



The Leeds Centre for
Reproductive Medicine



Isle of Man
Government

FROZEN EMBRYO TRANSFER CYCLE

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

Mrs M Moroney
Consultant Obstetrician & Gynaecologist
Nobles Hospital
Douglas
Isle of Man IM4 4RJ

Telephone:

- ❖ Monday to Friday (8.30am to 5.00pm):
 - Secretary 650330

- ❖ **EMERGENCY PROCEDURE**

If you have an urgent enquiry during normal office hours contact Mrs Moroney's secretary using the telephone number above. Out of hours in an emergency contact the gynaecological SHO on-call at Noble's Hospital via the hospital switchboard **650000**. Alternatively, contact the St James's Hospital switchboard **0113 243 3144** and ask for the duty IVF member of staff who can then be contacted and will return your call. There is someone available 24 hours a day who will be able to help in an emergency.

- ❖ Leeds Centre of Reproductive Medicine
 - Reception 0113 206 3111
 - Clinical enquires 0113 206 3102
 - Embryology enquiries 0113 206 3103

Website address: www.leedsreproductivemedicine.co.uk

Transfer of Frozen Embryos

What is the purpose of freezing spare embryos?

1. Transfer of frozen thawed embryos from your previous IVF cycle can give you another chance of achieving a pregnancy without undergoing a full IVF cycle.
2. Embryos from an IVF cycle (where a transfer is medically not appropriate) can also be frozen so that the clinical problems can be rectified before any embryos are transferred. For example:
 - a. Patients at risk of severe Ovarian Hyperstimulation Syndrome(OHSS).
 - b. Inability to transfer embryos because of obstruction or another abnormality in the cervix (neck of the womb)
 - c. Patients undergoing this treatment prior to treatment for cancer so that they can try to preserve some fertility in advance of treatment

How is it done?

The embryos are transferred back to the womb after suitable preparation of the lining of the womb. As the embryos already exist, this cycle does not involve stimulation of your ovaries or an egg collection.

Freezing & Thaw of Embryos

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



Embryo freezing:

1. 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 the embryos are deemed suitable. However, approximately 60% of embryos judged suitable for freezing will survive the freeze/thaw process 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 when your embryos are thawed you have embryos to transfer.
2. Embryo freezing can only be performed with your prior written consent. The legal storage limit for embryos is a maximum of 10 years from the date of freezing and this can be further extended if in the interim the female partner has reached the peri-menopausal years. You will be advised on The Centre's current policy regarding the advised duration of embryo storage and how extension and cost of storage may affect you.
3. The embryos are your property and responsibility. You also have to decide the fate of the embryos in the event of death or mental incapacity. 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:

1. With your written consent, thawed embryos can be maintained in culture until they stop growing or develop into the blastocysts (usually 2-3 days after thawing).
2. Generally embryos with little chance of development to a pregnancy will stop growth within these days.
3. Embryos that have showed growth after thaw are believed to have a higher developmental potential.
4. After thaw and transfer, we are not legally permitted to keep embryos in culture for observation alone unless there is a clear instruction from you to preserve them when appropriate.

Embryo donation:

If you do not wish to under go this treatment:

1. You can consider donating your frozen 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.
2. 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.

Long term storage:

This section is primarily for the storage of 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.

Posthumous use of gametes and embryos

Biologically only 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 provide written information about the implications of posthumous use of gametes and advise you to have a discussion with the counsellor if you have further issues.

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.

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 will have 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.

Embryo research: see below for further detail.

Humanely discard the spare embryos:

1. Only good quality embryos can be successfully frozen, donated to another couple or used for research.
2. If you do not wish prolonged culture with a view to freezing the embryos that continue growth, then you must instruct us to humanely discard your spare embryos as soon as embryo transfer has been performed.

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

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.

Please refer to your IVF-ICSI booklet for further detail.

What are the important issues regarding stored embryos?

Legal issues:

- As explained above, HFEA regulations permit that the embryo storage for a maximum of ten years.
- An extension to this storage period may be available in certain circumstances.
- Please view your embryos as your responsibility and us as merely their caretakers. The trust contacts you every year for your instructions with regards to these embryos. You may choose to maintain them in storage, discard them, have them replaced to yourself or donate them to other couples. The trust also charges you a fee for their continued storage on an annual basis.
- It is extremely important that you keep us fully aware of any change in address.
- Failure to remain in contact could lead us to discard the embryos if your consent with the trust for an agreed period of storage has expired.
- The embryos cannot be maintained in storage or donated without the full written consent and agreement of both partners.
- Similarly the embryos cannot be replaced or donated to another couple without the written consent of both partners.
- Donating embryos to others would require both partners to undergo a screening process, similar to that for sperm and egg donors.

