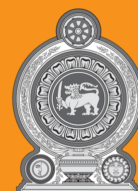
SUBFERTILITY

Manual for the Primary Health Care Provider



SUBFERTILITY

MANUAL FOR THE PRIMARY HEALTH CARE PROVIDER

FAMILY HEALTH BUREAU
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PREFACE

Subfertility is one of the most distressing problems a couple may encounter. This is further aggravated by the commonly believed myths, which prevent them from obtaining proper treatment. The primary health care provider who is the closest link to the client will be the most appropriate person to guide them with correct management. To perform this task adequately they should have a clear understanding of the subject. Furthermore subfertility is a fast advancing field, which has seen many new developments during the last few decades. Therefore this manual hopes to refresh the knowledge of the reader on important aspects of the problem of subfertility & also provide a glimpse of the new developments. All attempts have been made to provide advice that is appropriate to our health care system.

We would like to thank all members of the task force who participated in the discussions. We like to especially acknowledge the guidance, advise & encouragement provided by Professor H. R. Seneviratne & Dr. K. P. Wickramasuriya throughout the preparation of this manual.

We hope this manual will help the primary health care providers in their efforts to provide relief to the large number of subfertile couples in this country.

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INTRODUCTION

Most couples desire to have children. The inability to do so is an extremely distressing situation. Very rarely can a couple be labeled infertile. (i.e. incapable of having a pregnancy) About 1 in 7 couples however have difficulty in conceiving and therefore can be considered subfertile. The aim of this manual is to help you understand the causes of subfertility and the principles of management.

How do you define subfertility?

In a normal couple the chance of conception depends on the duration of unprotected intercourse (Table 1).

Table 1 - Rate of conception among fertile couples

Duration of unprotected intercourse	*Percentage of conceptions*
3 months	*50*
6 months	*75*
12 months	*90*
24 months	*95*

Even though there are differences of opinion regarding the duration most authorities agree that twelve months of regular (i.e. 2-3 times per week) unprotected intercourse without a pregnancy is sufficient to consider a couple subfertile.

Do you always have to wait for 12 months to commence Investigations?

This is the normally accepted period; if however there are risk factors that indicate the possibility of difficulties in conceiving such as;

- Female age over 35 years
- Irregular menstruation
- History of pelvic infection or surgery
- Abnormal findings on pelvic examination
- History of orchitis (testicular inflammation)
- History of testicular injury or surgery
- Any other concerns,

Investigations may be commenced earlier.

Even if there are no risk factors, if a couple seeks help they are entitled to a patient hearing. This opportunity should be utilized to educate them regarding the need for regular intercourse, the fertile period, the advantage of taking folic acid and being vaccinated against rubella etc.

What is primary and secondary subfertility?

Subfertile clients who have never conceived previously are said to be primarily subfertile. Those who have had a previous conception (live birth, still birth, abortion) are labeled as secondarily subfertile.

What are the common causes of subfertility?

The underlying cause for subfertility may lie in either partner. The causes for primary and secondary subfertility though common differ in their prevalence.

Table 2 - Causes for primary and secondary subfertiltiy

Ca seof s bfertiltiy	*Primary s bfertiltiy %*	*Secondary s bfertiltiy %*
Disorders in male	***25***	***20***
Ov lation disorders	***20***	***15***
T bal obstr ction	***15***	***40***
Endometriosis	***10***	***05***
Ca se nexplained	***30***	***20***

The 3 main requirements (Figures 1,3,6) for a conception are an adequate quantity of quality sperms, a regular release of mature ova and a pathway for these two to meet. It is therefore problems in these three aspects that result in the first three causes of subfertility.

Endometriosis is another common cause for subfertility. It is a condition in which the endometrium is also present outside the uterus and a process similar to what occurs in the endometrium during the menstrual cycle occurs elsewhere.

The patients in whom the first three causes of subfertility have been excluded by investigations and where there is no other apparent cause to explain their infertility are categorized as unexplained infertility. It is important to identify them because even though we do not know the cause they can be offered certain modes of management, which are known to be effective.

PHYSIOLOGY OF REPRODUCTION

What are the events that precede a conception?

