Egg Donation for Donors

Welcome
This booklet has been written to help fully inform you of the purpose and techniques of treatment. Please ask for clarification and let us have your comments and suggestions for future editions. It is important that you read and understand all the material as our intention is to keep the risk of an error in treatment at its minimum.

HOW TO CONTACT US!!

Address:
The Leeds Centre for Reproductive Medicine
Leeds Teaching Hospitals NHS Trust
Seacroft Hospital, York Road
Leeds, West Yorkshire LS14 6UH

Telephone:
❖ Monday to Friday (8.00am to 5.00pm):
  ➢ Administrative queries: 0113 206 3100
  ➢ Clinical queries: 0113 206 3100
❖ Saturday, Sunday & Bank Holidays (8.00am to 12.00pm):
  ➢ Clinical queries only: 0113 206 3102
❖ When in emergency:
  ➢ During working hours ring The Centre on he direct line or go to a local Accident and Emergency department
  ➢ Outside the above hours please ring the St James’s Hospital switchboard: 0113 2433144
    You will be put through to the duty person for The Leeds centre for Reproductive Medicine or go to a local Accident and
    Emergency department

Fax: 0113 206 3101
Email: leedsrmuenuquiries@leeds.nhs.uk
Website address: www.leedsreproductivemedicine.co.uk

Ethnic Minority Languages: We will be pleased to organise a session (with prior notice) for an official translator / interpreter (if available) to translate the contents of this booklet.
This information booklet describes why egg donation is needed. It is expected to supplement but not replace further opportunities for you to
discuss the implications and any other specific questions that you may have with a counsellor, nurse or a doctor. You should not feel under
pressure when making up your mind and we hope that this information may help you to decide if donating eggs or accepting donated eggs is
right for you.

Please bring this leaflet with you when you attend for your appointment in the centre. You may also find it helpful to underline/mark the areas
which you would like to discuss further.

1. Background:
The first pregnancy following the use of donated sperm was reported in 1884 but it was not until 1983 that the first pregnancy following the use
of a donated egg was reported. Sperm can easily be collected and frozen (cryo-preserved) for storage. Eggs, in contrast, are difficult to collect
and, at present, cannot easily be frozen for storage and future use. With the advent of the technique of IVF, however, it is now possible for a
woman to donate eggs (the egg donor) to another woman (the egg recipient). Only clinics that have been inspected and are licensed by the
Human Fertilisation and Embryology Authority (HFEA) can set up an egg donation programme. Such a programme has existed in Leeds since in
1993. This leaflet contains some general information about egg donation and some specific information for egg recipients.

2. Patient Support Group
On line internet support and information is available. The website is run by current and ex-patients who have had similar experiences and
who are prepared to share their experiences. They will also be able to get information regarding groups in your locality. We recommend
that you become a member of the support group for your own benefit and that of others. Contact the Assisted Conception Unit for the
address.

3. Emergency out of hours contact
The LCRM working hours are Monday to Friday 8.30am- 5.00pm
In an emergency or on weekends you can obtain advice from the on call member of the team OR from the gynaecology registrar or SHO on
duty via the hospital switchboard on 0113-2433144.

4. Why do some infertile couples need egg donation?
Some couples can only achieve pregnancy by using eggs donated by another (fertile) woman. They can be divided in 2 categories:

1) women whose ovaries cannot produce eggs at all, or produce poor quality eggs
   a) For a variety of reasons some women's ovaries are not able to produce eggs. The most common causes are:
   b) Women born without ovaries or with under-developed ovaries (eg Turner’s syndrome).
   c) Women whose ovaries stopped working prematurely. Most women go through the menopause in their mid to late 40's or early 50's.
      After the menopause a woman is no longer capable of conceiving because her ovaries stop producing eggs and sex hormones.
      However, to some women these changes can occur much earlier, even in their teens or twenties before they would even have
      contemplated to try to get pregnant. This is known as premature ovarian failure or premature menopause.
   d) Women who have become sterile after surgery, radiotherapy or chemotherapy.
   e) Women undergoing infertility treatment but whose ovaries do not respond to traditional fertility drugs (such as Clomiphene tablets
      or FSH injections).
   f) Women undergoing infertility treatment but whose ovaries consistently produce poor quality eggs when stimulated (particularly
      more common in the older age group).

For these women, egg donation is their only realistic chance of achieving a pregnancy.

2) women who are suffering from, or are carriers of certain genetic diseases
   a) Some women may be carriers of diseases such as Duchenne muscular dystrophy or haemophilia. These diseases can be passed on to
      their offspring. Rather than risk giving birth to a child who might suffer greatly and die at an early age, they may choose to avoid the
      possibility of having an affected child by using donor eggs from another woman who is not a carrier.

5. Who donates eggs?
Donors undergo the procedure voluntarily and for altruistic reasons. The HFEA provides guidance on financial reimbursements to the
donor, which covers expenses for travel and loss of earnings (SEED REVIEW: details can be accessed from the ACU staff and the HFEA
website).

Our donors are recruited from several sources,

Anonymous volunteer donors:
Women who are in a stable relationship, have already had children, preferably have completed their own family, and feel that they want to help
infertile couples. Such women have come forward on their own initiative and have only altruistic motives. No financial incentives are involved.

Close relative of the patient:
1) Some patients for ethnic, cultural or religious reasons and others as a personal preference choose to have a 'known donor' such as a
sister or close friend of the female partner. Donation between known donors and recipients is acceptable after careful implication
counselling. We adhere and remain within the law and its provisions at all times.
2) Nationally there is a shortage of anonymous donors and some donors as well as recipients prefer anonymous donation because it makes the likelihood of emotional conflict in the family or between friends less likely. We can match another donor recruited by a different couple for your friend/relative whilst you donate anonymously to a different recipient. In this way treatment can be expedited for both your relative/friend and for others.