Planning a Frozen embryo treatment cycle?

Even though survival of embryos upon thaw and their subsequent developmental potential remains uncertain, it is still important to agree 'a plan' with respect to the stored embryos. This is not quite as important when there are only a few embryos stored (<3) and multiple embryo transfer would be acceptable. However it is very important when a good number of embryos have been stored, a pregnancy has been achieved from the cohort already and it is desirable that the risk of multiple pregnancies is kept at a minimum.

- We therefore need to meet for a follow-up when your history can be updated and new developments if any or their absence is recorded.
- At this time you will explore your wishes regarding your future treatment with the Consultant considering how effective you want your next cycle to be, how many treatments you envisage from the frozen embryos and how effectively you wish to avoid a multiple pregnancy.
- On the basis of your personal plans, we would also discuss your options with respect to how many embryos are to be thawed and whether or not they are to be cultured so that surviving embryos are transferred after they have also demonstrated further growth, thus improving the selection of the most competent embryo.
- Such decisions are obviously based on results of thaw and subsequent development going according to that which is expected. There may be modifications necessary if thaw and survival does not go to plan.
- We will discuss the outcome of thaw, their growth and the fate of remaining embryos in our care with you on the day of transfer. Their continued preservation will incur charges from the trust on an annual basis as before.
- In this way with our guidance you will have the choice of deciding how many embryos should be thawed and transferred at any one time.

Other points of note:

- The frozen embryo transfer cycle can be conducted any time after your initial treatment.
- In our programme, the embryos are usually stored individually.
- Approximately two thirds of the frozen embryos (60-70%) survive the process of thawing.
- Not all cells in an embryo may survive.

- Approximately 3-5% of all cycles in our programme would not have any surviving embryos after thaw. Unfortunately you cannot know about the embryo survival until hours before the embryo transfer is scheduled.
- Frozen thawed embryos have a lower developmental potential than fresh embryos and hence the success rates may be somewhat lower. Please ask staff for up to date information.
- For a good chance, it is important to have several embryos available for freezing and an ability to select the best graded embryos after thaw. Where ever possible we culture embryos after thawing for 1-2 days in order to assess their continued ability to grow and develop after thaw.
- Although frozen thawed embryos have been successfully frozen thawed with a pregnancy, this is not common practice and it would be reasonable to expect a further lowering of the likelihood of a pregnancy with such embryos.
- After thaw, embryos are selected for transfer on the basis of their survival, the appearance and number of surviving cells in the embryo.
- It has been known for couples to achieve multiple pregnancies with the same batch of embryos.
- Transfer of multiple embryos after thaw can lead to a multiple pregnancy.
- There is no evidence that embryos are actually affected by the length of time they are frozen.
- We understand that any damage caused occurs either during the course of cooling embryos to freezing point or when warming them back to body temperature.

Pre-treatment assessments

▪ **Rubella status and Cervical Smear**

It is important to confirm before treatment that you are immune to rubella, with a blood test, and that your last cervical smear was performed within the previous 3 years and was normal.

▪ **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 assess 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 will be uneventful. If difficulties are encountered we may need to take specific actions e.g. perform cervical dilatation under a general anaesthetic prior to commencing a treatment cycle.

The 'Natural' versus 'Stimulated' Frozen Embryo Transfer' cycle

Naturally, the ovary continuously recruits and develops the eggs. The eggs develop within little sacs that are called '*follicles*'. The cells contained in these *follicles* produce oestrogens with which the lining of the womb (*the 'endometrium'*) develops in order to receive the embryos. After ovulation the *follicle* becomes *the 'corpus luteum'* which then produces the oestrogen as well as the progesterone in order to bring in the second phase of development in the lining of the uterus and those changes that are associated with endometrial receptiveness for the embryo to implant.

In a frozen embryo transfer cycle we can rely upon your natural cycle to do the right thing or modify your cycle with medication so that the necessary changes are ensured as far as is possible. Evidently the success rates are higher when we ensure that the changes are optimally occurring with medication. In a natural cycle, assessing the exact timing for thaw and transfer is much more complex and the success rates are lower because in a natural cycle the lining of the womb may not be prepared correctly.