SPERMATOGENESIS

Sperms are produced in the testes from primordial germ cells by a process called spermatogenesis, which takes about three months. They then travel via the epididymis and along the vas deferens to come out through the urethra during ejaculation.

Figure 1 - Spermatogenesis

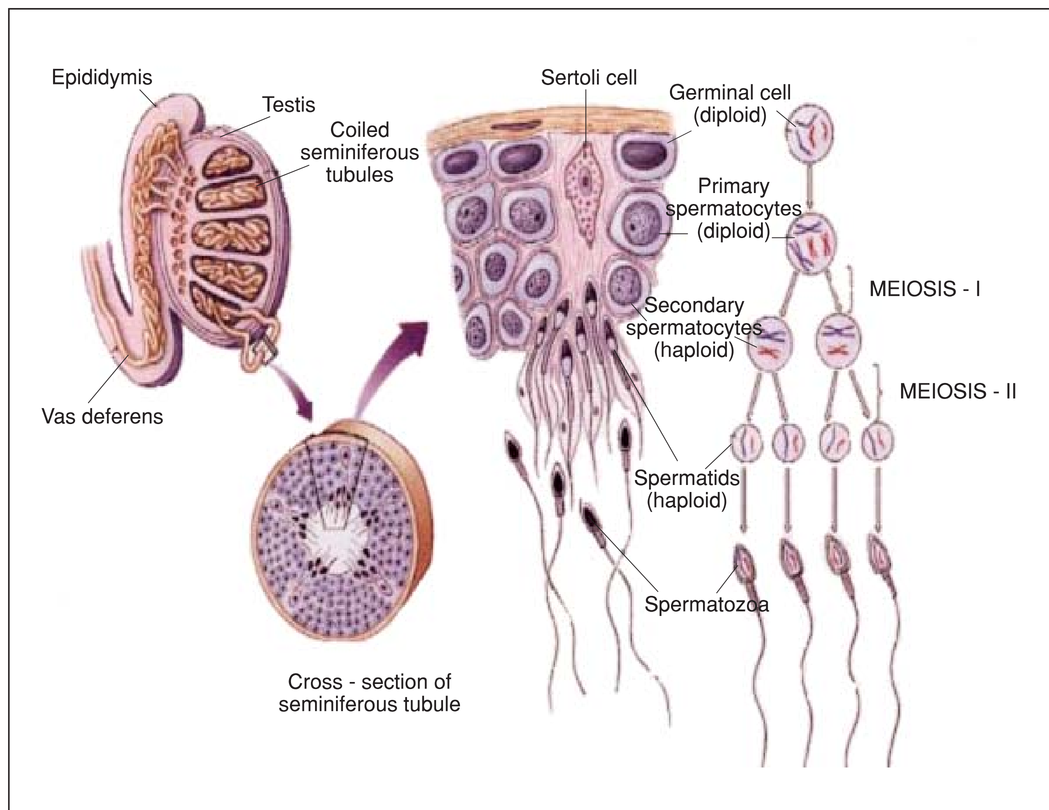
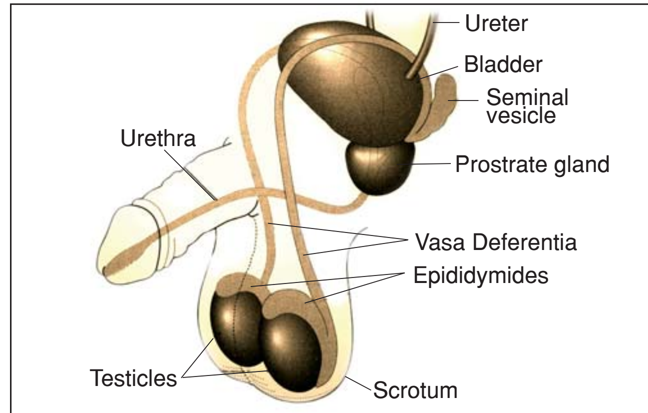