Infertility Patients:
Some programmes have an egg-sharing scheme where screened and counselled infertility couples donate some of their eggs in return for subsidised treatment for themselves. We have not initiated this scheme because we have been concerned with the effect that loss of permanent anonymity between donors and children might have in time on the children, donor and recipient couples. However, such a scheme is operational in several other centres with HFEA's permission.

6. Regulation of egg donation:
We suggest you read the leaflet "What you need to know about donating sperm, eggs or embryos" produced by the Human Fertilisation and Embryology Authority, the official government body regulating and licensing IVF units in this country.

1) Human Fertilisation and Embryology Act
Human Fertilisation and Embryology Act was passed by parliament in 1990 and became law on 1st August 1991. Simultaneously a statutory Human Fertilisation and Embryology Authority (HFEA) were established for the regulation of all treatments and research. It is our statutory obligation to report every treatment cycle and its outcome to the HFEA. This information is analysed annually and published in a 'Patient's Guide to IVF and DI treatments' which is available free of charge on request from the HFEA.

2) HFEA register
The Authority keeps a confidential register of identifying information on all patients and their treatments, donors and recipients and children born after all licensed treatments. This register was set up on 1st August 1991 and therefore contains information concerning children conceived from licensed treatments since that date.

From 2008, people aged 16+ (if contemplating marriage) or 18, who ask the HFEA, will be told whether or not they were born as a result of licensed assisted conception treatment, and if so, whether they are related to the person they want to marry.

3) The Law
Children born following treatment have the right to know of their genetic origins at the age of 18 years or at 16 years, if contemplating marriage.

This means that donors have to provide identifying information which the HFEA may release, on request, to people aged 18 years or more and who has been conceived with gamete or embryo donation.

All recipient couples and donors are advised to explore the implications of these regulations. Counselling services are available to all donors and recipient couples. When in doubt, please seek independent legal advice.

4) Legal Parenthood
The law defines the legal mother as the woman who gives birth and her partner as the father irrespective of the source of eggs or embryos created with donated eggs unless the husband/partner can prove that he did not consent to treatment. The donor has no parental rights or responsibilities.

Both partners of a recipient couple must provide written consent to the use of donated eggs/embryos in the treatment of their partner.

Under the current law, there is no need for the recipient couple to disclose the use of donor eggs/embryos to the Registrar of Births. Therefore you will not expect to be named at any stage.

Unmarried couples concerned about parental responsibility are advised to seek independent legal advice.

5) Welfare of Future Children
The law states that 'a woman shall not be provided with treatment services unless account has been taken of the welfare of any child who may be born as a result of the treatment (including the need of that child for a father), and of any other child (other children in the household or the family) who may be affected by the birth'.

This applies to every woman whether or not she is resident in a country of the United Kingdom. It is the statutory duty of every centre to have a written procedure for assessing the welfare of the potential child and that of any other child who may be affected.

6) Factors considered in assessment include:

i. the couple's commitment to having and bringing up a child
ii. ability to provide a stable and supportive environment for the child/children
iii. couple's medical history and that of their families
iv. both partner's health (including their ages) and consequent future ability to look after or provide for a child's needs
v. ability to meet the needs of the children in the event of a multiple birth
vi. risk of harm e.g. that of inherited disorders, transmissible disease or abuse, multiple birth, neglect or abuse
vii. risk a new born may put on the existing child in the family
It is our statutory duty to identify the person/s who will have the parental responsibility and who will be responsible for the raising of the child. Where necessary, we obtain reports from the general practitioner, other medical specialists, authorities and agencies e.g. social workers, police etc for information to ensure that the child would not be at risk. When treating single women or those in a single sex relationship we ask the couple to identify a father figure to ensure that the child’s/children’s right for both paternal and maternal nurturing will be met.

7) Donors’ rights
The donor has the right to change her mind up to the point the embryos have been placed in the recipient. Embryos created using donated eggs can only be stored for a patient with the consent of the donor. On the other hand, the donor has no rights once embryos have been transferred to the recipient.

8) Limitation to the number of pregnancies with each donor
Legally in the UK, eggs or sperm from any one donor can be used to produce a maximum of TEN children or TEN families. In reality, this possibility is extremely unlikely for egg donors. However, donors may set a lower limit should they wish to do so.

9) Consents
As stated above, we can only advise you with respect to the current law and the changes that we can envisage. You are advised to seek more specific and independent legal advice if you are concerned about how a retrospective change in the law might affect your legal position.

All donors and recipients are asked to sign appropriate consent forms after they have read the information booklets, have discussed the medical/ethical issues with the doctors/nurses/counsellor, and are satisfied that their questions have been answered fully. Consents are obtained prior to donation.

Your consent advises us of your informed choice. You always reserve the right to change your mind until but not after the embryos have been transferred to the recipient. It is however important that all issues are thoroughly considered beforehand so that sudden and unexpected changes that you may later regret are avoided.

10) Confidentiality
All information regarding your treatment is strictly confidential and subject to both the HFE Act and the Data Protection Act. We may communicate with your general practitioner, referring consultant and other carers only with your written consent.

Once the information has been disclosed to unlicensed individuals it can no longer be controlled by the HFE Act although it will still be under the Data Protection Act and General Law of Confidentiality. At your GP’s practice, information will be accessible to other GPs and staff. When changing GPs, your medical records will be transferred to your new GP practice without our involvement or written consent.

From time to time your notes may be inspected by HFEA members for audit, by Commission of Health Improvements (CHI), individuals working for Patient Safety Agency (PSA) and National Care Standards Commission.

You have a right to decline consent to communicate with specific people or agencies, in which we may need to consider the reasons for your refusal to consent in our assessments.

We advise you to keep your G.P. informed. They are your primary carers, will also be committed to confidentiality. Sometimes patients request their GP to keep written information regarding egg and sperm donation separate from the practice notes so that this information is not freely available to all the staff in their surgery. You may request them but they may not be obliged to do so.

