Pre-Implantation Genetic Testing for Aneuploidies (PGT-A)

Leicester Fertility Centre

Information for Patients and Partners

NHS
University Hospitals of Leicester
NHS Trust

What is Pre-Implantation Genetic Testing for Aneuploidies (PGT-A)?

Chromosome aneuploidy describes the condition in which there are an incorrect number of chromosomes in an embryo. Embryos are expected to have 22 pairs of chromosomes plus the two sex chromosomes. One of each pair is inherited from a mother and father in the egg and sperm at fertilisation. Most aneuploidies are lethal to the embryo and are a major cause of IVF failure and miscarriage. In rare cases, they result in pregnancy and an affected child.

Chromosomal irregularities can result in aneuploidy (embryos having an incorrect number of chromosomes – e.g., extra copy of chromosome 21 also known as Down's syndrome), translocations (chromosomes incorrectly rearranged), or other chromosome alterations that may be clinically significant.

Aneuploid embryos are associated with higher implantation failure and miscarriage rates. PGT-A can be performed in addition to a standard IVF (*in vitro* fertilisation) or ICSI (intra-cytoplasmic sperm injection) cycle. When the embryo is at the correct stage (blastocyst) a small sample of cells are biopsied (approximately 5-10 cells) and the chromosome number within those cells determined.

All of the embryos that are biopsied are then frozen while the results of the analysis are generated.

Embryos that are euploid (with the correct number of chromosomes) are then thawed and transferred to the patient.

By excluding the embryos with an incorrect number of chromosomes, the procedure may theoretically increase the chances of a successful pregnancy. PGT-A can help to prevent the possible transfer of embryos which are destined to either; fail to implant, result in miscarriage or result in a birth of a child with a chromosomal irregularity. However, PGT-A screening may also result in no euploid embryos being found and embryo transfer being unable to take place.

PGT-A is a selection tool used to identify embryos with the correct number of chromosomes with the aim to increase the likelihood of a healthy ongoing pregnancy and is not a guarantee of pregnancy or live birth.

How common are chromosome irregularities in embryos?

It has been shown that the risk of chromosome irregularities is greatly influenced by the age of the mother. For women in their early thirties, about 35% of embryos are aneuploid. However, over the age of 40 it is typical for at least 75% of embryos to suffer from aneuploidy.

The majority of aneuploid embryos (90%) occur when eggs with extra or missing chromosomes are fertilised. Sperm cells may also be aneuploid, but the prevalence is usually lower (around 10%).

Who may benefit from PGT-A?

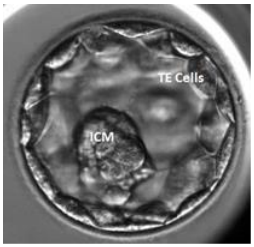
- Patients with advanced maternal age (usually defined as maternal age over 37 years)
- Patients with 2 or more previous unsuccessful IVF cycles (fresh or frozen)
- Patients with 2 or more previous miscarriages
- Patients who have had a previous pregnancy affected by chromosomal irregularities

In the UK, it is illegal to use this testing to select embryos on the basis of their sex for social/family balancing reasons.

What is the procedure?

You will be required to undergo an IVF/ICSI cycle (the full details of which can be found in our IVF/ICSI patient information booklet). The eggs will be assessed for fertilisation the day after the egg collection and any embryos that have developed will be kept in the incubator for 5-7 days until they reach the (blastocyst) stage. At this stage trophectoderm (TE cells) biopsy takes place. This involves the removal of a small number of cells which are then tested by the Cooper Genomics laboratory who can then give a prediction of whether or not the embryo has the correct set of chromosomes.

The removal of these cells should not harm the embryo. There are over 100 trophectoderm cells in a blastocyst so the removal of very few of these cells rarely impacts on the embryo.



TE cells - Trophectoderm cells, these are the cells that form the placenta.

ICM - Inner Cell Mass, this is the group of cells that would produce the potential foetus.

Patients electing to proceed with PGT-A will have their embryos cultured to blastocyst stage regardless of embryo quality. If embryos do not reach the blastocyst stage, then it is most likely these embryos are aneuploid and unlikely to result in a successful pregnancy. Embryos that do not reach a suitable blastocyst stage cannot be biopsied for technical reasons.

The embryos will be frozen immediately after the biopsy to await the results of the test. There will be no transfer of embryos until the results of the biopsy are available.

Once we have the results of the chromosome tests, we will know whether there are any suitable embryos available for transfer. One or two embryos will be thawed and transferred in a frozen embryo transfer cycle (full details in our Frozen Embryo transfer patient information booklet). We cannot transfer biopsied and non-biopsied embryos in the same cycle.

At any point patients can elect to proceed with an embryo transfer without the biopsy procedure taking place. A cancellation fee is applicable.

How is the genetic analysis performed?

The biopsied cells are sent to the Cooper Genomics laboratory for analysis. The chromosome number for each embryo is determined using a technique called Next Generation Sequencing (NGS). This technique will be able to detect if there are any extra or missing chromosomes in each of the embryos biopsied.

How will we find out the results?

