Covid-19 and pregnancy

INFORMATION FOR PARTICIPANTS

Would you like to participate in a research project to investigate the prevalence of Covid-19 in pregnant women, their partners and newborn children, and compare pregnancy and birth information with test results for Covid-19?

Covid-19: Consequences of Covid-19 infection for pregnant women, women in labour, their partners and newborns.

The project

The focus of this project is pregnant women and women who give birth during the Covid-19 epidemic. The project also includes partners of pregnant women. We would like to discover how many pregnant women have or have had Covid-19, with or without symptoms. We will compare this with the outcome of the pregnancies and births. We also want to discover whether differences in the participants' genetic material can predict how susceptible they are to contagion and symptoms of Covid-19.

The project is a collaboration between several departments at Amager-Hvidovre Hospital and is being headed by Professor Henriette Svarre Nielsen. The participating departments are: The Department of Gynecological Obstetrics, the Department of Clinical Biochemistry, the Department of Microbiology and the Department of Pathology. Sampling will take place at the Department of Clinical Biochemistry (blood sampling), at the ultrasound unit for pregnant women (section for fetal medicine) and at the maternity ward. The blood samples will be taken during your routine visits to the department.

Before you decide to participate in the project, we ask that you read this information letter thoroughly and ask any questions you may have. Taking part in the project is voluntary. You can withdraw your consent at any time and without explanation. This will have no consequences for your future treatment. If you do not wish to participate, you will still receive the same help and treatment from the hospital.

You will receive information in your e-Boks, via the hospital's website or when you visit the hospital, where you will receive additional information about the project and you will be able to ask any questions. You are welcome to have a family member, friend or acquaintance (virtually) present at the consultation e.g. via Facetime due to the corona epidemic. After the consultation, you will have 24 hours to consider whether you wish to participate and to sign the consent form.

This information letter includes information on the rights of clinical trial subjects in a health-science research project prepared by the National Committee on Health Research Ethics. The information is relevant to anyone participating in a scientific study.

Background

The Covid-19 pandemic has taken a firm hold. A large part of the population is already infected and more will become infected in the coming weeks/months. Some of the infected will become ill while others will only experience mild symptoms or no symptoms at all. Many infected pregnant women and their partners only experience mild symptoms or no symptoms at all. This can be due to many factors. For example, how exposed they have been to infection and how healthy they are generally. Differences in genetic material (genes) can also effect how susceptible the body is to coronavirus and how the body combats the virus once infected.

Pandemics like Covid-19 raise many questions, both in Denmark and in the rest of the world. No one knows with any certainty whether Covid-19 poses a serious risk to pregnant women, women in labour and newborn children. It is therefore important to gather information during this pandemic so we can provide correct recommendations for pregnant women, their partners and newborn children with regard to Covid-19.

Who can participate?
You can participate in the project if, up to 1 September 2020, you:

- Are pregnant and have an ultrasound at Hvidovre Hospital, or
- Have an induced abortion
- Have an examination in connection with a miscarriage
- Give birth at Hvidovre Hospital
- Are a partner of a woman delivering at Hvidovre Hospital
- Can read and understand information about the project in Danish, English, Arabic, Turkish, Farsi, Urdu or Polish.

Who cannot participate?
You cannot participate in this study if

- You do not speak and understand Danish, English, Arabic, Turkish, Farsi, Urdu or Polish

Cancellation of the project
We may have to cancel the project in the event of any unforeseen practical, financial or staff-related circumstances. However, we do not expect such obstacles.
As mentioned above, taking part in this project is voluntary and you can withdraw your consent at any time and without explanation.

How will the project be carried out?
All pregnant women in Denmark are offered prenatal ultrasound scans during the first half of their pregnancy (nuchal fold scan) and during the second half of pregnancy (general scan).

You will be able to participate in the project if you or your partner is pregnant and before 1 July you will receive an ultrasound at Hvidovre Hospital or give birth at Hvidovre Hospital. We will ask your permission to take the following samples:

- In connection with the general ultrasound and consultations related to induced abortions or miscarriages, we will ask permission to take a blood sample (13ml) from the pregnant woman. At this time, the woman will be asked whether she wants to participate in a supplementary questionnaire on mental wellbeing and concerns related to the Covid pandemic.
- In connection with delivery, we will ask permission to take a throat swab and a blood sample (13ml) from the pregnant woman and her partner as well as a vaginal swab during delivery.
- After delivery, we will take a blood sample from the umbilical cord (8ml) and a small sample of the placenta. The sample will be taken once the umbilical cord and placenta have been discarded and are no longer of use to the child.