We request photographic evidence of your identity (e.g. passport) which we will photocopy and along with a photograph of yourself placed in your notes, so that as treatment proceeds we can confirm your identity.

11) Treatment for single sex couples and single women is considered on an individual basis after careful consideration of the Welfare of the Future Child/Children (see below).

7. What to do if you are interested in becoming an egg donor?

You may have heard about becoming an egg donor via the newspaper or television, or via a friend or relative who is undergoing IVF or needs donated eggs. The first step is to go and see your GP and ask him to refer you to a unit with an egg donation programme. Only clinics that have been inspected and are licensed by the Human Fertilisation and Embryology Authority (HFEA) can set up an egg donation programme.

You will be sent an appointment to be seen in The Leeds Centre for Reproductive Medicine (LCRM) itself and will be seen by a doctor within the team. You can also make such an appointment yourself by telephoning the LCRM directly on the direct line in front of this booklet between 8am and 5.30pm.

It is preferable to come together as a couple with your partner. You will see one of the doctors in the centre. The doctor will discuss your motivation, the social, medical and legal aspects of egg donation; explain the techniques involved and the potential side-effects and risks. A full medical and family history will be taken from you.

It is of particular importance to mention any inherited diseases in your family.

It may be necessary to obtain further details from other clinics or your GP. You will be given some further literature to read at home and some time for reflection.
8. Implication counselling
Implication counselling is required for both donors and recipients.

In addition to this:
Free counselling service with a trained counsellor is routinely available to all upon request. It is carried out by HFEA licensed counsellor/s away from the unit in the Department of Clinical Psychology which you may find less stressful. Appointments can be made directly by yourselves or via the ACU. If you require an interpreter, you are advised to give sufficient notice for an independent interpreter to be arranged.

The counselling is entirely confidential and private between you and the counsellor and will not be judgmental or prejudicial. The counsellor is also HFEA licensed and has a statutory duty to give essential information that may affect the Welfare of future or existing children to the team. This is exceptional.

The effect of egg donation on the donor, her partner and any existing children is carefully discussed. Wherever possible the partner's participation and agreement is sought before proceeding with the donation. If the children of the donor are of an appropriate age the donor is also asked to discuss the matter with her children.

9. Screening of Donors
The donor by law has to be 18 to 35 years in age, of normal intelligence, in good health and with no past or family history of severe physical, mental or genetic disease. All donors are required to undergo a medical examination and details are asked about their personal, medical and family history. A donor may not be accepted whenever a risk is envisaged to her, her existing children or to the future child.

All donors are carefully screened according to current guidelines and best practice.

10. Which screening tests are performed?

a. Genetic Testing:
All prospective egg donors have an analysis performed of their chromosomes.

In addition, we routinely test for cystic fibrosis. The screening will be performed for only the 12 commonest gene mutations in the Caucasian and Northern European populations. These mutations account for 85% of all varieties known to medicine at date. Exclusion of these mutations reduces the risk of being a carrier for cystic fibrosis to about 1% for these populations. In other population's e.g. Asians, the incidence of cystic fibrosis is much lower than that among Caucasians. Whilst all 12 mutations known to be common in the Caucasian and Northern European populations are excluded, the risk of being a carrier among the Asian donors cannot be accurately determined.

In addition, wherever appropriate additional screening tests may be applied. For example:

- East European, South Asian and Middle Eastern donors are screened for Thalassaemia.
- Donors with African descent are screened for Sickle cell disease.
- Jewish donors are screened for Tay Sach's disease.

It is very important for the recipient couples to understand that not all known gene mutations are or can be possibly screened for and even after screening of some, there may be others for the same disease that are either uncommon or are not yet known. Hence the likelihood of developing these illnesses can be minimised with this screening but cannot be completely eliminated.

b. Screening for infections:
- All egg donors are screened for HIV, hepatitis B and C.
- Syphilis: All egg donors are screened for syphilis
- Cytomegalovirus (CMV): This virus commonly infects people and in normal circumstances gives a minor flu like illness. However it can become activated in pregnancy and can harm the baby. It is a very common infection in the normal population and many of us are exposed to it during our lifetime. We screen all donors and use CMV negative donors only for CMV negative recipients. On the other hand, CMV positive recipients can have gametes from both negative and positive donors.

11. What is the risk of a congenital abnormality?
The risk of a congenital abnormality after treatment using donor eggs is believed to be the same as for natural conception in a normal couple that is approximately 1 - 2%. The risk of having a child with Down's syndrome and other similar abnormalities, miscarriage or a still birth as a result etc is that in the donor's age group in the normal population. GP's and those responsible for the obstetric care (obstetricians and midwives) routinely advise the recipient couples about prenatal diagnostic tests as appropriate.

12. How are the Donors matched to the Recipients?
Physical characteristics such as height, weight, body build, hair colour, complexion, eye colour, race and blood group etc are recorded. We try to provide an acceptable match. There are fewer donors and detailed matching for physical characteristics can prove difficult. Matching for ethnic origin and rhesus blood group is always performed. Exceptions are always discussed with the recipient couple in advance.

13. Freezing of Embryos
Decisions regarding freezing, storing and discarding embryos formed with donated eggs must comply with written consents of both the donor and recipient. This includes how long embryos can be stored and whether or not they can be used after the death or mental incapacitation of the donor or recipient.

It is possible for either donor or recipient to withdraw consent to storage, in which case the embryos have to be allowed to perish.

We usually advise embryo freezing only if there are at least three suitable embryos. The embryos can be kept frozen for 5 years (up to a maximum of 10 years in certain circumstances) from the date of freezing.

- **Embryo donation:**
  Your eggs could be used to create embryos that are then donated by the recipient couple to another couple once they have completed their family or decided to discontinue treatment.