A report is generated by the Cooper Genomics laboratory and is sent to The Leicester Fertility Centre. Once the clinic has been informed of the results, we will contact you by telephone. This is usually 2-4 weeks after the biopsy procedure.

We will then arrange for you to attend the clinic to plan your frozen embryo transfer cycle. If there are no euploid embryos available to transfer, we will discuss your options**.**

Would you benefit from this test?

Aneuploidy screening may improve pregnancy and live birth rates, because only euploid embryos are selected for transfer.

Women in their late thirties and early forties may consider this option, particularly if they have already had unsuccessful IVF treatment or miscarriage.

Other couples who may find aneuploidy screening reassuring are those considering elective single blastocyst transfer to avoid the risk of multiple pregnancies. Other benefits may include a quicker time to pregnancy and fewer IVF cycles.

If all the embryos are found to be aneuploid the screening will enable you to make an important decision about embryo transfer and future IVF treatment.

Studies into PGT-A

Many years ago, the PGT-A test was performed by a technique called FISH (fluorescent in situ hybridisation), which only looked at a limited number of chromosomes in the embryo. These early studies were not effective at increasing the likelihood of a live birth. Technology has since improved, and the Cooper Genomics laboratory is now able to use tests that detect all of the chromosomes and are therefore more effective.

Recent studies using these new techniques showed that the chances of an embryo with a normal number of chromosomes producing a baby was more than 25% higher than those chosen based on the look of the embryo (morphology). While these results are extremely promising, they have not yet been replicated by other IVF centres. There needs to be further robust clinical and laboratory trials to assess whether or not PGT-A can

significantly increase live birth rates. These studies are currently being performed.

Although there are studies reporting improvements in IVF success rates using PGT-A, there is other research suggesting that chromosome testing is of no benefit. The HFEA currently rates PGT-A as follows on their treatment add-ons rating system:

Rated red for increasing chances of having a baby for **most fertility patients.**

Rated green for **reducing the chances of miscarriage for most fertility patients.**

Rated grey for **reducing the chances of miscarriage for older women.**

Rated grey for **improving chances of having a baby for older women.**

<u>Key to ratings symbols</u>:

There are potential safety concerns and/or, on balance, the findings from moderate/high quality evidence shows that this **add-on may reduce treatment effectiveness**.

On balance, findings from high quality evidence shows **this add-on is effective at improving the treatment outcome**.

We cannot rate the effectiveness of this add-on at improving the treatment outcome as there is insufficient moderate/high quality evidence.

Further information can be found on the HFEA website:
https://www.hfea.gov.uk/treatments/treatment-add-ons/

What risks are involved?

Our IVF/ICSI patient information booklet details the risks of undergoing a routine IVF/ICSI cycle. There are some additional risks when undergoing PGT-A.

Risk of an unsuccessful outcome and miscarriage

Performing PGT-A and having a euploid embryo transferred does not guarantee a positive pregnancy test, a viable early scan or a healthy live birth. PGT-A has large financial and emotional costs and counselling is available for either partner at any stage of treatment should you wish.

As with all pregnancies there is also a risk of miscarriage. PGT-A testing and replacement of a euploid embryo does not eliminate the risk of miscarriage; it can only serve to reduce the risk.

Risk of Embryo Biopsy

There may be a risk of damage to the embryo when the biopsy is carried out. It is currently unknown whether embryos derived from biopsied embryos have the same likelihood of implanting as embryos from un-biopsied embryos.

Risk of preparation of biopsied cells

After the biopsy procedure, the cells are placed in a small test tube for their testing. The cells are no longer viable in any way after this process and can only be used for PGT-A. Some of the cells may not yield a test result (<5%), some may not contain any genetic material; cells may be lost during the process of the test.

Risk of Misdiagnosis

Although PGT-A testing has a high level of accuracy, misdiagnosis can result in false positive results (euploid embryos being diagnosed as aneuploid) or false negative (aneuploid embryos being diagnosed as

euploid). The risk of clinical misdiagnosis is less than 5%. Due to the chance of misdiagnosis, however it is recommended that pre-natal testing is performed for any pregnancy that results from your treatment.

Risk of having nothing available for biopsy
There is a chance that no embryos will be suitable for biopsy as they haven't reached the correct stage of development. In these cases, it is highly likely that the embryos that have stopped developing are aneuploid and would not produce a viable pregnancy.

Risk of no embryos suitable for transfer
Sometimes there may be no suitable embryos available for transfer. This may be due to no eggs being retrieved or no embryos developing, or the test may find that none of the embryos are euploid, in which case there may be no embryo transfer procedure.
The likelihood that this will happen is influenced by a variety of factors, mainly female age and the number of embryos.

Risk of no diagnosis/partial diagnosis
Some embryos may have no diagnosis, due to the absence of chromosomes, or technical difficulties in the fixation process. Embryos without a result can still be transferred, but the possible advantages of PGT-A will not apply. In addition, sometimes the analysis may not be clear for one of the chromosomes tested. Embryos with such partial results may be transferred, but this must be discussed with either a geneticist or a consultant. The risks of having such an embryo back will be explained to you.

