



The Leeds Centre for
Reproductive Medicine

IN VITRO FERTILISATION (IVF) & INTRACYTOPLASMIC SPERM INJECTION (ICSI)

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 the 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 3120

Email: leedsrmuenquiries@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.

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1. Patient Support Group

This group 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. This is a very useful contact point for information, support and information on other support groups (local and national). We recommend that you become a member of the support group for your benefit and that of others. Any member of the team would be pleased to provide you with the contact details.

2. New Patient Seminar

Time:

Venue: The Leeds Centre for Reproductive Medicine, Seacroft Hospital, York Road, Leeds LS14 6UH

Setting: In this seminar there will be slide presentations by a doctor, a nurse specialist, an embryologist and counsellor.

Objective: Our intention is to explain the treatment process with the help of slides, highlight important legal and treatment issues, risks and precautions that we would take to protect your well being. This is also a good opportunity for you to ask questions and meet other patients who might undergo treatment at the same time as you. There is no cost, commitment or obligation undertaken by attending this seminar. We strongly encourage that everybody attends this seminar before starting a treatment cycle. You can attend as many times as you wish and no appointments are necessary.

3. Emergency out of hours contact

The ACU working hours are: Monday to Friday 8.00am- 5.00pm, Saturday and Sunday 8.00am-12.00pm.

In an emergency or on weekends you can obtain advice from the on call member of the team by ringing the St James's Hospital switchboard on 0113-2433144.

4. Human Fertilisation and Embryology ACT

The Human Fertilisation and Embryology Act was passed by parliament in 1990 and became law on 1st August 1991. Simultaneously the Department of Health established The Human Fertilisation and Embryology Authority (HFEA) for the regulation of all treatments and research pertaining to human eggs, sperm and embryos. This authority licenses centres, its staff and regularly inspects the centres for compliance with the law and the HFEA Code of Practice. By law every HFEA licensed centre is required to report every treatment cycle and its outcome to the HFEA. This information is analysed periodically and published on the HFEA website (www.hfea.gov.uk) and in a 'Patient's Guide to IVF and DI treatments' which is available free of charge on request from the HFEA.

- **HFEA register:** The Authority keeps a confidential register of identifying information on all patients, their treatments, donors, recipients and children born after HFEA licensed treatments. This register was set up on 1st August 1991 and contains above information from that date onwards.

From the year 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 HFEA licensed treatment, and if so, whether they are related to the person they want to marry.

The HFEA 'generally permits donors to preserve their anonymity'. Only information that HFEA could give at the time when treatment was conducted may ever be available unless there was a further change in the law. This includes information about the screening tests performed before donation and their results.

Prior to April 2005, the law did not allow children born with donated gametes or embryos to apply for identifying information from the register about current or past* donors, or of patients and their children. It is a criminal offence for the centres to disclose this information.

**Recipient couples and donors concerned about how a retrospective change in the law might affect their and their child's legal position should seek more specific independent legal advice.*

- **Legal Parenthood:** The law defines the 'woman who gives birth as the mother and her partner as the father' irrespective of the source of eggs, sperm or the embryos. This is the case unless the couple are judicially separated or the husband can prove that he did not consent to treatment.
 - When a child is born to an unmarried couple the male partner may not have parental responsibility for that child. In our centre, we provide treatment services to couples in stable relationships where both partners consent to treatment.

- All partners are advised to provide legal consent in writing for the use of donated sperm/eggs/embryos in the treatment of their partner.
- If the woman using donated sperm or embryos created with donor sperm is not married and is not in a civil partnership, she will be asked to consent in writing that she agrees to her partner being the legal parent of any child born as a result of this treatment. Her partner will also be asked to consent in writing that he/she agrees to being the legal parent of any child born as a result of this treatment.

**Unmarried couples concerned about how parental responsibility affects their legal rights should seek independent legal advice.*

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

5. Welfare of Future Children

The HFEAct 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 or a citizen of the United Kingdom. It is the statutory duty of every centre to have a written procedure for assessing the Welfare of the Future Child and that of any other existing child who may be affected by treatment.

Factors considered in assessment include:

- 1) the couple's commitment to having and bringing up a child
- 2) the couple's ability to provide a stable and supportive environment for the child/children
- 3) the couple's medical history and that of their families, considering factors that may risk the child's wellbeing
- 4) both partner's health (including their ages) and their ability to provide maternal and paternal nurturing to the child
- 5) the couple's ability to meet the needs of the children in the event of a multiple birth
- 6) any risk of harm e.g. that of inherited disorders, transmissible disease, neglect or abuse
- 7) any risk a new born may put on the welfare of the existing child with in the family

The HFEA Code of Practice (COP) also advises that views of all those who have been involved with the prospective parents should be taken into account. It is also 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.

We have a protocol that has been approved by our local ethics committee. Under specific circumstances, we may also need to contact your general practitioner, other medical specialists, authorities and agencies e.g. social workers, police etc for information. This is to enable the members of the team at The Leeds Centre for Reproductive Medicine or the Clinical Ethics Committee in the Leeds Teaching Hospitals Trust formally Consider the Welfare of the Future Child when appropriate.

Please note that fair and unprejudiced counselling services are available to everybody prior to, during or after the assessment process irrespective of the outcome of such an assessment.

6. Common causes of Subfertility

Nearly 1 in 6 couples will require some form of sub-fertility assistance. The exact prevalence of various conditions can vary demographically. Below is a simplified version of various causes.

6.1 Causes of Female sub-fertility include:

- 1) Chronic pelvic inflammatory disease and tubal damage: 30%
- 2) Male sub-fertility: 30%
- 3) Endometriosis: 10-15%
- 4) Ovulation disorders: 10-15%
 - a) polycystic ovaries
 - b) reduction in ovarian reserve
 - c) hyper-prolactinaemia

- d) hypo or hyper thyroidism
- e) other
- 5) Unexplained: 30%
- 6) Miscellaneous:
 - a) Fibroids
 - b) Endometrial polyps
 - c) Auto-immune disorders
 - d) Past treatments such as chemo or radiotherapy for cancers
 - e) Sterilisation
 - f) Genetic

6.2 Causes of male sub-fertility include:

- 1) Genito-urinary infections
- 2) Undescended testicles
- 3) Sterilisation or failure of reversal of vasectomy
- 4) Hereditary or Genetic causes
- 5) Orchidectomy for testicular tumours
- 6) Past chemo or radiotherapy for cancers

Genetic or hereditary male sub-fertility:

Whilst most of the above listed causes of male sub-fertility are self-explanatory, genetic causes require some further explanation. This is because the treatment of male sub-fertility for genetic cause may require additional tests for assessment and may also have an influence on the outcome of your treatment. The incidence of chromosomal abnormalities is approximately 13.7% in azoospermic males (no sperm in the ejaculate) and 4.6% in men with low sperm counts. The incidence in men with normal sperm counts is 0.5%. Identifying these abnormalities may not only give us the reason for your problem but will also have an influence on the risk of having a similar abnormality in your children born after ICSI.