- **Embryo research:**
  Research is carefully regulated and centres have to obtain specific research licences for the projects that they conduct or take part in. From time to time we are involved in research projects and we will provide relevant information to you if appropriate.

13. The Natural versus ‘The IVF’ cycle

Naturally the ovary continuously recruits and develops the eggs. The egg develops over 60-90 days but only the last 14 days are in the menstrual cycle and at a stage where we can make changes. Normally the ovary recruits a group of eggs and the number allocated each month vary with the ovarian reserve of eggs and certain conditions such as polycystic ovaries. In older women or when ovaries have been affected by a past illness/treatment, the total number of eggs in the ovary goes down and hence the number it can allocate per month also reduces.

From the number allocated normally one follicle is visibly larger by the 4th-5th day of the menstrual cycle and has started to grow ahead of others. This dominant follicle prevents other follicles from growing that month. By giving you stimulating drugs however we can allow more than one egg to develop. Naturally the glands interact and prepare for ovulation as the hormone levels rise. Normally this would only happen when the single follicle reaches a mature stage. However when more than one follicle is growing, the hormone levels go up faster and to higher levels which can confuse the Interacting glands to send messages related to ovulation prematurely. This will affect the quality of egg development. Hence we give medication to inactivate these glands. Often this will start before the stimulating hormones as in the long protocol but we can also use other hormones with similar effects but during the stimulation phase as in the ‘short protocol’.

Fertilisation represents a complex series of changes and interaction between the sperm and the egg. Normally the egg matures within the growing follicle, which is a small fluid filled sac like structure with in the ovary. The follicle stimulating hormone (FSH) allows development and maturation of the follicle and its egg. The luteinising hormone (LH/hCG) allows the mature follicle to prepare the egg for fertilisation. In natural cycles, only one follicle and egg develops fully. By contrast in an IVF cycle, the ovary is stimulated with hormones to allow multiple eggs to develop simultaneously. At the appropriate time these eggs are removed after they have completed their maturation in the ovary. The egg is surrounded by a shell called the ‘zona pellucida’ and a group of cells called the ‘cumulus oophorus’.
Naturally after the sperm are ejaculated in the vagina, they swim upwards, through the womb and into the fallopian tubes where they expect to meet the egg. On the other hand in an IVF cycle, the sperm meets the egg within the laboratory dish approximately 3 to 7 hours after the egg collection. The sperm then has to dissolve the cumulus cells to reach and fertilise the egg. Once the sperm reach the zona pellucida, it undergoes a series of changes before entering and fertilising the egg. Immediately after this the egg undergoes a complex reaction that will stop any more sperm from entering except when it is not of a good quality when this may happen. In couples with very low sperm counts or other defects of sperm function, a single sperm is injected into the egg to assist fertilisation. This procedure is called ICSI (Intracytoplasmic Sperm Injection). This is described in detail in the booklet.

After fertilisation, the egg forms a single-cell embryo which will then undergo a series of divisions. On the second day the embryo would have reached the 2 to 4-cell stage. By day 3 the embryos have 5-8 cells within. This is when the embryos are usually transferred. After culture to day 3-5 and with continued development, the embryo will become a tight ball of cells, 'the morula' by day 4 and a 'blastocyst' by day 5 or 6. At this stage, the embryo is ready to implant. If further development continues within the body after implantation, the embryo will release the hCG that can be detected with a pregnancy test.

In nature only 1 in 4 embryos implant and carry on development to be recognised as a pregnancy. Nearly 40-50% embryos are genetically abnormal both in nature and also when formed in the laboratory. The risk of abnormal embryos increases progressively with the age of both the female and the male partner.

When more than one embryo is transferred, your chance of becoming pregnant is increased but your chance of multiple pregnancy is also higher. The law permits a transfer of a maximum of 3 embryos in women >40 years in age because the risk of multiple pregnancy is very low in this group. In suitable patients, prolonged culture to day 3 or day 5 improves the selection of embryos for transfer when one embryo is transferred, your chance of becoming pregnant is increased but your chance of multiple pregnancy is also higher. The law permits a transfer of a maximum of 3 embryos in women >40 years in age because the risk of multiple pregnancy is very low in this group. In suitable patients, prolonged culture to day 3 or day 5 improves the selection of embryos for transfer when a single embryo may achieve the same success rate as two but without a high risk of a twin or a triplet pregnancy.

14. Treatment Procedure

14.1 A Typical Cycle:

This section has been written in the expected order of various steps in treatment. You may find helpful to refer to this section regularly during treatment.

a. First clinic appointment: A full discussion of the relevant personal and family history takes place in The Centre. We aim to minimise your visits and do not repeat investigations unless deemed essential for the conduct of your treatment.

b. Screening tests. These tests are arranged as explained above.

c. New Patient's Seminar. We very strongly recommend that you attend this open seminar by the team. Dates are available on request from the unit.

d. Implication counselling: You will be advised to see the counsellor so that implication of what you r donation to you, your spouse and your family can be discussed fully and all legal issues can be discussed.

f. Follow up clinic visit. You will attend the clinic for discussion of screening tests and you have this opportunity to clarify any outstanding issues that have arisen in your mind with respect to your treatment. At this visit, you will receive a prescription and also be advised to see the Egg Donation Nurse co-ordinator on your way out so that you can be given a start date for your treatment.

g. Consultation with the Nurse Specialist. Both Partners must attend this appointment (see details) because you both will be required to sign consents, receive instruction for self administration of injections and a cycle plan.

h. Suppression of your natural hormones. When the 'long protocol' is used, your naturally produced hormones are suppressed from the 1st or the 21st day of the menstrual cycle using a nasal spray, a daily injection or a single depot preparation. This is maintained until you are ready to receive hCG and can in total last for approximately 5 to 7 weeks. When the 'short protocol' is used, we prescribe a second injection in parallel with the stimulation drugs from an appropriate stage. A baseline scan is performed, usually prior to starting this phase, unless you have had another recent scan within the preceding 3 months.