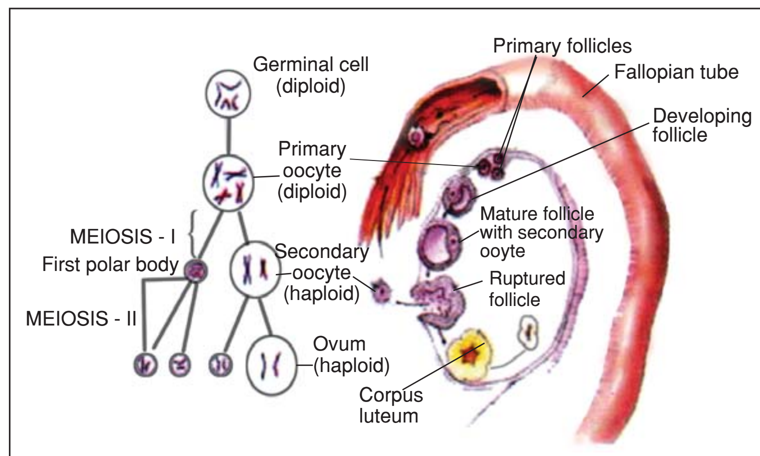
Figure 2 - Sperm Pathway



OVULATION

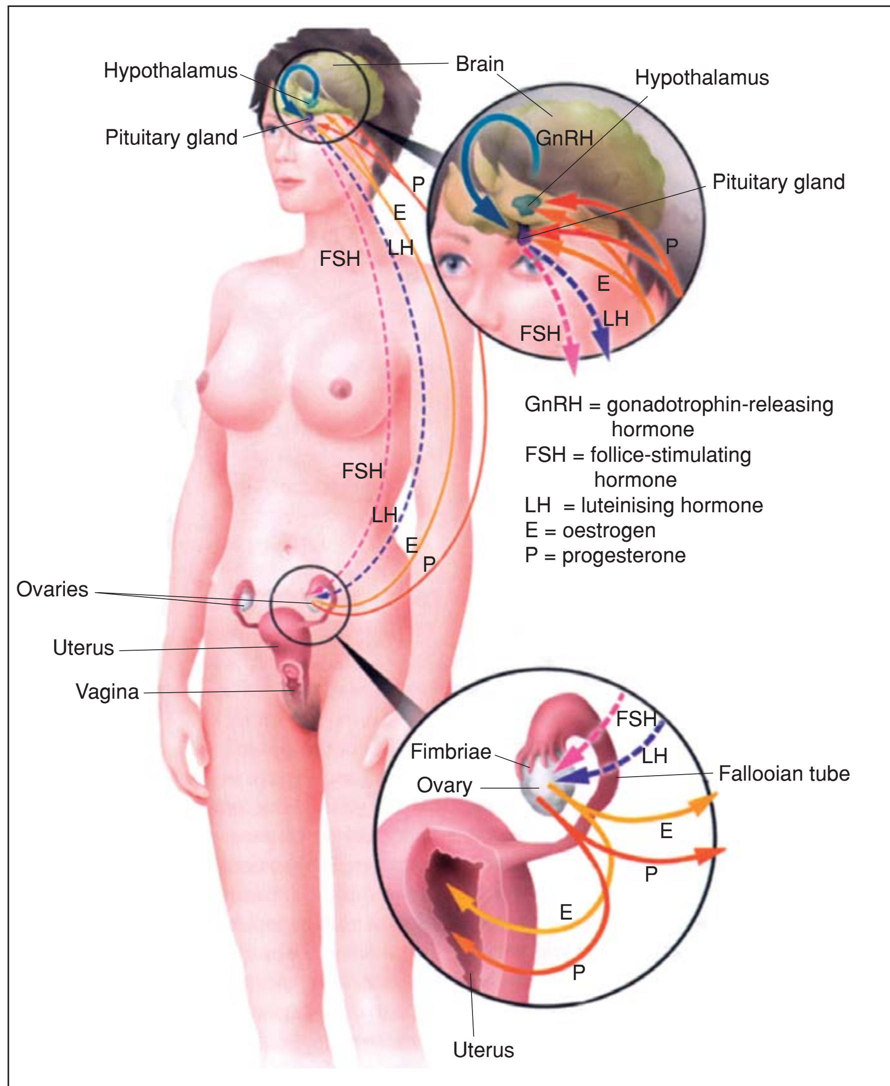
Ova are produced in the ovaries from primordial germ cells. One mature ovum is released in the middle of every menstrual cycle in a normal fertile woman. Figure 3 shows the ovulation process.