Normal chromosome pattern: This for every man is 46XY. There are 22 pairs of normal chromosomes (total 44) called the '*autosomes*' and these are responsible for the general characteristics and bodily functions. The 23rd pair is the sex chromosome and in men this is expressed as XY, where X codes for female development and Y codes for development as a male. Females have two X-chromosomes and hence an XX pattern. In males the Y chromosome is the dominant one and this dictates development of the baby as a male.

Abnormal patterns:

- 1) In the majority of men, there is no constitutional abnormality of chromosome numbers i.e. the total numbers are normal as 46XY, but a structural aberration of the sex chromosome exists with either missing or modified genetic information on the Y chromosome. This chromosome is responsible for testicular development and sperm formation. In the event of loss of genetic material or its modification, men may have a genetically determined low sperm counts and subfertility. As the same Y chromosome will be passed on by ICSI to the male offspring, there may be a risk of passing the same defect to the male child and his future fertility may thus be similarly affected. There are no other known additional risk factors. We do not yet know all forms of gene deletions or mutations although active research is bringing more new information forward at a considerable pace.
- 2) In some men, there is an extra sex chromosome giving a pattern of 47XXY or 47XYY. The ICSI success rate in this case is low and variable. If successful the risk of similar genetic defect in the offspring is also not known.
- 3) If there is a constitutional chromosome aberration i.e. when there is an abnormality with the main 22 pairs, then the success rates after ICSI are also lower, there is an increased risk of miscarriage and, in ongoing pregnancies there will be a risk of congenital abnormality and/or mental retardation. **Fortunately this situation is very rare in otherwise normal and healthy men.**

Choice of treatments:

- Where there is only a Female cause for Subfertility only IVF is needed
- Male Subfertility requires IVF in combination with ICSI
- Where Male & Female Subfertility is combined, IVF is performed in combination with ICSI
- Depending on the cause of male sub-fertility prior surgical sperm retrieval by PESA or MESA or TESE may be needed. We have separate information leaflets for this procedure

7. Referral and Clinic

There are two levels of services:

Secondary care: These couples have been referred by their General Practitioners from within the Leeds district for investigations of subfertility. The need for assisted conception is realised during the course of assessments.

Tertiary care: These couples are referred by other specialists from the neighbouring district general hospitals after appropriate investigations have already been performed and a diagnosis has been reached. Most of the assessments would have been performed recently and would not require repetition but we may perform further assessments in certain areas such as request a more advanced sperm analysis, hormone profile, genito-urinary infection screen and a baseline scan. We will proceed to treatment when you are satisfied have the appropriate time to fully consider all legal and treatment related issues.

8. NHS funding and 18 week target

Until such time that there are uniform nationwide criteria for NHS funding, your Primary Care Trust's criteria will define eligibility for NHS funding and the number of funded treatments. Patients entitled to NHS funded treatment will be able to start their treatment within 18 weeks from the time of GP referral unless they themselves wish to postpone treatment to a later date. We provide relevant information regarding your eligibility and time to treatment when you attend the clinic.

9. Funding of treatment

Each PCT defines its own criteria for access to NHS funded treatment. When you come to the clinic, we can provide relevant information regarding your PCT's eligibility criteria.

Amongst patients eligible for NHS treatment, PCT's and hospitals comply with the government's '18 Week Target' for time to start treatment.

Patients not eligible for NHS funding have the option of proceeding as Genesis patients. You will be advised of this at your clinic appointment when the indicated treatment is discussed with you. At that time a trust price list will also be provided.

Before the treatment, the finance officer in the unit will give you the relevant invoices. The Leeds Teaching Hospitals NHS Trust expects you to settle your account by credit card, cash or bankers draft before the nurse consultation appointment.

10. Counselling

Free counselling services with a trained counsellor are routinely available to all upon request.

Location: Counselling is generally provided within the premises of The Centre. When required, arrangements for counselling in the distantly located Department of Psychology at the St James's site can be made. Couples can request to be counselled together or individually. You may seek assistance at any time before, during or after treatment. It 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 in exceptional circumstances to give essential information that may affect the Welfare of future or existing children to the team.

Access: There are no limits to the number of times you attend and to make an appointment you can ring the unit directly any time during the working days of the week. Couples needing assistance of interpreters are advised to either bring a known interpreter with them or give sufficient notice for an interpreter to be arranged by the trust.

Counselling can take several forms, namely:

- Support: This is to discuss the social and emotional aspects of sub-fertility, help you at times of distress or confusion and to minimise the potential impact of treatment outcome to you and your partner.
- Discussion of Implications: We may advise you to see the counsellors in specific circumstances to discuss the implications of certain aspects of your treatments and the choices you may wish to consider. It is best if you request an appointment with the counsellor after you have had a chance to read our information booklets and attend the new patient seminar.
- Therapeutic: This is when the counsellor helps you devise coping strategies to understand your feelings, prevent guilt or self harm and help to develop the ability to come to terms with the situation.
- Assessment: Whenever there is a concern that you may not have understood the issues relevant to the Welfare of the Future or Existing child / children, the team may refer you for an assessment by the counsellor.

11. Consents

You will be asked to sign appropriate consent forms after you have read the information booklets, attended the new patient seminar, your concerns and questions have been answered and you have discussed the medical and ethical issues.

Both partners are required to sign all of the consent forms before we can proceed with your treatment.

The consents cover the following subjects that are discussed in detail below:

1. Right of Confidentiality
2. Your wishes regarding:
 - 2.1. freezing of eggs / sperm / embryos
 - 2.2. research on eggs / sperm / embryos
 - 2.3. long-term storage of eggs / sperm / embryos
 - 2.4. posthumous use of eggs / sperm / embryos

Your consent advises us of your informed choice but does not commit you to undergo any form of treatment. You always have the right to change your mind until, but not after the event. It is therefore very important that all issues are thoroughly considered beforehand and that sudden and unexpected changes that you may regret later do not happen.

You have the following relevant issues to consider:

11.1 Confidentiality

All information regarding your treatment is strictly confidential and subject to both the HFEAct and the Data Protection Act. We may communicate with your general practitioner, referring consultant and other carers only with your written consent. However you should be aware that medical practitioners by virtue of their knowledge and experience may already know or understand the nature of treatment that might be undertaken in your specific circumstance.