i. Ovarian Stimulation. Hormones are administered in this period to help your ovaries produce multiple eggs. This treatment can last for approximately 9-14 days. In women receiving the 'long protocol' a pre-stimulation / down regulation scan will be performed before to confirm that natural hormones have been suppressed. You will receive further scans to monitor growth of the follicles.

j. HCG injection. This injection prepares the eggs for ovulation and is given late in the night (usually between 10 p.m. and 2.00 a.m.).

k. Egg Collection. The eggs are collected approximately 35 to 38 hours after the hCG injection.

l. Insemination or ICSI. Male partner of the recipient gives a sperm sample (unless a frozen sample is already available) for preparation and insemination of the eggs by the direct method or by the ICSI procedure.

m. Checking Fertilisation. The recipient will receive a telephone call with necessary information on the day after the egg collection.
n. Embryo Transfer and Hormonal Support. The embryos are replaced in the womb of the recipient.

n. Luteal phase monitoring. This is provided to all those donors who we feel could be at risk of developing the ovarian hyperstimulation syndrome.

o. Follow-up consultation. This is arranged after the cycle has been completed.

14.2 Nurse consultation

This appointment follows your clinic appointments with the doctors and your attendance at the New Patient seminar.

- You should have become fully informed before you reach this stage so that you are happy that you are signing ‘Informed Consents’.

The primary objectives of this visit are for the nurse:

- to assist with the completion of your consents
- to discuss any further issues that have arisen and/or you are not clear about.
- to provide instruction regarding the administration of drugs
- to check your prescription or drugs that you should have already received before this visit
- to provide a prescription if you have not received one until then
- to give you a Cycle plan in a flow chart format to help you further
- to give you the ‘Common Questions and Answers’ booklet
- to book your next appointment

Please do not hesitate to ask, if after this appointment, you still feel the need for further discussion. Please also return to the New Patient’s Seminar as many times as you require to fully understanding the process.

14.3 Downregulation or the Suppression phase

During your treatment cycle the response from other glands (the pituitary) may interfere and affect the maturation of eggs. As this can lead to a lessening of the success rate, when using the Long Protocol we choose to inactivate this gland before stimulating your ovaries.

- Baseline scan
  A vaginal scan is performed before starting any medication unless the scan performed as part of Pre-assessments was done within the last 3 months. This is to ensure that there are no new developments that we should be aware of before starting the drugs.

- Pre-stimulation or Down regulation scan
  The scan is repeated at the appropriate time after starting the suppression phase. This should show inactive ovaries and a thin lining of the womb. The usual time taken for this phase is 10 days to 2 weeks.

- Drugs used
  A number of methods can be employed for the same ultimate effect. These, in our programme include the following:

  1. **Nafarelin Nasal Spray:** This is taken as one sniff in one nostril three times per 24 hours at 8 hourly intervals for first 2 weeks and then twice daily thereafter until the day of HCG. This medication is not suitable for those suffering from hay fever, chronic nasal discharge or who may not remember to use the spray regularly.

  2. **The Buserelin Injection:** This injection is taken once a day sub-cutaneously with a very fine needle-injection just under the skin. It is given daily at approximately the same time but an absolute and accurate precision is not essential (give or take 30 minutes).

  3. **Prostap Depot Injection:** This is a once only injection and works for 4-5 weeks in total. This is very convenient for many donors / patients except those with reduced ovarian reserve. If the suppression phase is prolonged because of the agonistic/stimulatory response from the ovary, a ‘top-up’ with Buserelin/Nafarelin in the later stages of the cycle may be needed.

- Side effects
  1. Hot flushes, night sweats, headaches, vaginal bleeding, temperamental behaviour. These are due to a fall in your oestrogen level, usually last for a short time and will disappear once we start stimulating your ovaries.

  2. Agonistic/ stimulatory response: In the initial stages all of the 3 preparations above can stimulate the ovary. This means that a follicle or cyst develops that has to resolve before we can proceed with treatment. It can naturally take up extra 2-3 weeks. If the cyst is aspirated the resolution may be slightly earlier and this requires an extra scan to see it disappear and for the endometrium to become thin. If you are prone to develop agonistic response seen in the form of cysts after starting this medication, we can use the oral contraceptive pill for a few days before starting the downregulation and this usually avoids such problems recurring.

- Time to start
  This treatment can be started on the first or the second day of your cycle especially when your cycle length is variable. It can also be started on the 21st day of the preceding cycle if your cycle is very regular.
Choices
We can prescribe any one of the above preparations and methods dependent on your preference and knowledge of past response. They are equally effective and are self-administered. There is a relatively small difference in their costs with Buserelin being the cheapest.

Important notice:
The Nafarelin nasal spray and/or the Buserelin treatment is continued in the stimulation phase. We will specifically advise in writing when to discontinue which is the day you are advised to take hCG. Those with Prostap normally do not have to take additional medication during the stimulation phase.

14.4 Stimulation phase
There are large variations between donors in the number of eggs recruited and developed in response to the same dose of the stimulating hormones (see below). This response is mainly dependent on the donor’s age, her body weight and past treatments or ovarian surgery. There are other genetic determinants also. Having preformed the pre-treatment assessments, we judge the starting dose bearing in mind all clinical circumstances. When uncertain we may perform additional early scans to use the option of ‘stepping-up’ or ‘stepping down’ during the stimulation phase for a better response.

What does it involve?
The hormones (Puregon/ Gonal-F/ Menopur) will be started when your ovaries have been adequately suppressed as judged by your pre-stimulation or the downregulation scan (see previous section).

My choices?
The difference in drugs is mainly in the way they are prepared, their purity, in the way they are administered and their costs. They are equal in terms of their success rate. We often choose them in combination or separately to suit.

How to inject?
Gonal-F, Puregon and Menopur are usually given by a subcutaneous injection (very fine needle-injection in the fat layer under the skin).