Figure 3 - Ovulation



Hormones produced by the hypothalamus and the pituitary gland in the brain controls the menstrual cycle and ovulation.

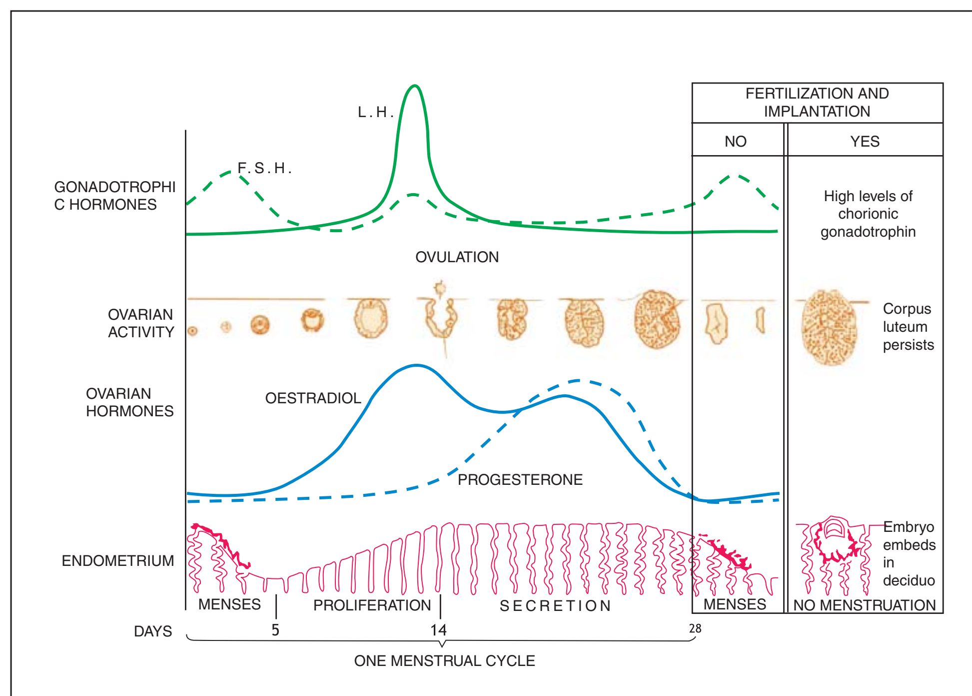
Figure 4 - Hormonal control of Ovulation



At the beginning of the menstrual cycle the hypothalamus produces GnRH, which in turn stimulates the pituitary to secrete FSH. This FSH acts on the ovary and causes about ten graffian follicles to start maturing. After a few days one follicle gets selected as the dominant follicle while the others degenerate. As the follicles grow they produce oestrogen, which acts on the endometrium causing it to grow (proliferative phase) in preparation for a possible pregnancy. Around

day 12 when the oestrogen levels in the blood stream reaches a critical level the pituitary releases a sudden surge of the hormone LH that acts on the graffian follicle triggering the release of the ovum. Ovulation takes place about 36 hours after the LH surge. Once the ovum is released the graffian follicle is converted to the corpus luteam, which starts to release progesterone. Under the influence of progesterone the blood supply to the endometrium increases and also starts secreting a glycogen rich product (secretory phase), which is useful for the growth of the embryo in the event of a successful fertilization.