Once we have disclosed the information to the unlicensed individuals it can no longer be controlled by the HFEAct but it will still be regulated by the Data Protection Act and General Law of Confidentiality. In general practice, information will be accessible to other GPs and staff working within the practice even if your consent specifically named only one of the several GPs in your practice. When changing GPs, your medical records will be transferred to your new GP practice without our involvement or written named consent from you.

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

You have a right to decline consent for communication but we need to consider your reasons for declining consent in our assessments.

We generally advise to keep your G.P. informed as they are your primary carers, will also be committed to confidentiality and can help you in an emergency but only if they are fully informed.

Sometimes patients request their GP to keep written information regarding assisted conception separate from the practice notes so that this information is not freely available to all the staff in their surgery. You may discuss this option when required with your GP.

11.2 Freezing of Eggs, Sperm and Embryos

Please note that you have to decide the fate of your spare gametes and /or embryos and that we act as per your written consents.

Regarding Surplus Sperm:

This issue becomes relevant where patients cannot give gametes when required e.g. in case of men requiring electro-ejaculation or surgical sperm retrieval. You may choose to freeze the spare sperm for your future use or discard them.

Embryo freezing: At the time of embryo transfer, we will discuss the fertilisation, growth rate and grade of embryos which is based on the embryo's appearance. We will offer embryo freezing when deemed appropriate. Approximately 60% of embryos judged suitable for freezing survive and embryos with lower grades would have an even lower chance of survival. Before undertaking a frozen embryo transfer cycle, we try to ensure (as much as is possible) that upon thaw you would have at least some embryos suitable for transfer.

Embryo freezing can only be performed with your prior written consent. The legal storage limit for embryos is a maximum of 5 years from the date of freezing and this can be extended to 10 years if in the interim the female partner has reached the peri-menopausal years.

The embryos are your property and responsibility. You also have to decide the fate of the embryos in the event of death or mental incapacitation. They deserve similar considerations as those for your unborn future child. Therefore we strongly advise you to always remain in touch with us, to advise us of your change in address, intentions and suggest that you consider replacement of your frozen embryos at the earliest possible opportunity.

Prolonged culture: With your written consent, embryos can be maintained in culture until they stop growing or develop into the blastocyst (usually on day 5 or 6 after egg collection). Embryos generally will stop growth within this stage. The day 3, 4 or 5 embryos generally have a higher developmental potential. We cannot keep embryos in culture for observation alone unless there is a clear instruction from you to preserve them when appropriate.

Embryo donation: You can consider donating your embryos to help another couple. This is very similar to egg and sperm donation, you would be required to have implication counselling and the necessary screening tests. We will advise you to consider this option for your frozen embryos after you have completed your family or decided to discontinue all future treatment for yourself.

Embryo research: Please see the relevant section below for details.

Humanely discard the spare embryos: Only good quality embryos can be successfully frozen, donated to another couple or used for research. If you do not wish prolonged culture with a view to freezing then you must instruct us to humanely discard your spare embryos.



Please see IVF consent forms for further details. We emphasise that these choices are entirely personal.

11.3 Long term storage

Long term storage is primarily for the storage of gametes and/or embryos prior to chemo or radiotherapy for cancer. We will be pleased to provide specific information on the length of storage permitted legally in your case. This can be quite a long storage period and up to your 55th birthday or for a total of 55 years. However this does not mean that the trust will be able to keep the sperm for this length of time. The duration of storage is agreed with yourself after discussion with your specialist, bearing in mind your reproductive intentions, how your fertility will be affected by chemo or radiotherapy and your prognosis.

11.4 Posthumous use of gametes and embryos

Men can opt to permit their female partner to use their sperm or embryos created with them posthumously. There are ethical and legal concerns that you must consider very carefully before making a choice. We like you to have a discussion with the counsellor when considering implications of posthumous use of gametes to your future child.

Ethical issues: In your considerations the 'Rights and Welfare of your Future Child/Children' must be paramount. These considerations must also precede and exceed your own wishes. The law clearly states that the child has a '*right to have a father or a father figure for paternal nurturing*'. It is our statutory obligation to ensure that this right is upheld. For instance, the law asks us to identify and counsel individuals who will have '*parental responsibility*' and who will be '*responsible for the paternal nurturing of your child*'.

Legal issues: The HFEAct provides that where a man's sperm or embryos created with his sperm are used after his death, that he is not to be treated as the father of the child, except for the purpose of recording on the Register of Births as the Deceased father subject to the Human Fertilisation (Deceased Fathers) Act 2003 being fulfilled and for no other purpose. For instance, the child will have no entitlements to the man's estate and if desired separate provisions will have to be made by the individuals concerned. The posthumous use of gametes or embryos is only possible if the sperm / embryos have been stored in the man's lifetime and with his written consent. The unit has a statutory duty to consider the Welfare of Future



Children born posthumously and to assess what arrangements have been put in place to meet the future child's needs when treatment is requested.

11.5 Embryo research

This is a HFEA licensed and very carefully regulated activity. All centres have to obtain specific research licenses for the projects that they may conduct or be a participant. This section intends to make you broadly aware of the issues that surround egg / sperm / embryo research and does not in any way constitute a request from us for you to participate.

In suitable circumstances (usually when considering the future of the frozen tissues / eggs / sperm / embryos in our centre) you may be asked, among others, an option to consider donation to research. We will be pleased to provide the necessary detail regarding the ethically approved project if we can accept your donation. If there are no active research projects, we may be unable to accept the donation when the stored eggs/ sperm / embryos may have to be allowed to perish when the storage period expires.

All research is experimental and gametes or embryos used or created during the project cannot be transferred for treatment and after completion of the research they must be allowed to perish.

You are not obliged to take any decision and your decision to participate or not in any research project will not affect your treatment. If you intend to withdraw for any reason during a research trial, you are free to do so at any time as long as the project has not already been conducted.

During research projects, cells of the embryo or the gametes may be fixed in what is called 'secondary research' that may have genetic applications.

For confidentiality, the gametes and embryos are anonymised. Currently all anonymisation is irreversible i.e. no specific feedback regarding your eggs / sperm / embryos is possible.

You will be offered implication counselling if, in a genetic research proposal, the anonymisation was reversible. In this case you may be able to get feedback after the research in case we have findings that may be relevant to you.

If the unit took part in Stem Cell research, you will receive more specific information about that project. In that case you will need to be aware that any stem cell lines created may continue indefinitely and that these lines may be later used in other relevant research projects.

12. Pre-treatment assessments

▪ Sperm Analysis

You will be given advice regarding preparation prior to giving the sample. On arrival you will be asked a few questions by one of the embryologists and taken to a private room where you can provide a semen sample. This sample is given by masturbating into a small pot. In analysis, we will perform several tests. You may occasionally require more than one appointment.