How are they prepared?
Gonal-F and Puregon are synthetic compounds, very pure and with an identical structure to PURE FSH only. Menopur is extracted and purified from menopausal women's urine and is therefore a combination of naturally produced hormones. This can contain protein impurities at a very low level which can rarely give a skin reaction. There are no other reported complications.

Side effects
As stated above, to date the only additional side effect with urinary preparations has been that of an occasional rash on the injection site and rarely a more generalised allergy has been reported. Other risks with protein impurities are purely theoretical and there have been no cases reported to cause concern.

Undesirable effects
This can happen with any of the preparations available. Sometimes the ovaries will recruit a large number of eggs especially in young women and those with polycystic ovaries. This can put you at risk of developing an illness called The Ovarian Hyper-stimulation Syndrome (see later for further details). We use ‘step-up and/or step-down’ method to adjust and protect you from this risk during the stimulation phase.

How effective are they?
We have used the Pure and Urinary preparations quite extensively and are happy with them all.

Who should give the injections?
The injections can be administered yourself or by your partner. We strongly advise you to consider learning self-administration. Independence will save you time, effort and stress of professionals not being available when needed. However, if you are extremely anxious then you may seek the help of your doctor’s nurse.

When to take the injections?
The injection is taken once a day at approximately the same time but an absolute and accurate precision is not essential. We will be able to estimate the day of your egg collection once the growth rate of follicles is established. It will also help in deciding the time of abstinence in preparation for the semen sample to be given on the day of egg collection.

The hCG (Pregnyl) Injection
When your follicles have reached an appropriate size, as assessed by scan, you are ready to be prepared for the egg collection. The hCG injection is essential to bring the eggs to the correct stage of maturation for this stage.

This injection is usually given late in the night normally between 10.00 p.m. and 2.30 a.m. It is specifically timed to be between 35-37 hours before the time of your egg collection.

Important notice: We will give you precise instructions as regards the time and day this injection has to be administered. It is essential that the hCG injection is given as close to the prescribed time as is possible. Please read the instructions before you leave the unit so that you can ask a member of The Centre if you do not understand any of the instructions.
14.5 Your Day Off !!

The day after the hCG injection, you may feel some heaviness or discomfort in the lower part of your abdomen. On this day, do not forget to take your bedtime Lorazepam tablet - this is given to reduce understandable anxiety and so that you can have a good night sleep before you arrive for your egg collection. Please remember that you are advised to refrain from driving or operating any machinery after you have taken the tranquilisers and not doing so could be hazardous for you and others. Please also remember to read the instruction sheet carefully.

14.6 Egg collection

Approximately 35-38 hours after the time of your hCG injection the egg recovery will be performed. This is performed in the Procedure rooms with the help of an Ultrasound machine. It is very similar to vaginal scanning except that we take sterile precautions to protect you and the eggs.

- Preparation

It is important to be as relaxed as possible for the egg recovery. Familiarity with your team will allow you to dispel some of the anxiety and fear. Your ovaries are considerably larger than their normal size which can lead to a dull ache and tenderness in the lower part of your abdomen before, during and after the egg collection. You will be advised to take an analgesic suppository on arrival and a further intravenous sedation and analgesia just before the procedure. We intend to relieve your discomfort as far as is possible. This is a short procedure and you should still be prepared for some discomfort as the needle enters the ovary. This procedure is outpatient based, you should be able to return home a few hours after the procedure.

It is necessary for your husband/partner/or a relative to drive you home and stay with you for the remaining part of the day. As you have received sedatives you should refrain from operating machinery, driving and should retire to bed after your return home.

![An egg collection procedure](image)

We will tell you the number of eggs collected during and at the end of the egg collection. Very occasionally the eggs can be difficult to identify and we will need to have another look in the laboratory. So your final egg number may be slightly less than that quoted to you immediately after the egg collection.

![Mature egg](image)

14.7 Insemination of the eggs

- **Time:** Although the time that the sperm sample is produced is not critical, we ask that the male partner attends at the specified time in order to avoid an undue delay in treatment. Many men would have frozen the sperm sample in advance of donation.

- **What happens?** After the sample is given, the sperm are washed and prepared. The live and progressively motile sperm are selected to inseminate the eggs 40-42 hours after your hCG injection i.e. 3-7 hours after the egg collection. Overall 50-70% of the eggs will fertilise but this number is variable in different patients and varies with age (both male and female).
14.8 Fertilisation of the eggs (Insemination or ICSI)

If the sperm count is normal and the sperm preparation is satisfactory we will conclude that the risk of failure of fertilisation is very low (not completely eliminated) and we will inseminate the eggs with a preparation of the sperm approximately 4 to 5 hours after egg recovery.

If the sperm count or motility is known to be low, there is a substantial increase in the risk of failure of fertilisation. We would have assessed this risk as part of our mandatory pre-assessments. In this situation, we would have also advised the recipient of the need for ICSI.

Sometimes the sample given on the day of egg collection is not satisfactory unlike the pre-assessment. In those circumstances we may feel that the risk of sperm not fertilising the eggs is increased. We would discuss this risk with the recipient and proceed with ICSI. Therefore all donors and recipient couples are advised to read through the section of 'risks of ICSI' very carefully. This is still considered to be an experimental procedure. We therefore ask you to consider this possibility in advance and also consent (if you agree) for this to happen at the time of your nurse consultation.

- **Insemination**
  This simply involves making a preparation of the sperm and transferring a measured number of sperm that are suspended in an appropriate fluid at the correct temperature and ph into the vicinity of the egg. The sperm will then find and fertilise the egg naturally.

