

WHAT TO EXPECT AT THE EXETER FERTILITY CLINIC

an Information Leaflet for patients by Mr. Jonathan West FRCS FRCOG, Consultant Gynaecologist, Royal Devon & Exeter Hospital Fertility Clinic (December 2007)

INTRODUCTION:

This guide is intended to help couples attending the Exeter Fertility Clinic understand the rationale behind the various tests and treatments that they may need to undergo.

It is written very specifically for patients attending this clinic since there are often variations of opinion among specialists about the interpretation of evidence and guidelines as to which investigations and treatments should be prescribed.

HOW COMMON IS INFERTILITY?

It is estimated that perhaps as many as one in ten couples may seek help at some time or another to try for a baby - and that a similar number may experience difficulties and not seek help. In other words although it may seem to couples trying for a baby that they are almost the only people in the world who are having trouble in this way, it is in fact quite a common situation. It's just that other people don't necessarily publicise the fact that they're trying. Even with normal fertility not all babies are conceived at the first month of trying and when there are no underlying problems, only about 50% of fertile couples conceive within 6 months, and after 12 months there may still be 10% of normal fertile couples who have not conceived. There are very few treatments that can improve on this 'natural' rate of conception. In addition there are some factors that influence the 'natural' rate of conception, particularly age. Women's fertility declines significantly from the age of 35 onwards and, for example, the chance of conception per month at the age of 40 is less than half that of women aged between 20 and 30 years. Unfortunately there is also an increased tendency to miscarriage and problems (e.g. high blood pressure) during pregnancy should conception occur. Male fertility also declines from age 45 onwards and pregnancies from men older than 55 may be at higher risk of chromosomal abnormalities.

WHAT FACTORS MAY CAUSE INFERTILITY?

There are six principal recognised causes of subfertility:

- failure to ovulate (produce an egg from the ovary) every month
- problems with egg quality
- problems with the ability of eggs to get from the ovaries into and down the tubes which connect them with the womb
- problems with sperm
- problems with the production of favourable cervical mucus
- problems leading to a failure of fertilised eggs to implant in the womb, - a condition known as 'recurrent early conceptual loss'

THE FIRST CLINIC VISIT:

In view of the above it would be unusual for couples to be referred to the clinic who have been trying for less than two years unless there are already some known factors that may make conception difficult. Clinic staff work as part of a multidisciplinary team and patients may be allocated appointments with either a consultant, another member of medical staff, or specialised nurses who works regularly in the clinic. The allocation depends upon how many patients are attending on the particular clinic day, the nature of the problem (if known), and whether any of the clinic doctors are away. Unfortunately it is not possible to say in advance which doctor or nurse specialist

patients will be seeing, but all efforts are made to ensure a consistent approach to problems.

PRE-PREGNANCY AND PRELIMINARY CHECKS AND ADVICE:

Couples who have been referred for new appointments will usually be sent a 'Preconsultation Pack', which contains:

1. A record sheet of preliminary investigations, which they could take to their general practitioners so that any that he/she could arrange could be put in hand prior to the first clinic appointment. If these basic tests have not already been performed they may be arranged at the time of the first clinic visit.

2. A questionnaire for some general details about themselves. Clinics such as ours, which are licensed by the Human Fertilisation and Embryology Authority (HFEA), are required to consider the welfare of any children born as a result of treatment as well as existing children before undertaking treatment. The questionnaire helps us with this. It includes a question about who it is intended will assume parental responsibility for a child born from treatment and we will normally only offer treatment to couples who are committed to a long-term stable relationship and who intend to be the legal mother and father of a resulting child. For some treatments, e.g. involving the use of donated or stored sperm or embryos it may be assumed that the man who originally consented to treatment or provided his sperm would be considered to have parental responsibility for a child born as a result unless he has informed the clinic about a change in circumstances. In cases where a child born from treatment would have no legal father the onus is on the woman or couple undergoing treatment to provide written assurance to the satisfaction of Clinic staff of arrangements to ensure that the needs of that child for a father would be met. In addition,