It is not appropriate to conduct discussions of a personal nature on the telephone and we respectfully advise you that embryology staff refrain from providing results of having a discussion on phone. You will receive a full explanation when you attend outpatients.

**Please discuss any difficulties you may have in giving the sample in clinical conditions. We can also arrange to freeze a back-up sample when required to relieve you of the stress of producing a sample on the day of your wife's / partner's egg collection.*

▪ Early follicular phase FSH, LH & Oestradiol

This is a blood test taken on the 1st, 2nd or 3rd day of your period. Its purpose is to identify those women whose reserve of eggs in the ovary may be below a critical level. When appropriate the dose of the hormone stimulation can be adjusted and likely outcomes can be discussed before the treatment. It is often necessary to update this assessment if this test has not been performed within the preceding 6 months or if shows an abnormality.

▪ Anti-Mullerian hormone

This is also a blood test but has the advantage of being accurate at any stage of the menstrual cycle. However this test is not widely available and hence when considered important we may do this ourselves in The Centre.

▪ Rubella status and Cervical Smear

It is important to ensure before treatment that you are immune to rubella (a blood test) and that your last cervical smear was normal within the previous 3 years.

▪ Pelvic ultrasound scan

A scan is performed to ensure that there are no pre-existing and as yet undiagnosed pelvic abnormalities such as fibroids, polyps, swollen tubes, ovarian cysts etc before treatment is planned. When present, a discussion of their implications and treatment options can take place at your next clinic visit. In addition we assess certain features within your ovaries to ascertain your risk of ovarian hyper or under stimulation.

▪ Genito-urinary Infection screen

It is prudent that we screen you for a potential coincidental infection in the genital tract which will reduce your success rate and increase your risk of infection after an egg collection or embryo transfer if not treated. This screening involves having appropriate swabs taken before treatment from both partners. We will provide information on tests required and usually your GP's or local genito-urinary medicine clinics (upon referral from your GP) can help with these screening tests.

▪ Mock Embryo Transfer

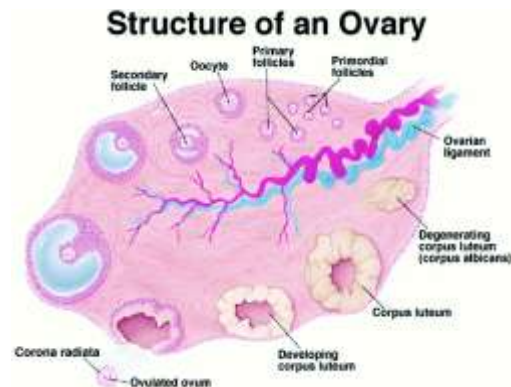
Those patients who have had previous surgery on the neck of the womb or who have fibroids will need a 'mock' embryo transfer. This is so that we can be as certain as possible that the real procedure is straight forward. If difficulties are encountered we may need to take specific actions e.g. perform cervical dilatation under a general anaesthetic.

▪ HIV, Hepatitis B, C & Syphilis screening

It is our policy to screen all patients, donors and recipients for HIV, Hepatitis B, C and syphilis prior to the start of treatment. Counselling is available prior to undergoing the screening tests. We can provide a safe environment for your treatment and your frozen embryos and gametes by ensuring that we are aware of the HIV and Hepatitis status of all our patients.

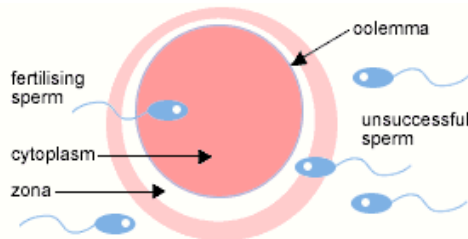
The sperm and embryos are stored in the vicinity of other similarly screened and negative samples. There is a very small theoretical risk of cross infection when a previously negative person becomes positive after storage. It is important to note that such an incident has never been reported to date.

Samples from screen positive individuals have to be handled in appropriately developed laboratory conditions and stored individually. At the present time we are unable to offer this service but will be happy to provide our counselling services and help in obtaining a referral to a suitable centre.



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 when 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*.

An

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 elsewhere in this 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 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 Treatment Protocols

As explained in the section above, we need to stimulate the ovary with hormones so that all eggs available for development in that cycle do not see ovulatory changes prematurely. This interacting gland is called 'the pituitary' and is located behind the eyes in front of the brain. We have several commonly used protocols.

▪ Long protocol

In this protocol we inactivate the pituitary before we start stimulating the ovary. This period of inactivation is termed as 'downregulation' or 'suppression'. We can use a number of ways to achieve this effect. As it takes longer to complete this cycle (5-7 weeks) it is called the 'Long Protocol'. This protocol is more suited to women with satisfactory ovarian reserve. It is also popular as it allows us to start stimulation on any day of the week that suits you and the unit. Please see below the relevant detail.

▪ Short protocol

Using this protocol we try to achieve the inactivation of the pituitary gland by using a different preparation. This medication is given as a single daily injection whilst the follicles are developing starting before the hormone levels have reached a critical stage. This effect can be assessed indirectly by measuring the size of the follicles and generally happens on day 6 of stimulation. Thus you may require an additional early scan to decide when to start this medication. As periods can arrive at any time of the week, we sometimes use the oral contraceptive pill for a few days so that we can still start stimulation on right day for you and the unit. This protocol can be used for all women, with good and also the reduced ovarian reserve. Using this protocol the cycle is shorter (4 weeks) and the treatment outcome is known early, hence the name 'short protocol'.

▪ Flare protocol

Unlike the long protocol, ovarian suppression is not performed in advance. Both hormones for suppression of the pituitary and for stimulation of the ovary are started together on the first day of the menstrual cycle. This allows us to use the initial stimulation that occurs with these hormones to recruit more follicles. This protocol is reserved for women with much reduced ovarian reserve.

14.2 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 where diagnosis is known. A full discussion of the relevant aspects of your treatment takes place in the clinic. 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 at your first appointment in the clinic.

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. 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 nurse co-ordinator on your way out so that the NHS funded patients can be given a start date for your treatment within the government target of 18 weeks. The NHS self funded patients will be added to the waiting list and the nurse co-ordinator will provide an estimate of the month in which you may receive treatment.

e. Appointment with the Finance officer. The Unit's finance officer will provide the invoice for the NHS fee paying patients, receipt payment and book a nurse consultation appointment in the weeks prior to your treatment start date.

f. 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.

g. 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.

h. 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.

i. 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.).