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 pregnancies 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.

Treatment Procedure

A Typical Cycle:

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

a. First clinic appointment: A full discussion of the relevant personal and family history will take place with Mrs Moroney at Nobles Hospital. Any necessary screening tests will be arranged and if any counselling issues arise then arrangements can be made for you to see a specialist counsellor at the Leeds Unit. A review of the number of embryos stored along with the stage of development at which they were stored will be verified. The treatment cycle will then be outlined and you will be given this information leaflet to take home. A month for starting treatment will be given to you and you will be asked to contact Mrs Moroney's secretary on 650330 when your period starts in that month.

b. Follow up clinic visit: When you telephone to start your treatment cycle you will be given an appointment to come and see Mrs Moroney on or around day 21. At that visit any outstanding test results will be reviewed, you will have a vaginal ultrasound scan to visualise the pelvic organs, the treatment cycle will be planned and you will be asked to sign the relevant consent forms. You will then be given a prescription for the necessary medications.

c. Suppression of your natural hormones (down-regulation): We do this by starting drugs on the 1st or the 21st day of the menstrual cycle using a single depot preparation (Gonapeptyl) or occasionally a daily injection (Buserelin). This is prior to starting oestrogen tablets and will be continued until instructed to stop. Ovarian suppression usually occurs with 3 weeks of starting down-regulation and you will be given an appointment to come for your next scan at that time

d. Down-regulation visit: A vaginal scan will be performed to check that the lining of the womb has thinned and confirm that you are ready to start endometrial preparation.

e. Endometrial Stimulation.

In order to develop your lining of the womb we start you on the oestrogen tablets at the correct time. This treatment can last for approximately 9-14 days and until the endometrium is sufficiently developed. To check that development is occurring normally you will have a further vaginal scan to check the thickness after you have been on the oestrogen tablets for about a week.

f. Reducing the risk of infection: After 8 days of oestrogen tablets you will be asked to start using an antibiotic vaginal cream (Dalacin) for the next 5 nights. This cream is inserted vaginally using a special applicator and will reduce the bacteria in the vagina to reduce any risks of introducing infection into the womb at the time of embryo transfer.

g. Endometrial Maturation: A few days prior to your embryo transfer you will start the progesterone. This is usually in the form of pessaries but occasionally injections are used. You will remain on both oestrogen and progesterone until the pregnancy test which can be up to 20 days later.

g. Thaw and planning the day of transfer. You will receive a call from the embryologist in Leeds on the day of thaw to inform you of the results and based on this we will plan the day/time of transfer.

h. Embryo Transfer. The embryos are replaced in the womb.

i. Pregnancy test. The date for this will have been arranged by Mrs Moroney. When you return to the Isle of Man after your transfer you should phone the Blood Clinic on 650415 and book an appointment to have the test. Arrangements will have been made for you to receive the results either by you phoning Mrs Moroney's secretary or her phoning you on the afternoon of the test. If the test is positive you will be given an appointment to see Mrs Moroney after 2 weeks to have your first pregnancy scan. You **must** remain on both your oestrogen and progesterone. A further scan will be performed 2 weeks later. Once pregnant these medications are continued until we know that the placental function is fully established which is usually at 9-10 weeks gestation. After this we can gradually withdraw all hormonal support and allow the pregnancy to progress naturally.

j. Follow-up consultation. This is arranged after the cycle has been completed if you have not conceived.

Downregulation or the Suppression phase

In women with a menstrual cycle undergoing the standard treatment, the pituitary gland may interfere and affect the development of the lining of the womb and as this can lead to a lessening of the success rate, we choose to inactivate this gland before stimulating your womb.

- **Baseline scan**

A vaginal scan is performed before starting any medication unless you have had one within the previous three 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 2 – 3 weeks after starting ovarian suppression.

- **Drugs used**

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

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

- **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 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 Buserelin treatment is continued in the stimulation phase. We will specifically advise in writing when to discontinue. Those on Gonapeptyl normally do not have to take additional medication during the stimulation phase.

Stimulation phase

There is some variation in how well the lining of the womb develops with some people being more responsive than others. Our aim is to give you medication in sufficient dosage so that your treatment has the greatest likelihood of being successful. We can assess the optimum dose many times from the knowledge of your past treatment even if in a different form before.