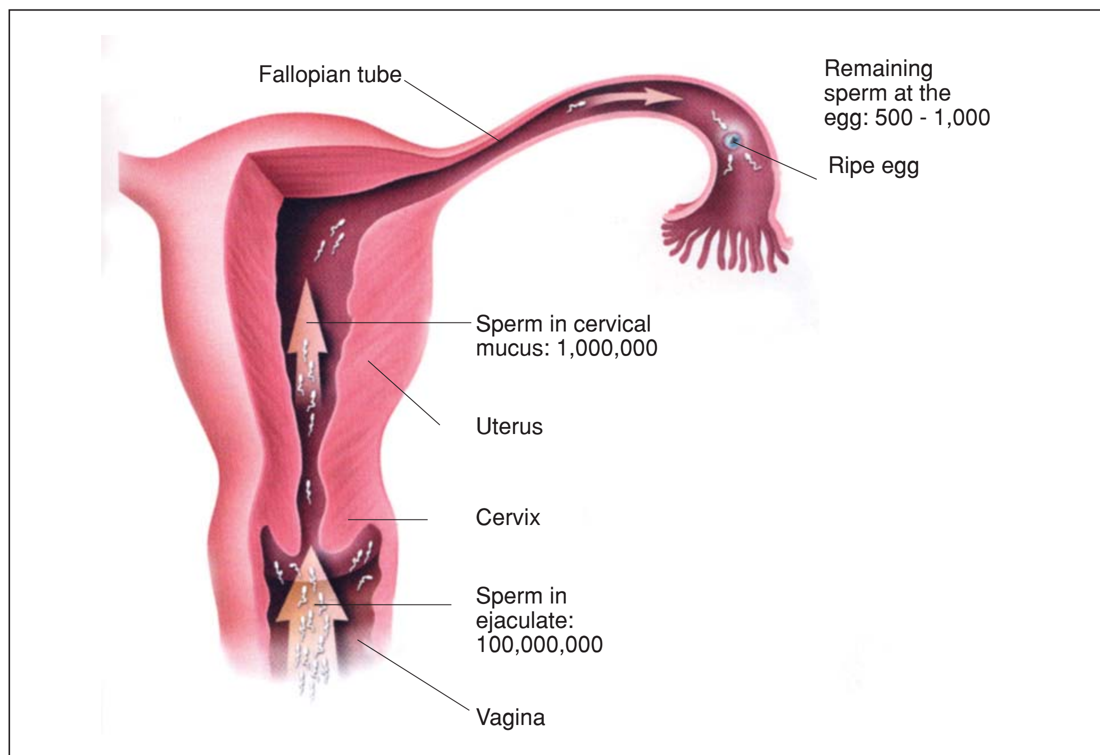
Figure 5 - Hormonal control of the menstrual cycle



FERTILIZATION AND IMPLANTATION

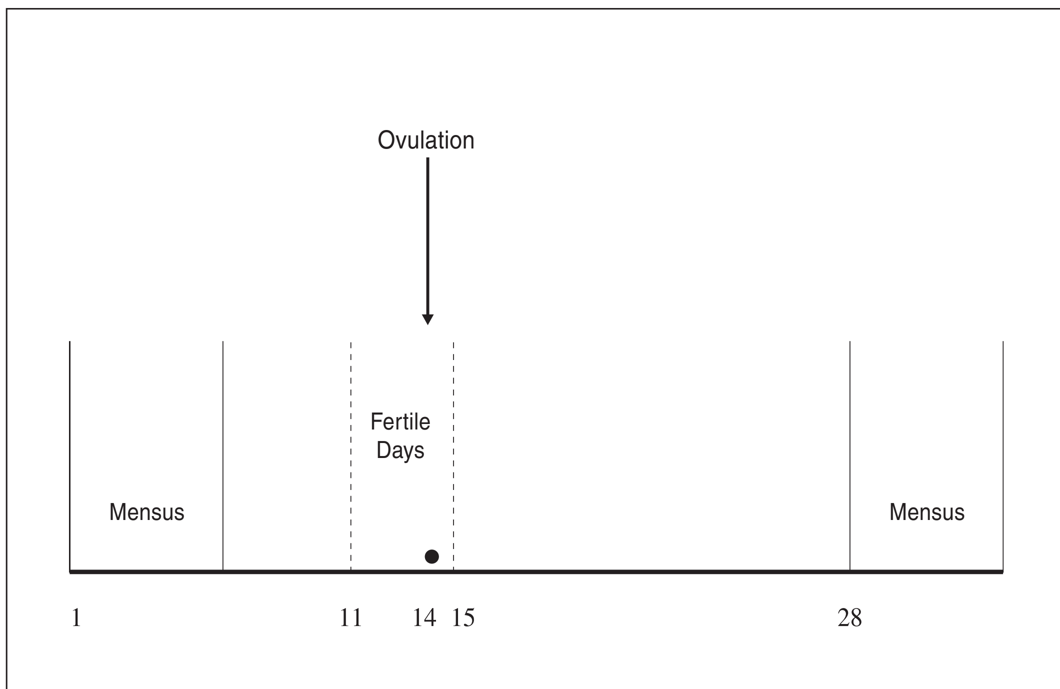
As already discussed the ovum is released in to coelomic cavity near the lateral end of the fallopian tubes and it enters the lumen of the fallopian tube where it remains fertilizable for about 24 hours. If a sperm reaches the lateral end of the tube during this period a conception can occur. Of the 100 million sperms deposited in the vagina during coitus only about 1000 sperms are able to swim up to the lateral end of the fallopian tube. This sperm migration occurs mainly by their own ability to swim but may be assisted by uterine and tubal contractions