The samples will be taken to check for any current or previous coronavirus infection and to analyse biomarkers that can determine the degree of severity of the illness. Some samples will be stored for later studies of genes that may affect whether a person becomes infected and how sick they become from the infection. In cases where the newborn child is infected with Covid-19, the placenta sample will be examined at a later date for any changes.

If you have previously taken a Double Marker test (a blood sample in connection with the Nuchal Fold scan), we will examine the sample for signs of Covid-19 (antibodies).

Treatment related to your pregnancy and delivery will not be affected by your choice to participate or not participate in this project.

What are chromosomes, genes and genetic material?
All cells in the body contain chromosomes. Chromosomes are small structures that contain our hereditary traits, known as genes. The information contained in genes determines our traits and controls the development of our organs, e.g. the brain, heart and kidneys. Normal body cells contain 46 chromosomes grouped into 23 couples. In each couple, one chromosome is inherited from the mother (the egg cell), while the other is inherited from the father (the sperm cell). The first 22 chromosome couples are identical for men and women. The 23rd couple is known as the sex chromosome. It is referred to as XX in women and XY in men.

Chromosomes contain DNA. A gene is a piece of our DNA. There are approximately 20,000 genes in each cell. All genes have a specific function. However, the function of all genes is not yet known. We carry our genes our entire life and the information contained in our genes is therefore different from other health information, which typically only provides a small snapshot of the whole picture. Gene mutations can be found in all humans. These mutations sometimes cause genetic disorders. Genetic disorders occur when one or more genes do not function correctly. This can be caused by defects in the gene or by changes to the information in a gene. Changes to a gene, known as a mutation, can be newly formed in a person or can be inherited from one or both parents. Similarly, different variations in our genetic material can affect how susceptible we are to developing illnesses, e.g. coronavirus.

Why are we studying genes?
Previously, it was only possible to study one gene at a time. It could therefore take many years to identify the genetic cause of a congenital disorder. Comprehensive mapping of genetic material means that it is now possible to examine all 20,000 genes at once. This means that, among other things, you can identify the causes of congenital disorders much faster than previously. Research is expected to bring new knowledge to light that will enable more targeted treatment of patients and thus increase the chances of successful treatment. Genetic analyses lead to a large volume of surplus information, so-called genome data. The genome data will be stored with the project in accordance with the General Data Protection Regulation and the Data Protection Act.

Mapping your genetic material
The blood samples will be used to complete an extensive **genetic mapping of your genetic material.** A genome analysis will identify any possible genes that affect how susceptible you are to infection and illness, e.g. coronavirus.
Prior to taking part in the trial, you will also be offered a consultation to further discuss the implications of the mapping of your genetic material. The genetic aspect of this research project is not a patient study and we therefore do not expect you to derive any personal benefit from it. You will therefore not receive the results of any findings of the genome study. The mapping may reveal unexpected information. You will be informed in the rare case that we discover a mutation in your genes that may lead to serious illness that can be prevented or treated. It may also be necessary to inform relatives if the information can prevent death or a serious deterioration of health. *It is important to think about this before you agree to participate in this project. In the consent form, you have the option to choose not to receive information on any genetic discoveries that may affect your health. Please note that we will not check for all pathogenic genes and will only contact you if we happen to discover a gene that may lead to serious illness.*

What happens with the samples after the trial?

Biobank

The samples (blood and swabs) will be stored in a research biobank until 17 March 2025. After this, the remaining material will be kept in a biobank for future research until 2035. The remaining material will then be destroyed and the data will be anonymised and archived in the Danish National Archives. All future use of the surplus materials for research must be approved by the Research Ethics Committees. Data privacy regulation will also apply to any future research. You can choose to transfer genetic data to the Danish National Genome Centre, ensuring that the data is available should it become relevant to you in the future. The project was approved by *Videncenter for Datanmeldelser* (the Danish centre for data registration) on 1 March 2020 (P-2020-255) and on 24 March 2020 (P-2020-300). The sample material will be examined in collaboration with our partners. The Data Protection Act and the Processing of Personal Data Act (applicable Danish legislation) will be complied with when sending samples to other countries and the samples will only be identified by an ID-number (pseudonymised).