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

k. Insemination or ICSI. Male partner gives a sperm sample for preparation and insemination of the eggs by the direct method or by the ICSI procedure.

l. Checking Fertilisation. You will receive a telephone call with necessary information on the day after egg collection.

m. Embryo Transfer and Hormonal Support. The embryos are replaced in the womb and you will receive further medication afterwards to provide hormonal support in this phase of the cycle.

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

o. Pregnancy test. You are given a date for the pregnancy test at the time of embryo transfer.

p. Pregnancy scan or Follow-up consultation. This is arranged after the pregnancy test and the outcome of treatment is known.

14.3 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*'.
- By this time self funding and the private patients should have also cleared their accounts so that you can proceed further unreservedly.

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 a treatment diary
- to give you the 'Pocket Consultant-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 understand the process.

14.4 Downregulation or the Suppression phase

As explained above, during your IVF cycle the response from other glands (the pituitary) may interfere and affect the maturation of eggs. As this can lead to a lessening of your 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 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 Prostag normally do not have to take additional medication during the stimulation phase.

14.5 Stimulation phase

There are large variations between patients 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 female partner's age, the cause of her sub-fertility, 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 your 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 (Merional / Fostimon) 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?**

Merional, Fostimon 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 'Risks' section 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 (Gonasi) 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.

14.6 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.

14.7 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



An egg collection procedure

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.

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

Mature egg

14.8 Giving a Sperm sample

- **Time:** Although the time that the sperm sample is produced is not critical, we would ask that the male partner attends at the specified time in order to avoid an undue delay in treatment.
- **Abstinence period:** We ask that all men abstain for at least 3 days prior to giving the sample. In men with normal sperm counts this 3 day period is adequate and longer abstinence is neither necessary nor appropriate. However in men with extremely low count (e.g. <1 million per ml) the abstinence period can be longer to ensure that sperm are found on the day of egg collection.
- **What happens?** Shortly 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) and / or the cause of your sub-fertility.
- **Freeze for Back up:** We know that providing sperm sample on demand in an unfamiliar and hospital environment, on a day of the stress of egg collection in your spouse etc can lead to anxiety and difficulties with ejaculation. We ask that you assess this risk carefully for your self and request sperm freezing for a backup if you perceive that you will have a risk. In such scenarios we do have the alternative of providing Viagra like medication for those suitable (it does have risks) or performing an emergency per-cutaneous sperm aspiration from the epididymis under local analgesia. Need less to say that both of these can be very traumatic for you both and there may also be costs incurred. If we are unable to find sperm the treatment may have to be completed at that point and neither freezing of mature eggs nor their survival can be guaranteed. It is therefore better to take precautions than to try and find alternatives in an emergency. **Please do not be embarrassed in discussing this matter with us*.*

14.9 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 still) 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 assessed this risk for you

increase in the risk of failure of fertilisation. We would have as part of our mandatory pre-assessments. In this situation, we would have also advised you of the need of ICSI at your follow-up appointment.

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 yourself and with your agreement we will proceed with ICSI. Therefore all 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**

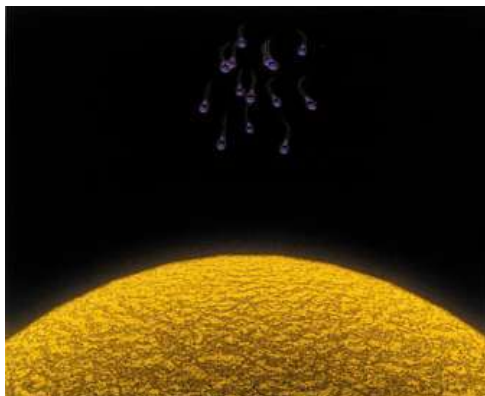
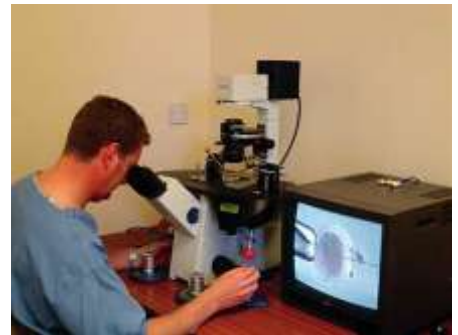
This simply involves making a preparation of the sperm and transferring a measured number of sperm that are suspended in an appropriate fluid at the correct temperature and pH into the vicinity of the egg. The sperm will then find and fertilise the egg naturally.



IVF

- **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.



14.10 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.

Normal fertilisation

Abnormal fertilisation

14.11 Prolonged culture of embryos

- **Purpose**

Prolonged culture of embryos provides us with more time to observe the developmental potential of the embryos and select those suitable for transfer better. It does not make the embryos more or less capable. It also does not help in removing all abnormal embryos from those that are available and your risks will remain as they would be appropriate for male and female partner's age and clinical circumstances. We would have discussed risks in specific circumstances beforehand but you can ask further if you wish when you attend the follow-up appointment before you start your cycle.



- **Why choose prolonged culture?**

This is a clinical decision. We choose to culture the embryos until such time we feel appropriate to select the best for transfer. Hence this is an option for only those couples where a number of equally good embryos are available. Pregnancy rate is higher when appropriately growing day 3 embryos or day 5 blastocysts are transferred than with day 2 embryos or day 6 blastocysts.

When there a lot of embryos with an them into prolonged culture in order to growth. It also gives us time to observe that we can avoid doing a transfer for time do not deprive those who remain rate. The developmental potential of frozen and thawed.



equivalent appearance and growth, we may put differentiate and select those with a better continued when you are at risk of ovarian hyperstimulation so those who develop problems early but at the same well from a fresh transfer which has a higher success fresh embryos tends to be higher than those that are

The spare embryos can also be maintained in culture until they are deemed suitable for freezing, stop growing or develop into the blastocysts when they can be frozen also if deemed suitable.

The risk of keeping embryos in culture is that you will find useful information about the embryo's development before your pregnancy test. None may progress sufficiently and despite having a number of embryos, none may be frozen because of suboptimal growth.

14.12 Embryo transfer

As explained above, the fertilised eggs are called `embryos`. These are examined the day following fertilisation and then daily to monitor cell division and growth to determine the day of embryo transfer. If the embryos have not grown after fertilisation, an embryo transfer is not performed.

Day 2: 2 cell embryo

Day 2: 4 cell embryo

Day 3: 8 cell embryo

Day 4: Morula

Day 5: Hatching Blastocysts

- **Risk of a multiple pregnancy**

This is a very important clinical matter for both us and you. We know that transfer of multiple embryos increases the likelihood of at least one continuing growth and implanting. However your risk of a multiple pregnancy is also increased with the transfer of multiple embryos. Your chance of conceiving a multiple pregnancy depends most of all upon your own age, cause of sub-fertility and also the programmes overall success rate. Occasionally embryos split to form two identical babies. This risk is also increased with IVF and ICSI.

