers for this Code. The Biobank Audit Committee supervises the Biobank.

Sharing data and bodily material in future studies with different research groups

By collaboration with other research teams and sharing data, we can answer new research questions.

Because of this, we would like to ask your consent to share data and bodily material with other research groups for future research into bacterial meningitis. The residual dried blood spot (heel prick) material will only be shared with other studies when approved by the METC.
We ask your consent to share body material from your child with commercial companies or institutions from abroad, for example manufacturers of vaccines. For sharing data with commercial companies we will ask permission from the Biobank Audit Committee. For sharing data with institutions from outside the EU it is possible that there may be other rules for personal data protection. We will share the data only via the code, never using the personal information (name, date of birth etc). If you do not wish us to share material for future research, you can state this separately on the consent form.

Renew consent and withdrawal of consent
At the age of 16 years, your child will be asked for consent for the use of his/her data and bodily material in the Biobank. If necessary, we will contact the Municipal Administration Department (Gemeentelijke Basis Administratie) to avoid making mistakes in approaching the right persons.
You can always decide to stop, at any time during the study, by filling in the “withdrawal form” (Appendix B). After withdrawal all data and material will be destroyed. If the samples have already been analysed, the results will still be used

8. Study subject insurance

This study is not associated with any risks for you or your child. The METC AMC has therefore declared that there is no need to take out additional insurance.

9. Informing treating specialist

The specialist treating your child is always made aware of participation in the study.

10. Costs or compensation

The study is free of charge. You will not receive payment for participation.

11. Any questions?

If you have any questions, please contact the study team. If you would like any independent advice about participation in this study, you may contact Doctor B. Jaeger (Paediatric Neurology AMC). She knows about the study but is not involved in it.
If you have any complaints, you may contact the complaints’ officer at your hospital. All the relevant details can be found in **Appendix A**: Contact details.

12. Signing the consent forms (C1-C4)

Your written permission indicates that you have understood the information and consent to the participation in this study (C1 and C3) and in the MeninGene Biobank (C2 and C4). The signature sheet is kept by the investigator. You will receive a copy or a duplicate copy of this consent form.

Thank you for your attention.

13. Appendices to this document

A. Contact details

B. Withdrawal form "MeninGene Biobank"

- B1: Withdrawal form "MeninGene Biobank" child
- B2: Withdrawal form "MeninGene Biobank" mother

C. Informed consent forms

- C1: Informed consent for **study participation child**
- C2: Informed consent for **storage data/material Biobank child**
- C3: Informed consent for **study participation mother**
- C4: Informed consent for **storage data/material Biobank mother**

D. Medical Scientific Research Brochure. General Information for Study Subjects (version 01-03-2017)

Appendix A: Contact details investigators

Contact details AMC

MA. Groenveld, MD, PhD student
Academic Medical Center
Neurology H2-224
Tel: 020 - 566 1564
E-mail: m.a.groenveld1@amsterdamumc.nl

Dr. M.W. Bijlsma, Pediatrician
Academic Medical Center
Neurology H2-217
Postbus 22660, 1100 DD Amsterdam
Tel: 020 - 5663942
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Independent expert

B. Jaeger, Pediatric Neurology
Academic Medical Center
Pediatric Neurology, H7-270
Postbus 22660, 1100 DD Amsterdam
Tel: 020 - 5663942
E-mail: b.jaeger@amc.uva.nl

Complaints’ officer

AMC Outpatient clinic, A0 (9.00 – 12.30)

Postbus 22660, 1100 DD Amsterdam,

Tel. 020-56 63355

E-mail: klachtenfunctionaris@amc.nl

GIVE TO PARENTS

To withdrawal consent in the future

Appendix B1: Child - Withdrawal of Consent Form for Biobank MeninGene

- I hereby withdraw my consent for participation of my child in the MeninGene Biobank
- I understand that if my child’s bodily material has already been analysed and used in research, this cannot be withdrawn or destroyed
- I understand that if my child’s medical data has already been analysed and used in research, this cannot be withdrawn or destroyed
- I hereby request the administrator of the MeninGene Biobank to destroy the collected and stored data and bodily material of my child.

Name Child: Date of Birth: __ / __ / __

Parent name 1:
Signature: Date:__ / __ / __
Parent name 2:
Signature: Date:__ / __ / __

Appendix B2: Mother - Withdrawal of Consent Form for Biobank MeninGene

- I hereby withdraw my consent for participation in the MeninGene Biobank
- I understand that if my bodily material has already been analysed and used in research, this cannot be withdrawn or destroyed
- I understand that if my medical data has already been analysed and used in research, this cannot be withdrawn or destroyed
- I hereby request the administrator of the MeninGene Biobank to destroy the collected and stored data and bodily material of me.

Name Mother: Date of Birth: __ / __ / __

Signature: Date:__ / __ / __