Genome data

We will be collaborating with the Icelandic company, deCODE genetics, in connection with the comprehensive genetic analyses. Even though the comprehensive genetic analyses will be carried out by deCODE genetics in Iceland, the genetic data will be processed in accordance with Danish law. deCODE genetics does not own the genetic data and will only have access to pseudonymised data, i.e. deCODE genetics will analyse the data without knowing the identity of the participant.

The genetic data will be transferred to Denmark, where they will be analysed and stored on Computerome. After completion of the project, the genetic data will be stored in accordance with the General data Protection Regulation and the Danish Data Protection Act.

Data security

The large amounts of genome data collected will be stored in the steel containers on Computerome, Denmark's national supercomputer. The computer is located at Risø and is under the supervision of the Technical University of Denmark. Computerome has very high security standards. All data is located in a so-called secure cloud, which means that data is split both physically and electronically and can only be combined by persons holding the correct access rights.

At your request, your genome data can be stored by the Danish National Genome Center.

The Danish National Genome Center is a government agency tasked with storing data from extensive genetic analyses for research and for future diagnostics and treatment of any illnesses you may contract in the future. After this project is completed, the genome data will be stored in accordance with the General data Protection Regulation and the Danish Data Protection Act. You can read more about your data rights in the Danish Data Protection Agency guidelines on www.datatilsynet.dk (in Danish only).

With your consent, we will also:

- Request permission to register the following information from your patient record in a research database: General information on your state of health, possible chronic diseases, previous illnesses, pregnancies and births, current week of pregnancy, first day of your last menstrual period, information on any prior fertility treatment, blood pressure, height, weight, BMI, pregnancy symptoms, type of treatment and findings in connection with ultrasound, and any medication you are on.
- Request permission to collect information from different registries: i.e. information concerning psychological and physical diseases from medical records, health registries and

databases, and information about your education, social status and income from Statistics Denmark.
- Request permission to collect information on your health and the health of your child using a questionnaire 1 month after delivery and then in 1, 2 and 5 years via your medical journal and the above-mentioned registries and databases.
- Request permission to possibly contact you via email, letter or telephone in 1, 2 and 5 years to check up on your health status.
- Request permission to couple your information with your partner's information.

You will still be able to participate in this project, even if you do not wish to be contacted by us at a later time.

We will also ask permission to collect health information on your child after the birth. This will be covered in a separate consent form.

Benefits of the study
Your participation will provide important knowledge regarding pregnancy and birth during this pandemic (coronavirus, Covid-19). We will share the results of the studies with you.
Once the data has been analysed, the findings will contribute important information regarding infection as well as any restrictions for pregnant women, their partners and newborn children during the coronavirus epidemic.

Disadvantages, risks and complications
As a general rule, there are no side effects or risks associated with participation in this project. However, there may be unforeseen risks and problems associated with sampling.
Some men/women find blood tests and swabs uncomfortable. However, we assess that there are no risks in connection sampling, and sampling will not result in additional treatment.

Your data
Your personal data will be processed as part of this study. The Data Protection Act and the General Data Protection Regulation will be complied with.

Information about your health, as well as other personal and confidential information about you that comes to light in connection with with project is covered by our duty of confidentiality.

Data from the project will be stored in an approved database and the results will be analysed anonymously. Information stored in the database will only be of a health-related nature and will include information on previous illnesses/hospitalisation, current treatments/ultrasounds and the birth in question. With your permission, we will collect information related to your pregnancy and the birth of your future child, including weight, length, duration of pregnancy, and any possible anomalies or additional hospitalisation on the maternity ward. Direct access to medical records is pivotal to completing, monitoring and controlling the project.

Results
The results of the study will be presented at scientific conferences. One or more articles are expected to be published in prestigious, scientific journals. The results of the study are expected to garner great interest due to the timeliness of the topic and its relevance to both Denmark and the rest of the world.

Financial information
This project was started by Professor Henriette Svarre Nielsen, consultant, MD, at the Department of Gynecological Obstetrics at Hvidovre Hospital. There are no financial costs for participants in the study. There is no payment for participation in the study.

Funding
The project has received DKK 5.808 million in funding from the Danish government's pool for Covid-19 research. The amount covers costs related to the collection and processing of biomaterial. It also covers expenses for Covid-19 analyses. Participants and the Research Ethics Committees will be notified when funding has been secured. The study will be carried out independently of the pharmaceuticals industry. The grant-maker has not influenced protocol preparation for this project and the doctors/research team attached to the project are not financially dependent on private enterprises, including our collaboration partner deCode genetics.

