# Typing of endometrial lymphocytes of (unexplained) recurrent miscarriage patients

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a. To investigate the phenotype and function of immunological cells present in endometrial and peripheral blood of women with a history of recurrent miscarriages and women without any known pregnancy complications.b. To investigate the association...

Ethical review	Approved WMO
Status	Pending
Health condition type	Maternal complications of pregnancy
Study type	Observational invasive

## Summary

### ID

NL-OMON44412

**Source** ToetsingOnline

Brief title TERM-study

## Condition

• Maternal complications of pregnancy

**Synonym** unexplained recurrent miscarriage

**Research involving** Human

### **Sponsors and support**

**Primary sponsor:** Radboud Universitair Medisch Centrum **Source(s) of monetary or material Support:** Ministerie van OC&W

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### Intervention

Keyword: Endometrium, Immunophenotyping, NK cell, Recurrent miscarriage

### **Outcome measures**

#### **Primary outcome**

Differences in phenotype and function of immunological cells present in

menstrual blood of patients and controls.

#### Secondary outcome

na

## **Study description**

#### **Background summary**

Recurrent miscarriages (RM) occurs in 1-3% of all women trying to conceive. Unfortunately, around half of the recurrent miscarriage cases remains unexplained, leaving the couples with the burden of uncertainty and clinicians without treatment options. It is well accepted that the immune system plays an important role in the implantation of the embryo into the uterus wall. Interaction between natural killer (NK) cells in the uterine lining and invading extravillous trophoblast cells (EVT) is important for proper placentation. When invasion of trophopblast cells is defective, the placenta is not formed properly which can lead to disorders like miscarriages. It has been suggested that women who experience RM lack certain receptors that recognize EVTs on their uterine NK cells. Also, some specific combinations of maternal KIR2D and fetal HLA-C have been correlated with pregnancy related complications. Besides NK cells, also other cells present in the endometrium or early decidua are thought to play a role, such as regulatory T cells (Treg) that can specifically suppress immune responses. A tightly regulated Th1/Th2/Th17/Treg balance is required for successful pregnancy as it has been shown that Treg were decreased while higher levels of Th17 have been found in peripheral blood and decidua of women with RM.

Up till now research into this problem has focused on peripheral blood and decidual tissue. Few have examined endometrial lymphocytes due to ethical constrictions related to taking biopsies. Our new technique to obtain endometrial cells via menstrual blood collection, now offers the unique opportunity to examine this tissue in more detail in RM patients versus controls. In this project we aim to determine immunological causes of unexplained recurrent miscarriage. These results will help to identify these patients and to eventually develop effective therapies.

#### **Study objective**

a. To investigate the phenotype and function of immunological cells present in endometrial and peripheral blood of women with a history of recurrent miscarriages and women without any known pregnancy complications.

b. To investigate the association between the maternal KIR and the paternal HLA-C genotype in recurrent miscarriages and uncomplicated pregnancies.

The ultimate goal will be to investigate whether menstrual blood can be used to detect patients that will likely suffer from a miscarriage in their next pregnancy.

#### Study design

Characterisation of the immunological cells present in menstrual and peripheral blood of recurrent miscarriage patients and controls.

In this study we will investigate endometrial blood from recurrent miscarriage patients and from women who had uncomplicated pregnancies. Patients and women without known pregnancy complications will be asked to collect menstrual blood during 1.5 day in 3 blocks of 12 hour. In addition, a peripheral blood sample will be asked during a regular visit to the Radboudumc. The male partner, i.e. the biological father of the child, of these women are asked to use a buccal swab to collect DNA to determine the HLA-C genotype

#### Study burden and risks

There are no direct benefits of this study for the participating subjects. The benefits may be related to the future understanding of the role of immunological cells in successful pregnancy.

The risk for the subjects associated with this study is minimal. The participant will be asked to get one blood withdrawal (1 tube of 10mL) during a regular visit to the Radboudumc. The use of the menstrual cup to collect menstrual blood is completely safe, there is no risk for toxic shock syndrome like with the use of tampons.

The male partner, i.e. biological father of the child, will be asked to collect DNA by the use of a buccal swab. This is completely safe and can be done at home. The only burden the partner will have is that he can\*t eat anything 30 minutes before taking the swab.

## Contacts

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## **Trial sites**

## Listed location countries

Netherlands

## **Eligibility criteria**

#### Age

Adults (18-64 years) Elderly (65 years and older)

#### **Inclusion criteria**

#### Patient group:

Normotensive women aged 18-45 years with a history of 3 or more consecutive, idiopathic pregnancy losses before <20 weeks of pregnancy. Patients are asked to collect menstrual blood. In case of a recent miscarriage, the patient is asked to collect menstrual blood during their second normal menstruation following the miscarriage.;Control group: Normotensive, fertile women aged 18-45 years without any known pregnancy complications, i.e. not tried to conceive yet and/or no problems to get pregnant and uncomplicated pregnancies.;The partner, i.e. biological father of the child, of these women will be included in the study as well.

## **Exclusion criteria**

- Use of immunosuppressive drugs, biological or antidepressants
- Use of birth control (exception condom)
- HIV positivity
- Auto-immune diseases
- Diabetes mellitus
- Smoking
- Participants who are not capable of signing the informed consent

- Patients will be excluded if there is a known cause for the miscarriages like e.g. the presence of anti-thyroid, anti-phospholipid and anti-nuclear autoantibodies, endocrine dysfunction, uterine malformation, hemostatic disorder, and abnormal karyotype.

## Study design

### Design

Observational invasive
Other
Non-randomized controlled trial
Open (masking not used)
Active
Diagnostic

#### Recruitment

NL	
Recruitment status:	Pending
Start date (anticipated):	18-07-2017
Enrollment:	80
Туре:	Anticipated

## **Ethics review**

Approved WMO	
Date:	30-01-2018
Application type:	First submission

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## **Study registrations**

### Followed up by the following (possibly more current) registration

No registrations found.

## Other (possibly less up-to-date) registrations in this register

No registrations found.

### In other registers

Register CCMO ID NL62693.091.17