Figure 6 - Pathway of Sperms in the Female Genital Tract



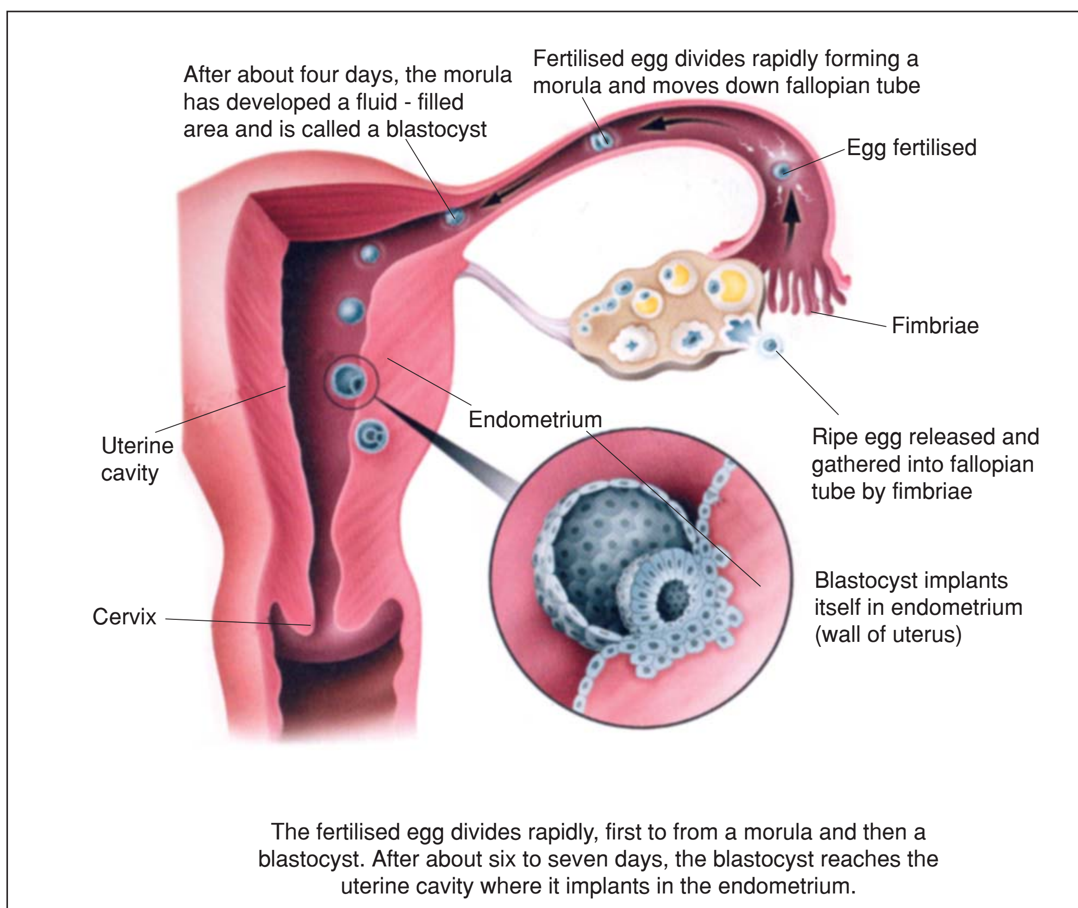
Sperms can stay alive for about 72 hours in the female genital tract. Hence an ovum, which is released on day 14 of the menstrual cycle, can be fertilized by a sperm entering the female genital tract from day 11 up to day 15. Therefore the fertile period is approximately about 4 days starting 3 days before the day of ovulation and ending one day after

Figure 7 - Fertile Period in a Regular 28-Day Cycle



Once a sperm enters the ovum fertilization occurs where the two nuclei form a zygote. This zygote then starts to divide and forms a ball of cells named the morula. This is moved towards the uterus by the cilia lining the fallopian tubes. It reaches the uterine cavity in 3 to 4 days. After floating in the uterine cavity for about 72 hours it embeds itself in the endometrium, which is in the secretory phase due to the peak levels of progesterone produced by the corpus luteum.