- **What does it involve?**

The hormone oestrogen stimulates the lining of the womb to grow. It is given in the form of oestradiol valerate tablets and it enters the blood in its natural oestrogen form after it is absorbed into the liver from the gut.

Occasionally we use oestrogen skin patches which allow the skin directly to absorb the natural oestrogen into your blood stream from the patch. We may make changes when needed and sometimes even use the combination of the two.

There is no difference in the drug that is eventually delivered to the womb via the blood stream. However there is a difference in the preparation and how it reaches there. Some absorb the drug better from the gut and others from the skin. There are individual variations also in how the womb reacts to the same dose of medication. There is little difference in terms of success rate provided the womb has responded well. We often choose them in combination or separately to suit.

- **How to take medication?**

Oral tablets can be taken in one or two daily doses. Skin patches are changed every three days. The medication can be given in the following regimens:

- **Fixed and continuously given moderately high dose** to ensure timely and adequate endometrial development. This regime makes it easy for you and the team to remember your drug dosage.
- **Step wise escalation** in the dose of oestrogen can also be performed to try and mimic the natural rise in oestrogen and to promote endometrial growth when the response is suboptimal.
- There are no differences in success rates with either of the two methods and regimen chosen can vary according to individual preferences.

- **Side effects**

- Oestrogen can give the feeling of nausea in some women. Other than that there are no notable side effects because the hormone is in fact one that your ovary produces naturally and your system is used to it.
- Theoretically oestrogen when passing through the liver can affect the way blood is helped to clot. This is usually an effect only in susceptible individuals and only after prolonged use e.g. when given as HRT and not when they are used for short periods such as in treatment even though in higher doses.
- Skin patches can give local reaction to the adhesive. We can use alternative patches as the reaction is to the adhesive and not to the drug.

- **Undesirable effects**

Lack of adequate endometrial proliferation is undesirable but not always preventable.

- **How effective are they?**

We have used both the tablets and the patches although the former are used most common. All regimens are also used freely to suit individual circumstances and clinical preferences.

Progesterone support

When your endometrium has reached an appropriate thickness, as assessed by scan, you will start progesterone support.

What does it involve?

The hormone progesterone after the initial growth of the lining of the womb brings in the second phase of development. It is given in the form of progesterone pessaries or injections. The pessaries can also be used in your back passage as a rectal suppository.

The pessaries once inserted in the vagina/rectum will dissolve and from there the lining of the vagina/bowel will absorb it and transfer it to the uterus through local and systemic blood supply.

The progesterone injections involve inserting the hormone into the muscle from where it is absorbed into the blood stream and transferred to the womb for necessary action. Blood levels of this hormone are much higher after injections than after inserting the pessary but it is thought that some progesterone gets to the womb from local transfer/ exchange mechanism.

My choices?

There is no difference in the drug that is eventually delivered to the womb. However there is a difference in the preparation and how it reaches there. Some absorb the drug better from the vagina or the bowel than others. There are individual variations also in how the womb reacts to the same dose of medication.

How to take medication?

Pessaries can be inserted in prescribed doses digitally into the vagina or the back passage.

Injections are given once a day into the gluteus muscle (buttock) or in the Quadriceps muscle (thigh). We ask you to rotate the injection site as repetitive injection at one site can cause pain and local reaction.

The oestrogen tablets and/or oestrogen skin patches continue during this second phase also as prescribed. They could continue as previously in the following regimens:

- Fixed and continuously given moderately high dose to ensure timely and adequate endometrial development.
- Step wise escalation to try and mimic the natural rise in oestrogen
- Step wise rise to promote endometrial growth when the response is suboptimal.

Side effects

Progesterone (as in the second half of the natural menstrual cycle) can cause abdominal bloating, breast tenderness, feeling of lethargy, tiredness and even a change in temperament or mood. These problems do not necessarily occur and stress of treatment is also an important factor to remember.

Undesirable effects

Early bleeding with pessaries and local pain at the site of injections are undesirable effects.

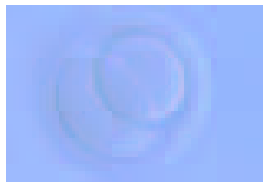
How effective are they?

There is evidence that injections achieve better results than the pessaries in fresh IVF-ICSI cycles. Whether this is also true for egg donation and frozen embryo transfer cycles is not known. We are involved in research projects that aim to assess these very issues at present and therefore cannot give conclusive answers.