- There should be no substantial risk that the child would inherit or contract a serious medical disease (e.g. Hepatitis or AIDS);
- The prospective parents should enjoy sufficiently good health such that the parental needs of a child could be met without serious difficulty;
- Neither prospective parent should be older than 60 years;

We may not be able or prepared to treat couples where there is a background on either side of child abuse or violence. We are required to expect couples to disclose any relevant information e.g. court orders relating to violent conduct or history of serious psychiatric disorder and couples must be prepared (if necessary) to give their consent for inquiries to be made of the police or social services to ensure that this is not the case. In some cases we may request the consent of couples to consult with their General Practitioners in case there are any other factors that may have a bearing on eligibility for treatment.

We operate a system whereby couples very often hold a copy of most of the relevant information from their own records. After the first clinic visit the medical 'consultation' notes and prescription records will usually be added to the pack. Although records may also be made and kept on the Clinic's computers **PLEASE REMEMBER TO BRING ALL OF THESE RECORDS WITH YOU TO EACH HOSPITAL AND GP VISIT** so that we do not have to print out a new set each time. In addition to medical record keeping and administration some of the information may be used for purposes of audit and, if anonymised and subject to official ethical approval, research. Couples are asked to indicate to clinic staff if they would not want

such anonymised data to be used for the latter. Such refusal would not affect treatment in any way.

SCREENING TESTS: These may include tests for immunity to Rubella (German Measles) and Chlamydia (an infection that may be 'silent' and cause damage to the Fallopian tubes). Women are asked to let us know if they have not previously had chicken pox. For some procedures e.g. IVF (test-tube baby treatment) we may also need to test for Hepatitis and HIV infections. The latter tests are routinely offered in any case to all women during pregnancy, most of whom choose to undergo them. If infection is found, advantages of having these tests performed include possible benefit from earlier treatment that could not only help the person tested but also protect an unborn child and sexual partners. Disadvantages of a positive test include a possible negative psychological impact on oneself, family, work and difficulty in obtaining insurance cover. People who are at low risk for these infections and who test negative should not be disadvantaged in any way, including insurance applications. Results and other information are normally communicated to the person concerned directly at a clinic appointment or else addressed to them by post in an envelope marked as confidential. Please note that correspondence may sometimes be misdirected or delivered to the wrong address. If you are concerned about the possibility of post being opened inadvertently by a third party and would like to be contacted in some other way (e.g. confidential e-mail) please let clinic staff know.

Handling and processing specimens from patients who test positive for HIV or Hepatitis requires special facilities and in this event couples may need to be referred to another clinic for certain types of treatment.

SEXUAL INTERCOURSE: Women with regular menstrual cycles ovulate approximately 14 days before the expected date for the start of the next period. Fertility is maximal at this time and during the week leading up to ovulation, when it is best to make love at least every 2-3 days. There is no benefit from avoiding sexual intercourse at other times or 'saving up' for the most fertile time, however, and there is some evidence that the more often the better (within reason).

FOLIC ACID: - Folic acid is a vitamin, which is most commonly found in fresh fruit and vegetables. There is some evidence that taking one 5mg tablet of folic acid per day prior to conception and in early pregnancy may help prevent certain types of abnormality in the baby (e.g. spina bifida). The tablets can be bought over the counter at most chemists.

SMOKING: - Smoking cigarettes during pregnancy is harmful to the developing baby. If you are trying for a baby and smoke, NOW would be a good time to try and give up. There are plenty of ways to help you with this if you need it and your general practitioner should be able to direct you to whichever is most appropriate. We also advise potential fathers not to smoke.

WEIGHT and DIET: - Except where there is a particular food fad or a disease which affects food absorption most diets are adequate in all the known essential nutrients for general health, conception and pregnancy. Being excessively underweight or overweight can, however, adversely affect both conception and the developing baby. The clinic may not be able to provide treatment in cases of extreme over or

underweight because of the risks to both mother and baby should pregnancy occur. Alcohol should be avoided in pregnancy except in small amounts.