Figure 8 - Fertilization and Implantation



The fertilised egg divides rapidly, first to from a morula and then a blastocyst. After about six to seven days, the blastocyst reaches the uterine cavity where it implants in the endometrium.

ASSESSMENT OF A SUBFERTILE COUPLE

As in other medical situations subfertility management requires the relevant history a thorough examination and the necessary investigations to be completed before treatment can be commenced.

HISTORY

What are the important aspects in the history of the female?

AGE - Fertility in the female starts to decline from the late twenties slowly at first, rapidly after 35 and very rapidly after 40.

DURATION OF TRYING FOR A PREGNANCY - The longer the duration lesser are the chances of a spontaneous conception occurring.

MENSTRUATION - The hormonal cycles shown in the Figure.4 should function properly for menstruation to occur and if this is so ovulation is also likely to take place. i.e. clients with regular cycles are very likely to be ovulating regularly. Severe pain associated with menstruation is often a symptom of endometriosis.

CONTRACEPTION - Temporary methods of contraception has only a very short duration of effect on fertility once they are stopped.

Table 3 - Return of Fertility after Use of Different Types of Contraceptives

Type of contraception	*Time at which fertility returns*
Condom	mmediate
OCP	2-3 months
DMPA	6 months
Implant	mmediate
IUD	mmediate

Contraception may even reduce the risk of subfertility. Condoms by creating a barrier while DMPA, Implant and OCP by making the cervical mucous thick reduces the risk of infection and thereby the possibility of future subfertility. These also help to prevent unwanted pregnancies and terminations, which are a common cause of tubal blockage and subfertility.

PREVIOUS ILLNESS - Diseases like hypothyroidism, renal disease and sexually transmitted infections can cause subfertility. Equally important are diseases such as diabetes mellitus, heart disease, hypertension and anemia that need to be assessed and treated prior to commencing treatment for subfertility in order to ensure that the patient is fit to go through a pregnancy.

SURGERY - Any surgery that involves the abdomen and pelvis can lead to subfertility if it causes damage to the tubes or ovaries either directly or by formation of adhesions.

INFECTIONS - There is a close association between pelvic infection and subfertility. It is said that one out of every eight patients who suffer from an episode of severe PID will become subfertile. This increases to fifty percent following three episodes.

WEIGHT CHANGES - Obesity as well as sudden loss of weight are known to cause anovulation and subfertility.

COITAL PROBLEMS - It is important to specifically inquire about any difficulties in having regular intercourse such as dyspareunia and lack of privacy since clients may be reluctant to divulge these.

DRUGS - It is important to ensure that the client is not on any teratogenic drugs before commencing treatment for subfertility as damage to the fetus is maximum during the first 12 weeks. It is also advisable to commence all females who are anticipating a pregnancy on Folic Acid one tablet daily in order to minimize neural tube defects in the fetus.

What are the important aspects in the history of the male?

AGE - In contrast to the female the fall in fertility in the male becomes significant very much later around 55 years.

OCCUPATION - The occupation may cause a couple to be subfertile by preventing regular intercourse. e.g. Armed Forces. Sometimes the working environment due to excessive heat or irradiation can cause a reduction in the spermatogenesis.

PAST ILLNESSES - Systemic diseases such as diabetes mellitus and any other severe medical illness can impair spermatogenesis in addition to causing impotence.

INFECTIONS - Mumps is the commonly known infection to cause orchitis and subfertility. However not all patients who develop orchitis following mumps will have their spermatogenesis affected. Other infections, which can cause subfertility are tuberculosis and Gonorrhoea.

TRAUMA - Any damage to the testis (e.g. Torsion, hemorrhage) can impair spermatogenesis.

SURGERY - Accidental damage to the vas during surgery such as herniorapphy and orchidopexy may lead to subfertility. Varicocoele and hydrocoele when treated by surgery may improve the quality of the sperms.