- **Intra-cytoplasmic Sperm Injection**
  This technique involves injection of one sperm inside the egg under microscopic vision. The egg is very small, smaller than a pin prick and the sperm is smaller still. The procedure is done under 300 times magnification where a sperm is lifted out individually using a micropipette or needle and this then is directed to the shell of the egg penetrating it and the membrane of the egg, the whole sperm left inside the egg. The sperm and the egg have to undergo necessary changes after this for fertilisation to take place.

14.9 Checking Fertilisation

This assessment is performed approximately 18-20 hours after insemination or ICSI procedure.

Please ensure that we have your day time contact number. Our embryology team will be pleased to ring you to give you the result of this assessment. If fertilisation has occurred we will also give you a provisional appointment for embryo transfer which could be the following day (day 2 after egg collection), the day after next (day 3) or even on day 5.

14.10 Hormonal Support after the Egg collection

Donors at risk of ovarian hyperstimulation are given depot Prostap injection which would inactivate the pituitary gland and reduce the risks.
14.11 Risks

There are no treatments that are completely free of risk. As you would have undergone an IVF cycle your risks include the following:

- **Ovarian hyperstimulation syndrome**

If your ovaries have shown an excessive response then you are at risk of Ovarian Hyperstimulation Syndrome. Everybody receiving drugs for ovarian stimulation in order to produce multiple eggs is at risk. However the risk is not the same in everybody and we have developed clinical tools with which we assess your individual risk. This can vary between mild, moderate, severe and very severe. Young and overweight women with polycystic ovaries are especially ‘at risk’.

**General advice:** You are advised to drink normally and check that you are regularly passing normal amounts of urine. Although mild symptoms are common, severe ovarian hyperstimulation is rare and occurs in only 1-2 % cases. If in doubt, please do not hesitate to contact the IVF team or the on call doctor (as per the instructions in the front) at any time. The switchboard at St James’s University hospital will be able to put you in touch with the on call gynaecological registrar at all times.

**Management of this risk:** We will assess your risk before deciding to give HCG, when we do an egg collection and afterwards until we do an embryo transfer. All women in categories a, b and c below receive monitoring within the unit for early detection of changes and as per our written protocols and those with symptoms will be treated as appropriate. This may include hospitalisation, administration of intravenous fluids and other treatment such as drainage of fluid from body cavities.

a. When in the category of very severe risk, we would not give HCG, advice abandoning the cycle and starting again with a modified regimen.

b. When the risk is severe, we may try to curtail the cycle prematurely with medication, will not do an embryo transfer and will freeze all developing embryos.

c. When the risk is moderately severe we may adopt an expectant individualised approach where we observe your progress carefully whilst we maintain at least some embryos in culture to day 5. If by then you develop signs or symptoms we may freeze all developing embryos still and take other precautions. If you remain well we may perform an elective single embryo transfer.

d. When in this category, you do not require monitoring or specific treatment but we advise you to contact the unit as and when you have problems and as per the contact address and details on the front of this booklet.

**Recognised complications:**

Fortunately with appropriate risk assessment, prophylactic monitoring, early detection and timely intervention most women will have no problems. Your co-operation is therefore essential in ensuring your safety. It is a self limiting disorder and there are no problems after the cycle is complete. In women who become pregnant the risk period extends into the first trimester of pregnancy and complications up to 12 weeks of gestation have been recorded.

Complications occur either as a result of thrombosis in large veins because of thickening of the blood and its sluggish flow or because of collection of fluid in body cavities such as the abdomen or the chest. Strokes, ascitis, pleural effusions, pericardial effusion, cardiac tamponade and deaths have been reported in the literature. The risk of death is less than 0.01%.

- **Risk of an unwanted normal or ectopic pregnancy:**

We may not collect all eggs and therefore there is always some risk of an embryo forming naturally and leading to a pregnancy. You are advised to abstain in this cycle or use barrier forms of contraception at all times until you menstruate.

- **Risks of the Egg Collection Procedure:**

At the time of an egg collection a needle is carefully passed through the wall of your vagina into the ovary under ultrasound vision. The risks include those of an infection, bleeding and damage to an internal organ requiring surgery and repair.

**Infection:**

1. The needle can transfer germs from your vagina into the pelvis and lead to an infection. The risk of this is greater:
   a. if you have chronically infected tubes, an active vaginal or pelvic infection, your tubes are swollen or distended with fluid that may still contain bacteria.
   b. if you have endometriosis and especially if you have Endometriomas that have to be entered during the egg collection.
   c. If you have extensive adhesions incorporating the bowel the risk of bowel injury is increased also.

2. We advise that all donors undergo screening for genito-urinary infections before they undergo a treatment cycle at least once but it could be prudent that you have screening done before each cycle. It can easily be done via your GP and requires the nurse to take a swab and check your early morning urine samples for NAAT analysis for chlamydia in particular.

3. We provide vaginal Clindamycin cream during the treatment cycle for you to use from the day of HCG administration (2 nights before egg collection) and maintain this at least until we do your embryo transfer.

4. We also take further precaution of thoroughly cleaning your vagina before an egg collection and use fluids that contain strong antibiotics. Further we may give additional antibiotics by mouth in special at risk circumstances.

5. You are advised to let us know if you are suffering from vaginal infections or an offensive discharge.
Bleeding or internal injury:
Potentially the needle can also enter a blood vessel leading to internal bleeding or perforate a loop of the small or the large bowel leading to internal infection, need for major surgery and further treatment as appropriate. The risk of this complication is quite remote and less than 0.001%.

Risk of equipment failure:
The trust maintains service contracts for all equipment that is regularly serviced. There are also many standard operating procedures in the laboratory that help us have an early warning for problems. Despite all our efforts and very uncommonly equipment failure may sometimes lead to loss of eggs or embryos. This is a Category A incident that will be immediately notified to HFEA, the trust and you. There would usually be a thorough investigation and steps taken to prevent a recurrence of similar problems. The HFEA also operates an Alert system which we use to learn from incidents elsewhere.