TESTS THAT MAY BE ARRANGED TO CHECK ON POSSIBLE FERTILITY PROBLEMS:

Body weight and height:- women whose body weight in Kilograms divided by their height in metres squared (known as the 'Body Mass Index' or 'BMI') lies outside the range 19-30 may not ovulate regularly simply because of being significantly under or over-weight. Sometimes just losing or putting on weight as appropriate may improve the chance of conception. Invasive investigations and/or treatments that may carry a risk of multiple pregnancy (e.g. stimulation of ovulation) may not be recommended or available when the woman's BMI is greater than 35 or less than 19.

Blood tests:- these may be requested to check, for example, on certain hormone levels that could give clues as to whether ovulation is occurring, and if not why not.

Basic Semen Analysis:- for this test the male partner needs to produce a specimen of semen into a special container for analysis. There is a problem with the interpretation of semen analysis, however, since some normally fertile men have quite low counts whilst others with apparently normal counts may nevertheless have reduced fertility. If all other factors check out, however, there is likely to be a reduced chance of conception when the best of two semen specimens contains less than a total of 20 million normal, living and moving sperm (known as the 'total effective count').

Post-coital test (PCT):- Not all clinics perform this test, which provides information about the ability of sperm to reach and survive in the cervical mucus. The woman needs to attend the Fertility Clinic around the middle of her menstrual cycle (usually on either day 12, 13 or 14 of her cycle - counting the first day of menstrual bleeding as day 1) having had sexual intercourse approximately 12 hours before the test (i.e. the night before, if the test is performed in the morning). A small sample of the cervical mucus is then tested (in a very similar way to the performance of a cervical smear test) to see if: a) the mucus is watery, signifying that it is likely that ovulation is occurring, b) (if the mucus is good) whether there are reasonable numbers of sperm present in it; and, c) to make sure that any sperm that are present are swimming normally, or whether the mucus is hostile to them. Interpretation of the test is complex, but a good test is a very good sign, whilst a test, which is not good, may be due to any one of or combination of many factors - both male and female. If an initial PCT gives a poor result it may be repeated after the woman has taken a prescription for oestrogen tablets (50 micrograms of ethinyloestradiol) from days 5 - 15 of her cycle to ensure that the reason for the poor result wasn't just due to performing the test at the wrong time of the cycle.

Ultrasound scan of the ovaries:- this test is usually performed, like the PCT, at the middle of the menstrual cycle. It may be helpful to monitor ovulation, especially where drugs are given to stimulate this. The appointments are arranged by telephoning the clinic during the early part of the woman's menstrual cycle. The test involves the use of a small hand-held ultrasound probe, which is inserted internally through the vagina. It is not necessary to have a full bladder.

Tests of the tubes that connect the womb and the ovaries (Fallopian Tubes):

The definitive standard test for this is called a 'Laparoscopy and Dye test'. Unless there is a good reason to suspect that there may be a problem with tubal damage (previous operation, infections etc.) it is not usually arranged until other factors have been checked out and treated if necessary. The reason for this is that it involves a small

operation, which in turn means being put to sleep. A special telescope is passed through a small incision under the tummy-button to examine the womb, tubes and ovaries directly. Coloured dye is injected through the neck of the womb and, looking down the telescope, it is possible to see if it can pass along and out of the tubes - thereby indicating whether there is a blockage. Alternatives to the laparoscopy and dye test may include simpler outpatient tests that instil fluid through the cervix that may show up on an X-ray or ultrasound scan. This only provides limited information but may sometimes be recommended as part of an overall investigation and treatment programme for pragmatic reasons.

Sometimes the tubes may be open but previous infection or damage may have caused them or the ovaries to have become stuck in a position that makes it difficult for eggs to get from the ovaries and into the tubes. This is a condition called 'adhesions' and can generally only be detected by laparoscopy. The operation also makes it possible to see whether there is a condition called 'endometriosis' present. This consists of small raw patches that may occur on the ovaries, the tubes, the womb, or indeed anywhere in their vicinity. It is quite a common condition and its cause is unknown. Mild endometriosis may be treated by cauterising the patches (down the telescope where possible). Severe forms of endometriosis may cause 'cysts' (sacs filled with chocolate-coloured fluid) on the ovaries, which can interfere with ovulation - and also with the ability of some of the tests to tell whether ovulation is occurring. Severe forms of endometriosis or tubal damage may require open surgery to try to improve matters, and in the most severe cases even that may not be likely to help. In suitable cases operations may be performed by 'keyhole' surgery.

