

# RIC Information for Patients



IMMUNO CONCEPTS IN INFERTILITY



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## 1. Pregnancy and the immune system

From the implantation of a fertilised egg to the delivery of a healthy baby, the maternal immune system has a major impact on the survival and development of the foetus. For successful pregnancy, the mother's immune system has to tolerate the immunologically foreign foetus, making the maternal environment potentially immunologically hostile.

The inability of a healthy woman to get pregnant or to suffer recurrent miscarriage has a number of causes, including chromosomal/genetic abnormalities, uterine problems and endometrial infection. When these have been excluded, exaggerated maternal immune activity is considered of prime importance. This exaggerated activity is apparent in several cells associated with the immune system. For instance, when the maternal immune system is overly active, NK and T cells are implicated or, in the case of anti-phospholipid antibody syndrome, B cells producing antibodies are involved.

Checking for increased or abnormal activity of these cells and the exclusion of autoimmunity (an immune response against the body's own tissues and foetus) allows timely pharmacological intervention that is critical for reproductive success.

The role of NK and T cells is particularly important and provides the core of our testing. For further information on the role of these cells, as well as other immunological components affecting pregnancy, please visit our website.

## 2. What is Reproductive Immunology Centre?

The Reproductive Immunology Centre (RIC) is based in Carshalton, Surrey and offers a comprehensive laboratory assessment of NK and T cell function as well as other immunological parameters, such as the functioning of the antibody system, in women with unexplained infertility.

RIC is well established and is one of only three laboratories in the world that provides in-depth analysis of the immune system in the field of infertility. Our services are used by many fertility specialists around the country, as well as several other laboratories lacking our expertise.

An extremely important characteristic of RIC is our programme of ongoing research, which builds on many years of earlier work that has been published in several peer-reviewed journals. This research continues to provide evidence which supports the benefits that our tests offer the clinician in the investigation of unexplained infertility.

### 3. What tests do RIC offer?

Besides the NK cell tests (NK activation and cytotoxicity) we also offer a range of other tests analysing cells and antibodies implicated in infertility. These include:

Tests to compare the suppressive effects of steroid, IVIg and intralipid on NK cell killing

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Th1/Th2 cytokine assay

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Anti Nuclear Antibody and subsequent testing for ENA and DNA antibodies if required

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Anti Thyroid Peroxidase Antibody

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Anti Cardiolipin Antibody (Both IgG and IgM type antibodies)

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Lymphocyte Subsets

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We can also screen for mutations associated with abnormal coagulation systems which may have an affect on pregnancy.

Factor V Leiden Mutation

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Prothrombin Gene Mutation

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We are currently working on developing an assay to measure Treg and Th17 cell levels.

### 4. How do I know that I need an NK cell test?

Your fertility specialist will be able to assess which tests are likely to be helpful in the management of your particular clinical problem.

The tests allow your fertility specialist to see if your NK cells are overly aggressive towards your embryo. Further testing can also assess which of the currently available therapies are best able to reduce the activity of these cells and thus may lead to improved pregnancy outcomes.

It should be noted that not all these tests are recommended by the Human Fertilisation and Embryology Authority (HFEA), the Royal College of Obstetricians and Gynaecologists (RCOG) or the American Society of Reproductive Medicine (ASRM) as the research community is divided in the interpretation of the data. With more research being required in the field of reproductive immunology, the tests offered are still considered research tests by some and you should be aware of this.

### **5. If these tests are not supported by the HFEA, why are you doing them?**

Research published by RIC in many of the leading fertility journals has shown that the absolute numbers of NK cells have no influence on the outcome of pregnancy following IVF. However, we and others have published results showing that abnormally high levels of activated (CD69+) NK cells or increased NK cell killing is associated with a reduced rate of successful pregnancy following IVF.

In addition to demonstrating the effects of NK cells on fertility, we have also shown that certain changes in T cell subsets are more frequent in those with recurrent failed IVF. Furthermore, research has shown that specific drugs can reduce unhelpful anti-fertility NK cell activity. These findings have been confirmed by other centres around the world.

For an up-to-date review of the NK and T cell literature go to our website.

### **6. Why has my doctor not suggested these tests before?**

There may be several reasons for why your doctor has not suggested these tests before, including:

- the lack of awareness of the availability of scientifically confirmed tests by an accredited laboratory in the UK.
- your specialist may have been pursuing purely non immunological causes for your infertility.
- some doctors may feel that the research literature is not sufficiently compelling at present and await further evidence.
- Alternatively, they could have a lack of knowledge in the area of reproductive immunology.

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## 7. How much do these tests cost?

The price of the NK cell test and other reproductive immunology tests can be obtained from the RIC website.

Unfortunately infertility treatment is almost never covered by private insurance and RIC is not aware of any of the leading UK private insurance companies supporting the cost of the tests or of the subsequent treatment.

## 8. How do I get an NK cell test done?

RIC advises all women to discuss the full details and implication of the NK cell testing with their specialist before making a decision. Your specialist will be able to advise you whether it is appropriate for you to have the testing done or not. They will also be able to contact us to arrange the blood test.

If you choose to have the blood tests undertaken before seeing a fertility specialist, please read the 'RIC for patients' information on our website before completing the blood test request and consent form. This will need to be signed by both yourself and your GP/fertility specialist.

Signing this form will constitute your consent to have the blood taken and the various tests performed, as well as your agreement to pay for the tests.

It is therefore very important that you take this form with you when you attend for your blood test. A map of where to go to have the blood test is available from our website.

After the blood has been taken, we will have the sample and the form couriered to our laboratory for immediate testing.

For further sample requirements, please see clinician's information.

## 9. Could my GP practice take the blood sample?

Your local GP or nurse can also take the blood sample. However, it is critical for the sample to get to us within 8 hours. Any delay beyond 8 hours affects the accuracy of the results owing to increased cell death. You will need to go to our website and download the blood test request and consent form, which needs to be completed and then signed by yourself and your GP or fertility specialist. Give the completed and signed form to the GP/nurse taking your blood. Please see our website for sample requirements. Both the form and sample should then be sent immediately to our laboratory for testing. A courier may be required for the transportation.

Please note that the cost of taking the blood sample and any transportation charges here are payable by the person whose sample is being analysed or their representative.

### **10. How long before I get the results of my NK cell test?**

The results will be available after 48 hours.

### **11. How do I get the results?**

Two copies of your results will be sent by post to your Doctor. The report can be faxed, but we are currently unable to email results.

If the test has been arranged by an individual rather than by a clinic, we will send you the invoice directly. Payment can be made by cheque.

### **12. If I have performed this test on my own, how can I understand the results?**

We recommend that the results are interpreted by doctors specialising in infertility and discussed in detail with their patient. However, all results include a written interpretative guide. It is important that patients should NEVER self-medicate.

## **Reproductive Immunology Centre**

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