Other risks
1. Although some have raised alarm over the risk of ovarian cancer with the use of hormones, these preparations have been used in treatment since early 1960's without any notified cases that can be directly linked to the use of these hormones. The available evidence suggests that there is no increase in your risk over and above that exists naturally. Infertility per se, delay in first pregnancy, and failure to breast feed, family history, obesity and smoking are known risk factors for the cancer of the ovary and the breast.
2. There have been no cases of complications with protein impurities in the urinary preparations. Theoretically some have worried those external proteins when injected could transfer viruses or prions that could lead to an illness like CJD at a later date.

This section is there for your information and to reassure you that as far as we know none of the publicised risks have been scientifically confirmed.

14.12 Risks of ICSI
ICSI was pioneered by a group in Brussels in 1992 and hence since rapidly become accepted in IVF centres around the world. The oldest child is therefore still very young. As it is significant invasion into natural processes where a natural fertilisation and pregnancy would not have occurred, its long term risks are not known. ICSI is an invasive technique and may also use sperm that would not otherwise be able to fertilise an egg. For these reasons, concerns about the potential risks to children born as a result of ICSI have been raised, and several follow-up studies have been published. These follow-up studies involve relatively small numbers of children and do not include effects that may be seen in older children or in the next generation. The HFEA considers follow-up studies to be extremely important and would encourage patients to talk to their treatment centre about participation in such studies. Clearly, more studies are needed, but the use of ICSI has been potentially linked with certain genetic and developmental defects as explained below:

These risks are only to the offspring and primarily relate to the recipient and the male partner's cause of Subfertility. It is therefore appropriate that you consider it an experimental procedure. Hence this section is not described here in detail. However further information can be provided to those who are interested.

15. Common causes of failure

These are as follows:
1. Failure to recruit optimum number of follicles with or without poor hormone levels.
2. Premature release of the eggs (very uncommon)
3. Unexpected illness
4. Failure to fertilise: This may be due to defective sperm, low number of sperm, functional abnormalities of the sperm, unknown technical failure and infection in the seminal sample (uncommon).
5. Failure of Cleavage: Occasionally fertilised eggs fail to divide and continue their development. Not all fertilised eggs will cleave to form embryos.

Although these are common causes of failure, sometimes failure also occurs even when everything has apparently gone well. Sometimes we may not have an explanation for why a pregnancy fails to occur. Mostly in these cases the embryos have failed to maintain their growth and development because of indigenous, not necessarily repetitive genetic abnormalities. We know that the risk of genetic abnormalities in naturally formed embryos and in normal couples is nearly 50%. Embryos created in IVF cycles have the same incidence overall but this risk exponentially increases with age and is substantially increased in women at or above the age of 40 years.

Most genetically abnormal embryos fail to implant, maintain growth to become pregnancies or may miscarry after a positive test. In this situation usually the prognosis for future attempts is good and we will discuss any specific predisposing factors that you may have. We may consider the removal of hydrosalpinges (swollen tubes), endometrial polyps or fibroids (if present) in some cases before repeating the treatment cycle.

16. Glossary of terms

- **Ovary**: Female gonad responsible for development of the eggs and female sex hormones.
- **Pituitary gland**: Master gland near the brain that controls most other glands in the body.
- **GnRH Agonist**: These hormones first stimulate and then suppress the pituitary gland function in relation to the ovary.
- **GnRH Antagonist**: These hormones instantly suppress the pituitary gland function in relation to the ovary.
- **Gonadotrophins**: Hormones produced by the pituitary gland for the stimulation of the ovary.
There are 2 types: FSH and LH.

- **FSH**: This is the follicle stimulating hormone and promotes development of follicles (see below) with eggs in the ovary.
- **LH**: This is the luteinising hormone responsible for preparing the follicle for rupture and release of the egg. It also prepares the egg for fertilisation by the sperm.

- **HCG**: This is the human chorionic gonadotrophin produced naturally only in pregnancy by the embryo's placenta. It has similar effects to LH but it is more potent. It is therefore used for inducing ovulatory changes in the egg before collection and for the stimulation of the ovary after egg collection to produce progesterone.

- **Urinary Gonadotrophins**: Purified extract of the menopausal women's urine containing both the FSH and the LH.
- **Synthetic Gonadotrophins**: Pure FSH only synthesised in the laboratory using new technology.
- **Oestrogen**: Produced by the follicles in the ovary. Responsible for the development of the lining of the womb.
- **Progesterone**: Hormone produced by the follicle after ovulation and responsible for preparing the lining of the womb for implantation.
- **Eggs**: Specialised female cell that develops in the ovary
- **Follicles**: Sac in the ovary that contains an egg. One develops every month naturally. Several develop in an IVF cycle leading to ovarian enlargement.
- **Sperm**: Specialised male cell that develops in the testis
- **Gametes**: A name for eggs and sperm
- **Fertilisation**: A term for the process by which the sperm enters the egg and its genetic material joins that of the egg.
- **Cleavage**: A term for growth of the egg after fertilisation with an increase in cell numbers by division.
- **Embryos**: A term for the growing ball of cells after fertilisation. Capable of developing into a human being.
- **Blastocyst**: An advanced 5-6 day old embryo containing a large ball of cells that has divided to define parts that will form the placenta and the foetus. It contains a cavity of fluid. At this stage the embryo is ready to hatch and embed into the lining of the womb.

16 USEFUL ADDRESSES:

In addition to the counselling facilities that exist at St James's you may wish to contact:

**HFEA (Human Fertilisation and Embryology Authority)**
21 Bloomsbury Street, London, WC1B 3HF
Tel: 020 7291 8200
Website: [www.hfea.gov.uk](http://www.hfea.gov.uk)

The details of other useful contacts can be obtained from ACU staff.

Please do not hesitate to discuss any aspect of this information booklet with us.

We wish you good luck.

Mrs Vinay Sharma,
Mr Anthony Rutherford
Professor Adam Balen