There is also a test called 'hysteroscopy', which can be performed as an operation on its own or in the course of a laparoscopy and dye test. This involves looking inside the womb from below with a miniature telescope for abnormalities that may interfere with conception or predispose to miscarriage. Special equipment may be used to deal with some abnormalities inside the womb or treating certain types of tubal blockage using the hysteroscopy telescope.

WHAT TREATMENTS ARE POSSIBLE FOR THE VARIOUS CONDITIONS?

Treatment to induce ovulation: -

Lack of regular ovulation is usually one of the most treatable problems for women of normal weight, age and hormone levels. In the first instance treatment involves taking a few tablets (usually clomiphene, or 'Clomid') on days 2 to 5 of the menstrual cycle each month. These have the effect of boosting the production by the body of the hormones that stimulate the ovaries to ovulate. There is a small chance (about 1:25) that the treatment may result in twins. Higher multiple pregnancies e.g. triplets or more are possible but very unusual. If the initial dose of tablets fails to produce regular ovulation the dose may need to be increased and sometimes oestrogen tablets to improve the cervical mucus from days 10 to 14 of the cycle and/or an injection around day 14 to ensure that eggs get released may be recommended.

Long-term use of clomiphene (more than one year) may possibly be associated with an increased risk of developing ovarian cancer later in life. Even if this proves to be correct it is not clear whether the clomiphene actually causes the problem or whether the increased risk is likely to be related to other problems related to infertility. Since it is doubtful whether continuing clomiphene treatment beyond one year is likely to be

of much benefit, long-term treatment is not recommended unless there are exceptional circumstances.

When there is a failure to respond to the tablets it may be necessary to switch to treatment by injections of a hormone called 'FSH'. This type of treatment is quite complicated and needs to be monitored very closely to make sure that a balance is achieved between achieving ovulation and overdoing it - a situation called 'superovulation' or 'hyperstimulation'. The chance of a pregnancy being multiple following this treatment is higher, at about 1:5. There is also a small risk, if hyperstimulation occurs, that it may lead to the temporary development of painfully swollen ovaries. In the most severe and rare cases of hyperstimulation it may be necessary to be admitted to hospital because it can lead to a temporary dangerous upset in the salt balance of the body together with an increased risk of thrombosis. Some hormones or drugs used in fertility treatments are derived from human sources or genetically-modified cells. They must pass stringent tests before being licensed for use but the theoretical possibility exists that as yet undiscovered risks from their use may come to light in the future. It is also common to prescribe some licensed medications in ways that differ from their official product license. This may limit the liability of manufacturers in some situations.

Some women are affected by a relatively common condition called '**polycystic ovary syndrome**' (PCOS). This is not a disease as such, but thought to be a hormonal configuration that evolved to help humans adapt to times of food shortage. Women affected by PCOS are less sensitive to a hormone called 'insulin' which, among other effects, regulates body sugar and fat levels. Among the consequences of this are a tendency to put on weight and irregular periods. Sometimes the only effective way to manage the condition is by strict control of weight and diet.

Treatment for poor egg quality

Poor egg quality is difficult to detect except by IVF, when it may be suspected because of the appearance of the eggs under the microscope, poor fertilisation rates with apparently normal sperm, or the development of poor quality embryos. It is usually a feature of increased age. There is at present no proven treatment to improve the quality of eggs, but treatments that stimulate the production of a large number of eggs per treatment cycle may increase the chance that one or more may be of sufficiently good quality to lead to pregnancy. Unfortunately poor egg quality often goes hand in hand with reduced responsiveness to such treatment, and on the other hand if there is a good response it may be especially difficult to avoid the risk of high multiple pregnancy, although this is very unlikely in such situations.