In the past even though approximately 85-90% of our cycles receive 2 embryos only, 25-30% of all our births were still twins. The risk is greatest in women under 35 years of age and in those who respond well. Legally we are permitted to transfer up to 3 embryos in women above the age of 40 years because of a very much lower multiple pregnancy rate using their own eggs (<1%).

The complications of multiple pregnancies include miscarriage, prematurity, fetal growth retardation, increased risk of pregnancy complications in the mother and the need for delivery by caesarean section. Additional complications of identical twinning include polyhydramnios and twin to twin transfusion syndrome. These complications have high risks for premature delivery. Extremely premature birth has the risk of death in infancy or survival with long-term mental and physical handicap in the children.

- **Our mission 'One at a time'**

Our intention is to give the best chance of a pregnancy but without a high risk of a multiple pregnancy. Whilst trying to come to a decision we balance the probability of a pregnancy against the risks of a multiple pregnancy. We therefore analyse our data extensively and we know of a number of features that will help us identify those couples



who are specifically at high risk of a multiple pregnancy. The same couples also have a good chance of getting pregnant even with a single transferred embryo provided we select well. We therefore choose methods of prolonged culture and optimal day of embryo transfer so that we do not compromise your success rate



but at the same time we give you a low risk of a multiple pregnancy.

Our embryology team will keep you informed of the embryo's progress and choose the best day for your transfer as per our centre's 'strategy to minimise multiple pregnancies. All couples will have a further discussion on the day of the embryo transfer.

- **Fetal reduction**

The term 'fetal reduction' is used for an ultrasound directed procedure that selectively terminates one fetus while permitting the other to continue growth and development as normal. Sometimes this procedure is employed to reduce the number of fetuses that have implanted after infertility treatment e.g. for reducing a triplet pregnancy to twins. Some pregnancies with a triplet implantation will spontaneously reduce to twins or singleton. Details regarding this 'natural' risk of 'spontaneous reduction' are available in our annual report and we can discuss this with you. If you have an ongoing triplet pregnancy of non-identical foetuses, then fetal reduction may be considered in line with the requirements of the Abortion Act. Equally you may consider this option if you conceive a set of identical twins with a non-identical triplet at the same time after the transfer of 2 embryos. Further discussion with your obstetrician will be necessary at that time.

This procedure is performed by passing a fine needle into the pregnancy sac and injecting potassium chloride into the fetal heart. The procedure carries a 4-5% risk of miscarriage. The world's combined data suggests that the duration of pregnancy is unlikely to be altered greatly by embryo reduction. Please ask for more up to date information or clarification regarding our own programme.

- **Technique of embryo transfer**

Usually at least 80-90% of those eggs that have shown normal fertilisation will grow in culture to day 2. However some of these will slow down or discontinue growth completely between day 3 and day 5. We check the embryos every morning before we call you for an embryo transfer. If there is no growth after fertilisation, we regret that we will need to cancel the

transfer and arrange a follow-up. In others, we will discuss the number, growth rate and appearance of the embryos and what we have selected for your transfer when you arrive.

- **Preparation for embryo transfer**

The procedure of embryo transfer itself is quite simple and normally pain free. The embryos are very sensitive to light, temperature and pH changes. Ideally therefore for the embryo survival and growth the transfer procedure should be quick, simple and atraumatic.

We take the following preparation for this to happen.

1. You are advised to have a full bladder before the transfer because in most circumstances doing so straightens the uterine shape and makes the transfer procedure straightforward.
2. The outer sheath of the embryo transfer catheter is inserted first to ensure easy insertion of the catheter whilst keeping the embryos in the correct environment until you are absolutely ready to receive them.
3. The selected embryos are put into a fine catheter and transferred gently into the uterus in a very small volume of fluid.
4. Occasionally and especially when the bladder is not full, an instrument to hold and straighten the neck of the womb may become necessary. This can give you temporary discomfort.

The embryos are not visible to the naked eye at this stage but can be seen with the microscope or on the television screen attached via a camera to the microscope. The embryo transfer procedure literally takes under a minute and you do not require pain relief. After the embryo transfer, we will check that the embryos have left the catheter and reached the uterus. Very occasionally, the embryos will not have left the catheter and the transfer procedure has to be repeated. You may rest for a few minutes afterwards before returning home.

- **After the embryo transfer**

You are advised to continue with your daily routine as normal and there is no need to take special rest. However, we would advise you to refrain from strenuous physical exercise, taking of any form of drugs or medicines without checking with us first and avoid contact with contagious illnesses including 'flu like illnesses' as much as possible.

You may experience discomfort in the lower part of your abdomen because of enlargement of your ovaries after the egg collection. These once again enlarge to provide hormonal support for the implanting embryos. There are sac-like structures in the ovary called 'corpora lutea' and may be mistakenly called 'cysts'. These have an important role and are essential for a pregnancy to take place. This enlargement of the ovary and discomfort after the egg collection is normal and expected. You may take some paracetamol tablets or suppositories safely if needed.

In this cycle your symptoms of premenstrual syndrome are likely to be exaggerated because of high hormone levels. If unluckily you fail to conceive then the pattern of menstruation may also be different.

If you have any worries you can get in touch with us at any time of the day during the week on our direct telephone line and at other times via the hospital switchboard as instructed in the front of this booklet. We would very much advise you to contact us during the working week as far as is possible so that you receive timely advice. We do not mind if you ring us for what you may consider a trivial matter.

****Please note that this is a much specialised form of treatment. Although your G.P. would gladly attempt to help you, he/she will not be fully aware of the details of your treatment or the necessary action. Hence it is in your interest to contact us first and before the problem is too advanced.****

14.13 Hormonal Support after the ET

On the day of embryo transfer, you will be given a letter which will explain further essential hormonal support in the second half of your cycle. Firstly this helps your uterus prepare for the embryos better. Secondly we know that without any support, some women will bleed too early after an embryo transfer and before the embryo implantation has declared itself in the form of hormonal signals. Hence medication is given after the egg collection or embryo transfer to ensure that premature bleeding does not occur and that you have the best chance of maintaining an embryo implantation.

This support can be given in several ways and clinicians as well as patients can have their preferences:

1. **Progesterone pessaries (Uterogestan or Cyclogest):** These are usually given in the dose of 200 mgms, 6 hrly or four times every 24 hours. Cyclogest 400 mgs is usually given once at night. They can also be used rectally as a suppository.