Other factors
In accordance with current legislation, representatives from the Danish Health Authority and the Research Ethics Committees are permitted to access project records kept by the hospital and the clinic. We therefore ask that you provide full power of attorney when you sign the consent form. This study is covered by normal patient insurance.

Information about the study
This project has been approved by the Research Ethics Committee for the Capital Region of Denmark (Journal no.:H20022647) as well as the *Videnscenter for Dataanmeldelser* (centre for data registration) for the Capital Region of Denmark. In accordance with the Danish Act on Free Access to Public Records, you have a legal right of access to trial protocols.

Contact details
To learn more about the project, you are welcome to contact:

Project manager/sponsor
Professor Henriette Svarre Nielsen, consultant, MD.
Department of Gynecological Obstetrics, Hvidovre Hospital
Kettegård Allé 30, 2650 Hvidovre, Denmark
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We hope that this information has provided you with sufficient insight into what participation in this project involves, and we hope we have given you the best grounds on which to base your decision. You are always welcome to contact the staff at the department or the doctor in charge of the project if you have any questions.

If you would like to participate in this project, please sign the consent forms on the following pages. You and your any partner will also need to grant consent to collect information relating to your child.

Thank you for your time.

Kind regards,
Research team

Rights of clinical trial subjects in a health-science research project

As a participant in a health-science research project, please note that:

- your participation in this project is entirely voluntary and you may only participate once you have been informed both verbally and in writing about the project and you have signed the consent form.

- you may withdraw your consent verbally, in writing or by other clear indication at any time and leave the project. Withdrawing your consent will not affect you right to current or future treatment or any other rights you may have.

- you are entitled to have a family member, friend or acquaintance with you (virtually) at the introductory consultation.

- You are entitled to a period of reflection prior to signing the consent form.

- information about your health, as well as other personal and confidential information about you that comes to light in connection with with project is covered by a duty of confidentiality.

- processing of your personal information, including information contained in your blood samples and tissue, will be in accordance with regulations in the General Data Protection Regulation, the Danish Data Protection Act and the Danish Health Act. The data controller of the test will provide you with additional information on your rights in accordance with the data protection regulations.

- in accordance with the Danish Act on Free Access to Public Records, you have legal right of access to protocols. This means that you can access all documents concerning the organisation of the study, except for the sections that contain trade secrets or confidential information about other people.

- in accordance with the Danish Act Governing the Right to Complain and to Obtain Compensation in the Danish Healthcare System, you may lodge a complaint and seek compensation. If you are injured during the trial, please contact the Patient Compensation Association; for more information visit www.patienterstatningen.dk.

Consent form for the pregnant woman

Informed consent to participate in a health-science research project.

Title of the research project:
Consequences of Covid-19 infection for pregnant women, women in labour, their partners and newborn children.

Statement by the trial subject:

I have received written and verbal information and I have sufficient knowledge of the objective, method, benefits and disadvantages to agree to participate. I know that it is voluntary for me to participate and that I can always withdraw my consent without losing my current or future rights to treatment.

I have been informed that this research project includes comprehensive mapping of genetic material. I have also been informed that, in rare cases, mutations in my genes may be discovered that could lead to serious illness that can be prevented or treated. If so, I will be contacted.

I give consent to take part in the research project and that my biological material be extracted with a view to storage in a research biobank. I have received a copy of this consent form and a copy of the written information about the project for my own use. I have been offered a copy of this consent form and a copy of the written information about the project for my own use.

Trial subject:

Full name: _____

I have been informed that in connection with some analyses, e.g. comprehensive survey of genes, there is a risk of discovering mutations (changes) that could result in illness (please tick one only):

□ I would like to be informed of any findings significant to my health for which prevention or treatment is possible.

□ I do **not** want to be informed of any findings.

I have been informed that it is my own decision whether my genome data is stored by the Danish National Genome Center to help diagnose any illnesses I may develop in the future, to help my future treatments or for research purposes (please tick one only):

□ I would like my genome data to be stored by the Danish National Genome Center.

□ I do **not** want my genome data to be stored by the Danish National Genome Center.

Date: _____ Signature: _____

Statement by the person providing information:
I declare that persons who have parental responsibility for the trial subject have received verbal and written information about the trial.

In my view, sufficient information has been provided to ensure that a decision can be made regarding participation in the trial.

Name of the person providing information:

Date: _____ **Name:** _____ **Signature:** _____