The only other treatment is to undertake IVF using donated eggs.

Treatment for a low sperm count:-

If the sperm count is low it is first necessary to establish whether this is because the testicles are not producing enough normal sperm, or else whether there is a blockage in the tubes leading away from the testicles. Examination of the testicles by the doctor and a hormone blood test can usually distinguish between these situations, but in either case treatment may not be effective in improving the man's natural fertility.

If there is a blockage (the more unusual situation) it may be possible to perform an operation to bypass or correct it. Such blockages may be associated with a genetic problem that could increase the chance of fathering a baby with cystic fibrosis and a

blood test may be recommended to investigate this. If there is no blockage very low sperm counts may be associated with genetic problems that may be passed on to a child (especially a boy) and in some cases blood tests may also be recommended to investigate this.

If the man's body is not already working to produce as many sperm as possible (as determined by a hormone blood test) it may be worth trying various measures. It is only fair to say, however, that there is considerable doubt as to whether any treatment to improve sperm count or quality has yet been found that genuinely improves the chance of conception.

Such measures may include:

- to cut down or abstain from smoking or alcohol, since the sperm counts of some men may be particularly susceptible to either
- keeping the testicles reasonably cool for as much of the time as possible (e.g. loose-fitting underwear)
- tablets (called 'Tamoxifen', 40mg/day) to boost the production of hormones by the body that lead to sperm production
- a moderate degree of vitamin/mineral dietary supplementation - especially Folic acid (5mg/day), vitamins C (1g/day) and E (400mg/day), selenium (225mcg) and zinc (15mg/day)

If after three months of treatment the sperm count has not improved sufficiently to make conception likely, the only other options to consider are 'assisted conception' procedures such as IVF; artificial insemination with anonymous donor sperm (also called AID, or 'donor insemination (DI)'); or adoption. Artificial insemination using the man's own sperm is not likely to be of help unless the problem is quite minor.

Some men produce antibodies to their own sperm. In this case treatment with steroid hormones may help but the treatment carries risks, is controversial and we do not usually undertake it in our clinic.

Treatment for hostile cervical mucus:-

If this is due to an infection antibiotics may be prescribed. If there is high mucus acidity simple treatment with a vaginal douche containing alkaline sodium bicarbonate may be prescribed. Occasionally the woman may produce antibodies against sperm but although specific tests for antisperm antibodies are available, current authoritative opinion is that such tests are of little value. Hostile cervical mucus may be caused by failure to ovulate or of the developing egg to produce satisfactory levels of oestrogen hormone. Treatment may therefore involve the use of tablets or injections to boost ovulation. Alternatively extra oestrogen hormone may be prescribed in the form of tablets from days 10-14 of the menstrual cycle.

If these measures do not work it may be possible to bypass the cervix altogether by a treatment called 'Intra-Uterine Insemination (IUI)'. This is most likely to be effective when combined with the use of injections to stimulate ovulation and to time insemination with egg release. A specially-prepared specimen of sperm is then injected with a fine plastic tube through the cervix and into the uterus. IUI may also be performed without stimulation of ovulation but although the risk of multiple pregnancy may be reduced it is also less likely to succeed. It may, however, be recommended in some circumstances.

IUI treatment is very unlikely to succeed in the presence of even minor damage to the fallopian tubes and will not usually be offered in these circumstances.

Treatment for blocked tubes:-

The decision about what to do when there is tubal damage or adhesions can be a very difficult one since the success of operations to correct such problems is unpredictable, and in some cases operating may make the situation worse. On the other hand certain types of tubal damage (this requires expert individual assessment) may be well worth operating on.

When there is very minor tubal damage or just one tube blocked it may be best to correct all other correctable factors and then wait at least six months before deciding to perform an operation to try to clear adhesions or open the blocked tube.

Moderate damage on both sides, but provided the tubes are not grossly swollen or the adhesions too severe, may be worth trying to correct by surgery from the outset.

