INSITU

Imperial College Healthcare NHS Trust

INVESTIGATIONAL STUDY INTO TRANSPLANTATION OF THE UTERUS

PARTICIPANT GENERAL INFORMATION & INVITATION LEAFLET

Study title:	**Investigational Study into Transplantation of the Uterus**
Short title:	**INSITU**
REC reference:	**18/LO/0217**
IRAS project ID:	**235711**

This is an invitation to take part 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. Please take time to read the following information carefully and feel free to discuss this with your partner, your family and with your doctor. Ask us if there is anything that is not clear or you would like more information. Take time to decide whether or not you wish to take part.

Why have I been invited to participate?

You have been invited to participate because you have been diagnosed with absolute uterine factor infertility (AUFI), a condition which affects one in 500 women of childbearing age. Women with this condition have infertility due to either the absence of their uterus (womb) or they have an anatomically or physiologically non-functioning uterus. This may be congenital (from birth) or acquired (for example following hysterectomy to treat gynaecological cancer, benign gynaecological disease or following severe haemorrhage after childbirth).

What is this study about?

This study will seek to offer up to 10 women with AUFI the opportunity to receive a womb transplant from a compatible donor. The donor will be deceased, having been declared brain dead after suffering permanent and irreversible brain injury. Prior to undergoing the transplant, each participant will have her fertilised eggs preserved by freezing (cryopreservation) in readiness for transfer into the transplanted womb from 6 months onwards following the operation. Following conception each woman will be closely monitored and looked after as a 'high risk' pregnancy. The subsequent birth of the baby will be by elective Caesarean Section at approximately 37 weeks' gestation.

How have patients/public been involved in the development of this study?

You will initially undergo a pre-screening selection process which involves using a questionnaire to determine if you meet the main selection criteria. The questionnaire was developed and validated with the assistance of a patient group, some of whom, have undergone organ transplant themselves.

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Do I have to take part?

No, it is up to you to decide whether or not to take part. If you decide to participate you will be given this leaflet to keep and be asked to sign a consent form when you are satisfied that all your queries have been answered fully.

Pre-screening Process

To determine which women are most suitable to undergo a womb transplant a pre-screening process will be carried out. A questionnaire has been created that will be used to elicit previous medical, surgical and psychological history, along with various lifestyle and social factors. Following the return of the questionnaire, selection criteria will be used to establish which women would be appropriate to partake in the process. A scoring system will then be used to identify those most suitable to undergo the process.

What will happen to me if I decide to take part?

Those selected will undergo an investigation process to confirm that you meet the selection criteria to take part in the trial. More detailed information will be provided in the corresponding information leaflets for each stage of the study process:

- Fertility treatment
- Transplant & immunotherapy Antenatal care
- Caesarean section/postnatal care
- Hysterectomy

As part of the selection process you will undergo a number of pre-operative investigations including various blood tests, an electrocardiogram (ECG), a magnetic resonance imaging (MRI) scan of the abdomen and pelvis along with swabs to check for genito-urinary infections. If the MRI scan indicates an abnormality that requires further investigation of intervention, then you may need to undergo a keyhole operation in your abdomen (laparoscopy), but this is unlikely. Your partner will also need to undergo blood tests to exclude infection and also undergo a check for genito-urinary infections. If you are both found to be physically and psychologically suitable you will be enrolled in the clinical trial.

Prior to the womb transplant, if you do not have embryos stored already, it will be necessary to undergo fertility treatment to create ten embryos that will subsequently be transferred following transplantation. The process of creating embryos is the same as what you would need to undergo if you were undergoing surrogacy. This treatment will take place at the Lister Fertility Clinic at the Lister Hospital in London.

You will meet the transplant team at the Churchill Hospital in Oxford and the team at Queen Charlottes Hospital who will look after you whilst you are pregnant. You will have the opportunity to ask questions about every aspect of the trial. You will also meet with Dr Maria Jalmbrant, the clinical psychologist for the trial, who will undertake an interview of both you and your partner and undertake a number of questionnaires to assess your psychological wellbeing. You will continue to see Maria throughout the process, and

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complete various questionnaires to continually assess your wellbeing. Support will also be given as needed, including the option of enrolment in a stress reduction programme.

From this point, you will be placed on a waiting list until a suitable donor is identified. It is planned that the transplants will be performed over a two-year period so you may be waiting for an organ to become available for up to two years. Initial funding has been secured for the first three transplants and further procedures will not be performed until further funding has been raised. The first three women who proceed to transplantation will be chosen based on blood group, to optimise the chances of finding a compatible donor. When a donor becomes available and it has been confirmed that you are a suitable match for the organ, you will receive a call from the transplant coordinator to come to the Churchill Hospital. It is likely this will be at short notice (12-24hours).

Once the donor womb has been retrieved they will be ready to proceed with your operation. The transplant is a major operation that will be performed by the consultant surgeon. The operation usually takes between 6-8 or longer. You will be in the Churchill Hospital for approximately 7 days after the transplant. While you are living with your transplanted uterus (womb) you will need to remain on medication called immunosuppression, which works by reducing the body's natural defence system (immune system), to prevent your womb being rejected.

If all remains well you will undergo embryo transfer from 6 months following the transplant. This allows sufficient time to ensure that the uterus (womb) is working properly, to monitor for rejection and ensure that you are on a stable dose of immunosuppression that will not cause any problems to the pregnancy or a growing fetus. For the embryo transfer to have the best chance of success you will be treated with various hormones to help prepare the womb for the embryo. Only one embryo will be used at a time to reduce the risk of multiple pregnancy.