Advantages: Apart from the inconvenience of frequent vaginal and rectal administration, it is painless and easy to administer.

Disadvantages:

- a. The medication can flow out of the vagina or the rectum and hence not have the full benefit.
- b. The absorption of the hormone from the vaginal skin into your body can also vary between patients.
- c. Some patients may thus experience premature bleeding despite this support.
- d. Occasionally women can develop an allergic reaction to progesterone in the form of urticaria or skin rashes and sometimes the allergy can be severe.

2. **Progesterone Injections (Prontogest):** This is a daily intramuscular injection of progesterone.

Advantages:

- a. For some once daily administration is an advantage.
- b. It also ensures that premature bleeding does not occur. In fact most women would not have had bleeding until we do the pregnancy test 14-16 days after the embryo transfer.
- c. We have an unpublished observation that it provides some protection against the risk of OHSS. This has not been scientifically tested and hence we are conducting a prospective trial.

Disadvantages:

- a. This is a painful injection and causes local discomfort. We advise you to rotate sites of injection in order to ensure that no one site becomes excessively inflamed.
- b. Occasionally women can develop an allergic reaction to progesterone in the form of urticaria or skin rashes and sometimes the allergy can be severe.
- c. When you become pregnant, we continue this support in early pregnancy until placenta is well established in the uterus (normally at 9-10 weeks gestation).

3. **Human Chorionic Gonadotrophin:** This is a very potent hormone injection. One Injection is given on the day of embryo transfer and another is given three days later.

Advantages:

- a. It ensures that premature bleeding does not occur and there is no need for continued support in early pregnancy.
- b. There are only two injections and no other medication is needed during the 2nd half neither of the cycle nor in early pregnancy.
- c. There are no incidences of allergies.

Disadvantages:

- a. When given to all patients, this has been associated with an increased risk of ovarian hyperstimulation (OHSS). NICE recommends that it should not be used.

14.14 The Pregnancy Test

▪ **When to come?**

You are asked to come to TLCRM, 14 to 16 days after the embryo transfer for a pregnancy test, irrespective of whether you have menstruated or not. This involves you bringing an early morning urine sample. If this test is positive then we will ask you to return to us 2 or 3 weeks later for an ultrasound scan.

We obviously hope that every patient will become pregnant but in reality 55-70% patients depending on your age group do not conceive. You will understandably feel a sense of grief in the event of failure. Please do not hesitate to ask for help in the form of counselling support with our psychologists. We will also arrange a review consultation after the completion of each treatment cycle. At this time we will have an opportunity to discuss those factors that may have become apparent during your treatment and consequently may require modification in further attempts.

14.15 Risks

There are no treatments that are completely free of risk. In an IVF cycle there are the following risks:

▪ **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 & complications up to 12 weeks of gestation have been noted.

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%.

▪ **Miscarriage:**

The risk of miscarriage after a positive pregnancy test alone is approximately 10-20%. This is no different to that after a normal conception. Once the pregnancy sac has been seen and the fetal heart action identified then the risk of miscarriage is substantially less. The risk of a congenital or genetic abnormality in babies born after IVF has not been higher than that in spontaneously conceived pregnancies. Your personal risk is more likely to relate to your age, your family history and whether or not you have a multiple pregnancy. Please see the section on multiple pregnancies for further detail.

▪ **Risk of an ectopic pregnancy:**

The embryos are not ready to implant at the time of their replacement. At that time they are in a very small volume of fluid which we expect to spread like a thin film on the surface of the lining of your womb. The embryo may sit in a fold of the lining of the uterus until it reaches the stage of implantation. The risk of embryo floating away in the direction of the fallopian tube exists in all patients. In normal circumstances we expect that the fine hair in the tube that beat in the direction of the womb will prevent such a migration. However in some cases this may not happen and the embryo enters the tube. Unable to return to implant in the uterus and especially in women with damaged tubes, it may attach itself to the tube and thus a tubal pregnancy occurs. If left undiagnosed, the tube may rupture and internal bleeding may take place. We endeavour to make an early diagnosis by performing an ultrasound scan at 7 weeks of pregnancy (3 weeks after your pregnancy test).

Notes:

1. It is therefore important to attend for the pregnancy test even if you have bled and for the scan after a positive test. If a pregnancy sac is not seen on scan, a blood test is taken to measure the pregnancy hormone (hCG) level in

your blood. You may be asked to attend for more tests after a few days interval. If this level is rising or static then we may perform a laparoscopy.

2. If you are unlucky and have a tubal pregnancy then you will require the removal of the tube. We may also counsel you regarding the future of your remaining tube in case it is already known to be irreparably damaged or is found to be such at surgery. We advise you to consider removal of both tubes in those circumstances in order to avoid a recurrence of this complication in future. This is an important decision as it is sterilising and no steps are taken without your written consent and complete agreement.
3. For the operation you will be admitted to St James's to prevent an untoward occurrence whilst travelling. The risk of an ectopic pregnancy is approximately 3-4%.
4. Occasionally you can have a combined intrauterine and an ectopic pregnancy (*heterotopic pregnancy*). These are more difficult to diagnose. If present, then often but not always, the tubal pregnancy can be removed without harming the uterine pregnancy.
5. We perform a risk assessment for this complication too in our pre-assessments. If you are already known to have damaged tubes you may choose to have removal of the tubes (*salpingectomy operation*) performed before the treatment cycle in order to minimise the risk of this complication. This is a sterilising procedure and future pregnancies will only be possible after IVF. Therefore you have to be completely at terms with your infertility if you undertake this procedure. It is performed in most cases laparoscopically (*key hole method*) and you do not need prolonged recovery or delay to treatment afterwards.

▪ **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 both partners 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.

▪ **Risk of a multiple pregnancy:**

Most assisted conception procedures carry with them the risk of a multiple pregnancy. Please read the section on the number of embryos to be transferred and multiple pregnancies where this risk has been discussed in greater detail.

▪ **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 that 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.

14.16 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. It is a significant invasion into natural processes where a natural fertilisation and pregnancy would not have occurred, its long term risks are not known. It is therefore appropriate that you consider it an experimental procedure.

The risks described in this section reflect the current state of our knowledge and the guidance provided by the Human Fertilisation and Embryology Authority. We regularly update this section, as and when new information becomes available. Please read carefully and ask for clarification as and whenever necessary. We will be pleased to discuss this and any other issue with you in detail. Also note that this section deals with everything that we know to date and the contents of these sections will be subject to change and variation, as more information becomes available.