Risk of Mosaicism
Mosaicism can occur when the chromosome number varies in each of the cells tested. For example, 4 cells may have the correct chromosome number and 1 cell may have an incorrect number. When this happens, the embryo is deemed mosaic. Mosaic embryos are associated with lower implantation rates and higher miscarriage rates. They can occasionally result in a viable pregnancy. If this is the case with your embryos, we will discuss the implications of transferring these embryos.

Natural pregnancy
It is important that you take precautions to avoid a natural pregnancy during your treatment as any embryos created naturally will be unscreened and may be aneuploid.

Costs

PGT-A is not NHS funded and only available on a private basis.

Currently the testing laboratory we use - CooperGenomics, uses the next generation sequencing test (NGS) for PGT-A

Please see price list

What follow-up care is available?

We understand that this is a very difficult time for you emotionally. Should you wish to access any supportive counselling regarding your treatment or your fertility you may contact the counsellors on 0116 258 5922.

We work in conjunction with our highly experienced Clinical genetics colleagues at the University Hospitals of Leicester NHS Trust. You may wish to contact the UHL Clinical Genetics Counsellor on 0116 2586044.

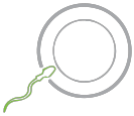
Explanations

What are chromosomes and genes?

Chromosomes are tiny rod-shaped structures that exist in virtually every cell in the body. Each embryo should have exactly 46 chromosomes: 23 from the egg and 23 from the sperm. The chromosomes carry the genes which are the chemical instructions that tell the embryo how to develop into a baby. The genes are thought of as being blueprints.

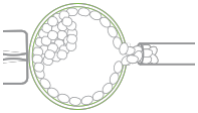
IVF

Multiple embryos are produced through an IVF cycle



Embryo Biopsy

A few cells are carefully removed from the part of the embryo that will form the placenta. Samples are sent to the laboratory whilst the embryos are frozen at the clinic



PGT-A

The Genetic testing service uses a cutting-edge technology to test the genetic material present within each embryo

Transfer and improved chance of success

Embryos most likely to result in success are selected for transfer or can be frozen for future use

Our commitment to patients

We are constantly striving to improve our services to patients, and we will welcome your comments or suggestions for improvement.

Leicester Fertility Centre contact details

Tel: 0116 2585922

E-mail: LFCinfo@uhl-tr.nhs.uk

Website: www.leicesterfertilitycentre.org.uk

Useful addresses

Human Fertilisation and Embryology Authority: www.hfea.gov.uk

NICE guidelines: www.nice.org.uk

NHS - Response line: 111.nhs.uk / 111

NHS - Smoking helpline: 0300 123 1044

Fertility Network UK: www.fertilitynetworkuk.org / 0121 323 5025

British Society for Genetic Medicine: www.bsgm.org.uk/

Cooper Genomics: www.coopergenomics.com

Screening tests in pregnancy (NHS Choices): www.nhs.uk/pregnancy/your-pregnancy-care/screening-tests/

Information about PGD (Genetic Alliance): https://geneticalliance.org.uk/information/service-and-testing/preimplantation-genetic-diagnosis-information-for-patients/

Do you feel that you are at risk of verbal or physical abuse? If so, you may find the following numbers useful:

Domestic Violence Helpline:

United against violence & abuse (UAVA)

Helpline:	0808 802 0028
Email:	info@uava.org.uk
Text support:	07715 994 962

This information was correct at the time of printing. While the Trust makes every reasonable effort to keep its information leaflets up to date, very recent changes may not be reflected in the guidance and you should discuss this with the clinical staff at the time of your appointment.

Questions

If you have any questions write them down here to remind you what to ask when you speak to your consultant.

Today's research is tomorrow's care

We all benefit from research. Leicester's Hospitals is a research active Trust so you may find that research is happening when you visit the hospital or your clinic.

If you are interested in finding out how you can become involved in a clinical trial or to find out more about taking part in research, please speak to your clinician or GP.

If you need information in a different language or format, please call the number(s) below or email equality@uhl-tr.nhs.uk

اگر آپ کو یہ معلومات کسی اور زبان میں درکار ہیں، تو براہِ کرم مندرجہ ذیل نمبر پر ٹیلی فون کریں۔

على هذه المعلومات بلغةٍ أُخرى، الرجاء الاتصال على رقم الهاتف الذي يظهر في الأسفل

જો તમને અન્ય ભાષામાં આ માહિતી જોઈતી હોય, તો નીચે આપેલ નંબર પર કૃપા કરી ટેલિફોન કરો

ਜੇ ਤੁਸੀਂ ਇਹ ਜਾਣਕਾਰੀ ਕਿਸੇ ਹੋਰ ਭਾਸ਼ਾ ਵਿਚ ਚਾਹੁੰਦੇ ਹੋ, ਤਾਂ ਕਿਰਪਾ ਕਰਕੇ ਹੇਠਾਂ ਦਿੱਤੇ ਗਏ ਨੰਬਰ 'ਤੇ ਟੈਲੀਫੋਨ ਕਰੋ।

Aby uzyskać informacje w innym języku, proszę zadzwonić pod podany niżej numer telefonu

0116 258 4382 or 0116 250 2959