If your pregnancy test is positive your care will be transferred to the obstetric team at Queen Charlotte and Chelsea Hospital for pregnancy care. During this time you will continue with hormone therapy until 12 weeks' gestation. If the pregnancy test is negative then the process will be repeated.

Following an uncomplicated pregnancy your baby will be delivered by caesarean section at 36–37 weeks' gestation under a spinal anaesthesia. This will be undertaken by the obstetric team at the Queen Charlotte's and Chelsea Hospital. The baby needs to be delivered by Caesarean section due to the risks of vaginal birth on the transplanted uterus.

If you experience complications during the pregnancy this will be carefully monitored and any decision to deliver your baby earlier will be made by the obstetric team in conjunction with the neonatologist and the surgical team.

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Following your Caesarean section, you will be transferred to the postnatal ward for a few days while you recover and establish infant feeding. You should be able to breastfeed on immunosuppressive therapy if you want to. If your progress is normal, you will be discharged into the care of your community midwife who will visit you at home.

Subject to an uncomplicated course, it may be possible to repeat this process and try for another child. Once you have completed your family, approximately 6 months following the birth of your baby you will undergo removal of the transplanted womb at the Hammersmith Hospital. Following hysterectomy, you will be able to stop the immunosuppressive medications and all other medicines that were started as part of the transplant process. Six weeks after hysterectomy you will be seen at the clinic and debriefed by the surgeons.

If no pregnancies are achieved within five years following the transplant then, to reduce the risk of long term immunosuppressive medications, the transplant will have been deemed unsuccessful and hysterectomy will be advised.

Will taking part be kept confidential?

Yes, please be assured that as an NHS patient your data will be protected under the data protection act. Data collected throughout the study will be stored on a password protected database, on a secure password protected NHS computer in a locked NHS office, and identifiable details will be amended under a study number. Manual files, including consent forms, will be stored within the study file. This is kept safely within the locked research filing area located in a secure research team office at Hammersmith Hospital. This office will be locked and the research file will only be accessible to research team members. Video recording may be used during the operation if you consent to it. The area filmed will only be the operative site. Any video recordings containing patient sensitive information will be treated securely on a secure password protected NHS computer in a locked NHS office. The recordings, which do not contain sensitive information, or identify any participants, may be used in future for teaching, presentation or in journals. The video recordings, along with all other research data, will be stored for 30 years. In the event if data being transferred between sites, data will be anonymised, compressed and encrypted prior to transfer, to ensure it remains secure.

What will happen to my information & samples afterwards?

The data collected from the study will be used to contribute towards a PhD research degree for Dr Benjamin Jones. Research information obtained during the study will be retained for 30 years. We will store certain tissue samples so that they may be used for future ethically approved research.

What will happen if I decide to withdraw from the study after I have given my consent?

If you decide to take part you are still free to withdraw **at any time** without giving an explanation, or, a decision not to take part, will not affect the care you receive in any way at

present or in the future. Data and samples already taken will be retained for research purposes but no future data will be collected or stored.

Who is funding the study?

This study has been funded by the registered charity Womb Transplant UK (Charity no 1138559).

What are the possible benefits to me if I take part?

This study will offer women with absolute uterine factor infertility, the opportunity to conceive and grow a pregnancy to term and give birth to a biologically related infant.

What are the risks or side-effects to me if I take part?

This is a complex study with numerous interventions and various stages over a long period of time. Each stage of the transplant process carries different and significant risks, which are explained in detail in the corresponding information leaflets. There are multiple major surgeries planned, including the transplant itself, up to two Caesarean sections and a hysterectomy. Each operation has associated anaesthetic risk, as well as risk of bleeding, infection, damage to internal organs and blood vessels and blood clots in veins or the lungs. One of the biggest risks is rejection of the transplanted uterus which may lead to it being removed. Conversely there are also risks with the immunosuppressive medications given to reduce the risk of organ rejection, including infection, diarrhoea, diabetes and cancer. This increased risk is largely transient as these medications will be stopped after hysterectomy. There are risks with the fertility treatment, including bleeding and infection related to the egg retrieval, and the ovaries can also be overstimulated which causes a condition known as ovarian hyperstimulation syndrome (OHSS). There is also a risk that the fertility treatment is unsuccessful, leads to miscarriage or results in a poor pregnancy outcome. These risks are explained further in the individual patient information leaflets addressing the fertility care, the transplant and immunotherapy, the Caesarean sections and the hysterectomy.

What if something goes wrong?

Imperial College Healthcare NHS Trust holds standard NHS Hospital Indemnity and insurance cover with NHS Litigation Authority for NHS Trusts in England, which apply to this study. This does not affect your legal rights to seek compensation.

If you are harmed due to someone's negligence, then you may have grounds for a legal action. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been treated during the course of this study then you should immediately inform the Investigator. The normal National Health Service complaints mechanisms are also available to you and you will be able to liaise with the Patient Advice and Liaison Service (PALS) at the hospital who can provide confidential advice, support and information. If you are still not satisfied with the response, you may contact the Imperial AHSC Joint Research Compliance Office.

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Who do I contact if I want to know more about the study?

If you have any further questions please do not hesitate to contact the study coordinator who will direct your queries to the appropriate member of the study team.

Mr J Richard Smith – Chief Investigator

Telephone: 0207 730 0431
Email: admin@jrsmithgynaecology.com

Thank you for reading this leaflet and considering whether to take part in the study

The approach, consent and assessment process prior to uterine transplant will take place ***at Imperial College Healthcare NHS Trust, Hammersmith Hospital***