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:

A. Possible inheritance of genetic chromosomal abnormalities:

- **Increased incidence of Cystic Fibrosis (CF) mutation status in azoospermic men**

Some men who have no sperm in their semen (approximately 5-10% of men with azoospermia) are found to have Congenital Absence of Vas Deferens (CBAVD). In this condition, the tubes that carry sperm from the testis to the penis are missing. Two thirds of men with CBAVD are also carriers of certain cystic fibrosis mutations. Men with CBAVD and their partners may therefore wish to undergo genetic testing before proceeding with ICSI. This is not compulsory as long as you are aware of and understand the risks of not taking this genetic test. It has also been recommended that genetic testing should be offered to other azoospermic men. Such a screening test may have to be performed locally via your GP.

Genetic counselling is strongly recommended for all azoospermic men with CBAVD along with their partners. This will help both for an improved understanding of your condition and also to become aware of implications of genetic testing.

- **Male fertility relating to Y chromosome (sex chromosome) defects**

A small proportion of sub-fertile men have parts of the Y chromosome missing (deleted). Certain genes on the Y chromosome have been shown to be involved in the production of sperm, and deletions of these genes may be responsible for some men having few or no sperm in their semen. Consequently, using sperm with such deletions to create an embryo may result in the same type of sub-fertility being passed from father to his son. It is recommended that sub-fertile males and their partners contemplating ICSI treatment should be aware of this possibility.

- **Sex chromosomal anomalies**

Abnormal numbers of structures of chromosomes, particularly the sex chromosomes (X and Y), may be associated with infertility in both men and women, and babies born from ICSI treatment may have a slightly increased risk of inheriting these abnormalities. Studies have found that up to 3.3% of fathers of ICSI babies have abnormal chromosomes. It is estimated that up to 2.4 % of the wider population have a chromosomal abnormality. Therefore, where ICSI is used in the treatment of men with severe azoospermia or oligospermia there is an increased risk of sex chromosome disorders. Sex chromosome abnormalities such as 47XXX: 47 XXY and 47YY occur at a relatively high frequency in the neonatal populations - about 1 in 700 birth for each of the aforementioned abnormalities.

- **Novel chromosomal abnormalities**

The complexity of the process of egg and sperm production means that even if an individual possesses a normal number of chromosomes, their gametes could potentially have an abnormal number. It is not possible to detect beforehand which eggs or sperm have chromosomal abnormalities, and gametes that might not have been able to participate in natural fertilisation could therefore be used in ICSI. Babies born after ICSI have been reported to have new chromosomal abnormalities in 3% of cases. The rate in general population is around 0.6%.

B. Possible developmental and Birth defects

- **Birth defects**

There is not as yet any clear evidence whether ICSI results in higher rates of birth defects. The number of babies reported to have major birth defects, such as cleft palate, is between 1-5% in both the general population and in babies born following ICSI. Studies suggest that minor abnormalities occur in up to 20% of ICSI babies, compared to up to 15% of the general population. More studies are needed in order to gain further insight into these possible effects.

- **Developmental delays**

One recent study that followed up a relatively small number of children has given an indication of possible delays in mental development at one year in some children born following ICSI. Other studies have not shown this link and further research is needed in this area.

C. Possible risks during pregnancy:

- **Miscarriage**

With ICSI, it is possible that abnormal gametes, which would not usually be able to produce a viable embryo could be used, increasing the chance of an abnormal embryo being formed. Many abnormal embryos will not implant into the womb and do not grow, but some might, leading to a possible higher risk of miscarriage. It has been reported that the risk of miscarriage increases in proportion to the severity of male infertility.

14.17 Scans and visits to the unit

We try to minimise your visits to the unit. On an average you may have 9-10 visits to the unit over a period of 2-3 months. You are almost never hospitalised except when you have had one of the problems listed above.

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 in either of the partners.
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.

17. USEFUL ADDRESSES:

In addition to the counselling facilities that exist at The Leeds Centre for Reproductive Medicine you may wish to contact any of the following for information, help and support.

Androgen Insensitivity Support Group
2 Shirburn Avenue, Mansfield NG18 2BY
01623 661749

British Agency for Adoption & Fostering
Skyline House, 200 Union Street, London SE1 01Y
0207 593 2000

British Fertility Society (National Society for Healthcare Professionals)
16 The Courtyard, Woodlands, Bradley Stoke, Bristol BS32 4NQ
01454 642211
www.bfs.co.uk

British Infertility Counselling Association (BICA)
96 Divisional Street, Sheffield, S1 4GE
01342 843880
www.bica.net

Childlink Adoption Society
10 Lion Yard, Tremdoc Road, London SW4 7NQ
0207 498 1933

Cot Death Foundation
14 Halkin Street, London SW1X 7DP
0207 235 1721

COTS (Childlessness Overcome by Surrogacy)
Loandhu Cottage, Gruids, Lairg, Sutherland, Scotland IV27 4EF
01549 402401

Daisy Network (premature menopause support group)
PO Box 293, High Wycombe, Bucks, HP15 7SH

Department of Health Social Care Group
Wellington House, 133-155 Waterloo Road, London SE1 8UG
0207 972 4347/4084

Department of Health & Social Services

Child Care Branch, Dundonald House, Upper Newtownards Road, Belfast B24 3SF
01232 520000

Donor Conception Network

PO Box 265, Sheffield S3 7YX
0208 245 4369
www.dcnetwork.org

Human Fertilisation & Embryology Authority (HFEA)

Finsbury Tower, 103-105 Bunhill Row, EC1Y 8HF, London
0207 291 8200
www.hfea.gov.uk

Infertility Network UK

National support organisation with newsletters & helpline.
Charter House, 43 St Leonards Road, Bexhill on Sea, E Sussex TN40 NJA
01424 732361
www.infertility.uk

International Social Service of the UK

Cranmer House, 39 Brixton Road, London SW9 6DD
0207 735 8941

Miscarriage Association

c/o Clayton Hospital, Northgate, Wakefield WF1 3JS
01924 200700

Multiple Births Foundation

Hamm House, Hammersmith Hospital, Du Cane Road, London W12 0HS
020 8383 3519

National Endometriosis Society

50 Westminster Palace Gardens, Artillery Row, London SW1P 1RL
020 7222 2776

Turner Syndrome Support Society

1/8 Irving Court, Hardgate, Clydebank G81 6BA
01389 380385
turner.syndrome@tss.org.uk
www.tss.org.uk

Twins & Multiple Births Association (TAMBA)

PO Box 30, Little Sutton, South Wirral L66 1TH
01732 868000

Verity (National PCOS Support Group)

Graystone Centre, 28 Charles Square, London N1 6HT
veritymembs@aol.com
enquiries@verity-pcos.org.uk
www.verity-pcos.org.uk

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

We wish you good luck.

Mrs Vinay Sharma