We have used both the pessaries and the injections for many years and all preparations are used freely to suit individual circumstances and clinical preferences.

Embryo transfer

As explained above, the fertilised eggs are called 'embryos'. These are examined after thaw to assess the number of surviving cells and their appearance. This assessment allows us to decide the optimum day for transfer and this could be on the same day or after 1-3 days of further in-vitro culture. This decision is based on the number of thawed and surviving embryos, their likelihood, as assessed, by us to continue development to assist in selection. If there are only a few surviving embryos we may be able to make the choice on the same day. If there are several surviving embryos we may advise culture so that we improve our selection of the embryo for transfer and also minimise the risk of multiple pregnancy by transferring fewer but selected embryos only.



Day 2: 2 cell embryo



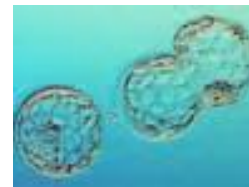
Day 2: 4 cell embryo



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 when embryos were frozen, cause of your 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 as described above 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

Not all embryos will continue their growth after thaw even if they appear to have survived the process initially. When in culture, we check the embryos every morning before we call you for an embryo transfer. If there is no growth after thaw the success rate is very much reduced but we will discuss whether or not to transfer the embryos in you in any case. 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 which is good.
2. The outer sheath of the embryo transfer catheter is inserted first in order to only remove the embryos from their environment when all at your end is 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.

In this cycle your symptoms of premenstrual syndrome are likely to be exaggerated because of higher than normal 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.

- **The Pregnancy Test**

You will be asked to have a blood pregnancy test 12 to 14 days after the embryo transfer, irrespective of whether you have menstruated or not.

You should attend the Blood Clinic at either Nobles Hospital or Ramsey Cottage Hospital at approximately 8.45 am. If you plan to attend the clinic at Nobles then please book an appointment time by telephoning them on 650415.

The result will be available a 2 pm and:

- a. you should contact Mrs Moroney's secretary on 650330
- b. Mrs Moroney's secretary will contact you

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 if you require. 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.

Risks in a Frozen Embryo Transfer cycle:

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

- **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 above..

- **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.

- **Risk of equipment failure:**

The Leeds Teaching Hospitals 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.

Your patient support group

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

USEFUL ADDRESSES:

In addition to the counselling facilities that exist at St James's you may wish to contact any of the following for information, help and support.

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

WOMEN'S HEALTH

A resource and information centre
 52, Featherstone street, London EC1Y 8RT
 Tel: 0207 251 6580
 Health enquiry line: Mon-Fri 9.30 am -1.30pm
 E mail: Health@womenshealthlondon.org.uk
 Website: www.womenshealthlondon.org.uk

NATIONAL ENDOMETRIOSIS SOCIETY

50, Westminster Palace Gardens
1-7 Artillery Row, London SW1P 1RL
Helpline 0808 808 2227
Website: www.endo.org.uk
www.womens-health.co.uk/endo1.htm

PCOS

Websites of interest
www.womens-health.co.uk/pcos.htm
www.pcos-support.org/what.htm
www.verity-pcos.org.uk
www.netdoctor.co.uk/womenshealth/facts/pcos.htm

ISSUE (The National Association of the Childless)

114 Lichfield Street, Walsall WS1 1SZ
Tel 01922 722 888
Fax 01922 640070
E Mail Webmaster@issue.co.uk

CHILD

Charter House, 43, St Leonard's road, Bexhill-on-Sea, East Sussex TN40 1JA
Tel 01424 732361
Fax 01424 731858
E Mail office@child.org.uk
Website www.child.org.uk

FORESIGHT

The Association for Pre-Conceptual Care
The Old Vicarage, Church Lane, Witley, Godalming, Surrey GU8 5PN
Tel: 01483 427 839

THE MISCARRIAGE ASSOCIATION

PO Box 24 Ossett, West Yorkshire WF5 9XG
Tel: 01924 264579

THE DAISY NETWORK

Premature menopause support network
PO Box 183, Rossendale BB4 6WZ

DONOR CONCEPTION NETWORK

PO Box 265, Sheffield S3 7YX
Tel & Fax: 0208 245 4369
E mail: address available to members only
Website: www.Dcnetwork.org.uk

SANDS (Still and Neonatal Death Society)

Leeds contact: Catherine Frieze Tel 0113 240 9021

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