

A randomised controlled trial of prednisolone for women with recurrent miscarriage and high levels of uNK cells in the endometrium. (Version 6, 1/05/08)

You are being invited to take part in a research project. Here is some information to help you decide whether or not to take part. Please take time to read the following information carefully and discuss it with friends, relatives and your GP if you wish. Ask us if there is anything you do not understand or if you would like more information. Take time to decide whether or not you wish to take part. Thank you for reading this.

What is the purpose of the study?

Recurrent Miscarriage (RM) can be a very distressing condition to the woman and her partner. In half of the cases we do not know the reasons why it happens. We would like to find out if certain cells that are called the Natural Killer (NK) cells from the lining of the womb (endometrium) contribute to the miscarriage. Natural killer cells are white blood cells that help to fight against infections, viruses and cancer. However, we have discovered that some women with recurrent miscarriage have high levels of NK cells in their womb. Furthermore, we have found that a steroid drug, known as prednisolone decreases the number of these NK cells. We now want to do a further trial to see if the steroid treatment increases the chance of you having a live baby.

Why have I been chosen?

You have been chosen because you have a history of recurrent miscarriage where the cause has not been found. A maximum of 700 patients will be studied over the period of 10 years.

Do I have to take part?

It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason. This will not affect the standard of care you receive.

What will happen to me if I take part?

Step 1 screening with endometrial biopsy

If you decide to take part, a small sample of the lining of your womb will be taken on Day 21 of the menstrual cycle. The sample will be taken in a similar manner to taking a cervical smear. You may experience some mild discomfort whilst the biopsy is being taken. The risk of any damage to your womb during the procedure is absolutely minimal and if any damage should occur it will heal spontaneously. If we took the biopsy whilst you are pregnant, it could possibly cause a miscarriage but the risk is very small. **Therefore, you need to use barrier method of contraception in the month that you have your biopsy (for example use condoms).** The biopsy will be analysed for the NK cells and various other cells that line your womb. You have a 30% chance of having high levels of NK cells.

Step 2 trial of prednisolone therapy against placebo

If you have high levels of NK cells then, you will be asked to ring the NK cell study answering machine when you are pregnant. You will be telephoned back within one day and given an appointment for a scan. If the scan shows that the pregnancy is in the uterus, you will be asked if you would agree to enter the trial. That is, you will be entered into one of two groups randomly. One group will receive a packet containing prednisolone daily for 8 weeks, and the other group will be given a packet containing identical dummy tablets. You will not know which drug you are taking and neither will your doctor (although if your doctor wants to find out he/she can do so). You may experience minor side effects of steroids such as mood changes, weight gain, increased

appetite, indigestion, high blood pressure and high blood sugar levels and a rare complication called avascular necrosis (This causes severe pains on your hip joint). You will be kept under regular review whilst you are on the medication. You will be contacted via telephone at 14 weeks gestation, and asked about any side effects you had.

The prednisolone is thought to cause the developing fetus very little harm. However, there is some evidence to suggest that it could be associated with cleft lip and poor growth in the uterus.

What are the possible benefits of taking part?

The information we get from this study will help us to find out if prednisolone is an effective treatment for women with recurrent miscarriage and high levels of NK cells.

We would like to keep your sample for examination of other factors in the lining of your womb that may be important in miscarriage. This part of the research is at an early stage hence we will not be able to give you the results. If you agree to this you can sign an extra box on the consent form. We would like to keep this sample for up to ten years.

What if something goes wrong?

If taking part in this research project harms you, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for a legal action but you may have to pay for it. Regardless of this, if you wish to complain about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms may be available to you.

Will my taking part in this study be kept confidential?

All information collected about you during the course of the research will be kept strictly confidential. Any information about you, which leaves the hospital, will have your name and address removed so that you cannot be recognised from it. Dr Quenby or another doctor involved in the research project may look at your medical notes and those of any baby born, to obtain information relevant to this study. Because you may be taking this medication, your GP will be notified of your participation in the study and a medical alert card will be given to you stating that you may be taking prednisolone or placebo drug.

What will happen to the results of the research study?

The results will be published in scientific journals and presented at conferences to further our understanding of recurrent miscarriage. All published data will be anonymous.

Who is organising and funding the research? Liverpool Women's Hospital. The Moulton Charitable Trust

Who has reviewed the study? The Liverpool Research Ethics Committee

Contact for Further Information

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Tel: Dr Quenby's Secretary 0151 702 4271

The Miscarriage Association: <http://www.miscarriageassociation.org.uk/>
helpline: 01924 200799 (Mon-Fri, 9am - 4pm)

Thank you for reading this. You will be given a copy of this information and a signed consent form to keep should you decide to take part.