Severe damage on both sides with very swollen tubes and/or extensive tough adhesions is virtually impossible to correct successfully and the main hope of conception is from 'in-vitro fertilisation (IVF, or 'test-tube' baby treatment). Indeed it is sometimes even advisable to remove swollen tubes in order to give IVF the best possible chance of success.

Women should be aware that in any case of tubal damage, whether there has been surgery or not, if pregnancy *does* occur there is an increased possibility of the baby implanting in the tube instead of the womb. This is called an '**ectopic pregnancy**' and is a **highly dangerous condition**. If a woman with known tubal damage becomes pregnant she should let her doctor know as soon as possible so that this can be checked out.

Treatment for recurrent early conceptual loss:-

Most miscarriages or early pregnancy losses occur with no identifiable predisposing cause. The 'natural' rate of miscarriage is about 1:25 when a baby's heartbeat has been detected on ultrasound and possibly as high as 1:4 or more if pregnancies lost before the baby has started forming are taken into account.

If three or more miscarriages or early pregnancy losses occur consecutively this situation is known as 'recurrent early conceptual loss' and usually investigated further. Tests may include blood tests for chromosome abnormalities of the man or woman; a check on certain of the woman's hormone and vitamin levels, particularly for polycystic ovary syndrome; tests for a subtle disorder call 'antiphospholipid syndrome (APS)'; and, a check of the woman's womb for internal fibroids or other abnormalities by hysteroscopy (see earlier).

Specific problems found by the above tests may be treated where possible but in most cases no identifiable cause is found and the outlook for future pregnancies is good. Sometimes extra hormone support with injections of one of the natural pregnancy hormones (HCG or progesterone) for the first three months of the pregnancy may be prescribed together with regular monitoring by ultrasound scanning.

Treatment for unexplained infertility:-

If no factors are discovered to explain why conception has not occurred, or of it still fails to occur despite correcting all correctable causes, then the options are:

- just to 'wait and hope', bearing in mind that the longer that time goes by without conception occurring the less likely it becomes
- to pursue adoption
- to try something 'empirical'

Of the treatments, which may be tried empirically, those, which are often considered, are:

- the use of 'fertility drugs' in the woman to induce ovulation
- 'assisted conception', a collective term for IUI, IVF and a number of similar procedures.

N.B. Extra note about Multiple Pregnancy: -

Most treatments for subfertility involve the use of tablets or injections to stimulate ovulation in the woman. These carry an increased risk that should pregnancy occur it may be multiple. When conception has occurred after the use of fertility drugs an early ultrasound scan is advisable in all cases to check for this. If the pregnancy is multiple, especially triplets or more, the possible impact of this on you, your existing family and the developing babies should not be underestimated. Multiple conception carries a higher risk of a difficult pregnancy, miscarriage, premature birth, and possibly handicap. Even if all the babies survive and are healthy there may be difficulties for the parents in providing them with adequate care and attention without themselves becoming exhausted.

Assisted Conception Procedures*:-

IUI and IVF treatments are available to a limited degree on the NHS in Exeter for couples meeting criteria set by their local Primary Care Trusts. Assisted conception procedures may be expensive, stressful both physically and emotionally and, even in the best of circumstances, success rates are only about 1:3-4 per treatment cycle. Couples should always bear in mind (as with all fertility treatments) the possibility that the treatments ultimately may not work and give genuine consideration to the alternative of trying to come to terms with ***not*** pursuing further investigations and treatment and attempting to find happiness and fulfilment through other aspects of their lives.

Support:

A specialised independent counsellor works closely with us. Information about this is available from the clinic's secretary or on our website at www.fertilitypc.com. There are also national patient support and 'self-help' groups.

Feedback and Complaints:

We try to resolve complaints in a constructive way by discussion and correspondence and sometimes learn from them to provide a better service. Formal complaints can be made in writing to Mr. Jonathan West FRCS FRCOG, Consultant Obstetrician and Gynaecologist or where NHS treatments are concerned may be made directly to the Royal Devon & Exeter Hospital's Complaints Office. Positive feedback is also always welcome, including contact from couples for whom treatment has been successful.