DRUGS - Cimetidine , steroids , nitrofurantoin , spironolactone and anti cancer drugs are some examples of drugs which may impair spermatogenesis. Antihypertensives and drug abuse can cause subfertility by causing impotence.

ALCOHOL & SMOKING - These cause subfertility by both impairing spermatogenesis and also causing impotence.

COITAL DIFFICULTIES - As in the female information may not be given unless specifically inquired. The problems that may be encountered by the male are impotence (inability to have an erection) premature ejaculation (ejaculation occurring before penetration) and retrograde ejaculation (ejaculate going backwards into the bladder)

EXAMINATION

What should you look for when examining the female?

GENERAL EXAMINATION - weight and height measurements to exclude obesity, hirsuitism, acne, galactorrhoea, breast development, goitre with a view to excluding possible thyroid causes, pallor, heart and lungs to assess fitness for a pregnancy.

ABDOMINAL EXAMINATION - masses such as fibroids, lower abdominal tenderness indicative of pelvic inflammatory disease and scars denoting previous surgery.

EXTERNAL GENITAL EXAMINATION - discharge, state of hymen, clitoral abnormalities.

SPECULUM EXAMINATION - discharge, polyps, abnormalities of the cervix.

BIMANUAL EXAMINATION - uterine size, position, mobility, and adnexal masses and tenderness.

What should you look for when examining the male ?

GENERAL EXAMINATION - signs of hypoandrogenesim, gynaecomastia.

GENITAL EXAMINATION - presence and the size of testis, check for varicocele, hydrocele , hernia and any thickening or tenderness of the epididimis.

Examine the penis for structural abnormalities such as hypospadius and status of hygiene.

INVESTIGATIONS

What are the basic investigations that need to be performed?

As mentioned at the beginning the three main causes of subfertility are what needs to be checked initially.

Male

SEMINAL FLUID ANALYSIS

This is done after 72 hrs of abstinence from ejaculation. Normal values are as follows;

Composition of normal seminal fluid
Volume 2-5ml
Count > 20 million / ml
Motility > 50%
Morphology > 30% normal forms

Female

CHECK FOR OVULATION - As shown in the Figure 4 progesterone is secreted only if ovulation occurs. These are therefore tests for presence of progesterone in the second half of the cycle.

Basal body temperature chart - One effect of progesterone is to raise the basal body temperature (temperature checked early morning before any activity) by about 0.5 deg centigrade.

Figure 9 - Basl Body Temperature Chart of a woman who is ovulating

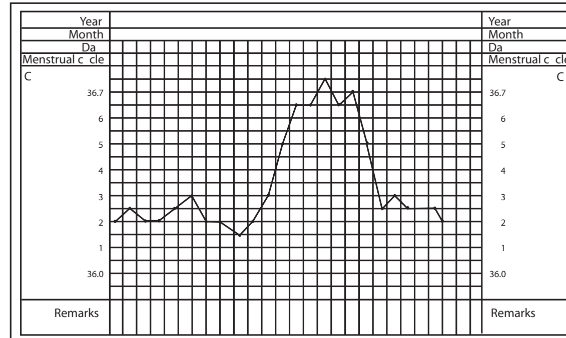
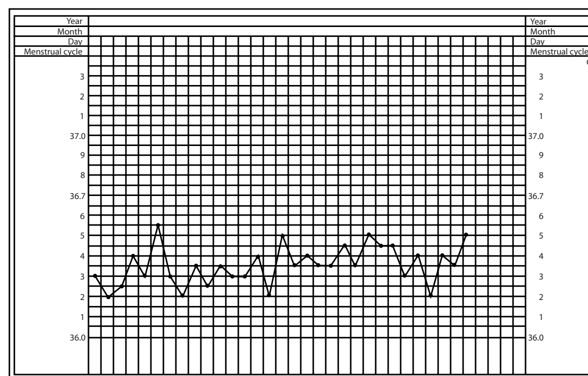


Figure 10 - Basal Body Temperature Chart of a woman who is not ovulating



Endometrial biopsy - When samples of endometrium obtained by dilatation and curettage in the middle of the 2nd half of this cycle shows a secretory phase ovulation is confirmed. This is a non-repetitive test.

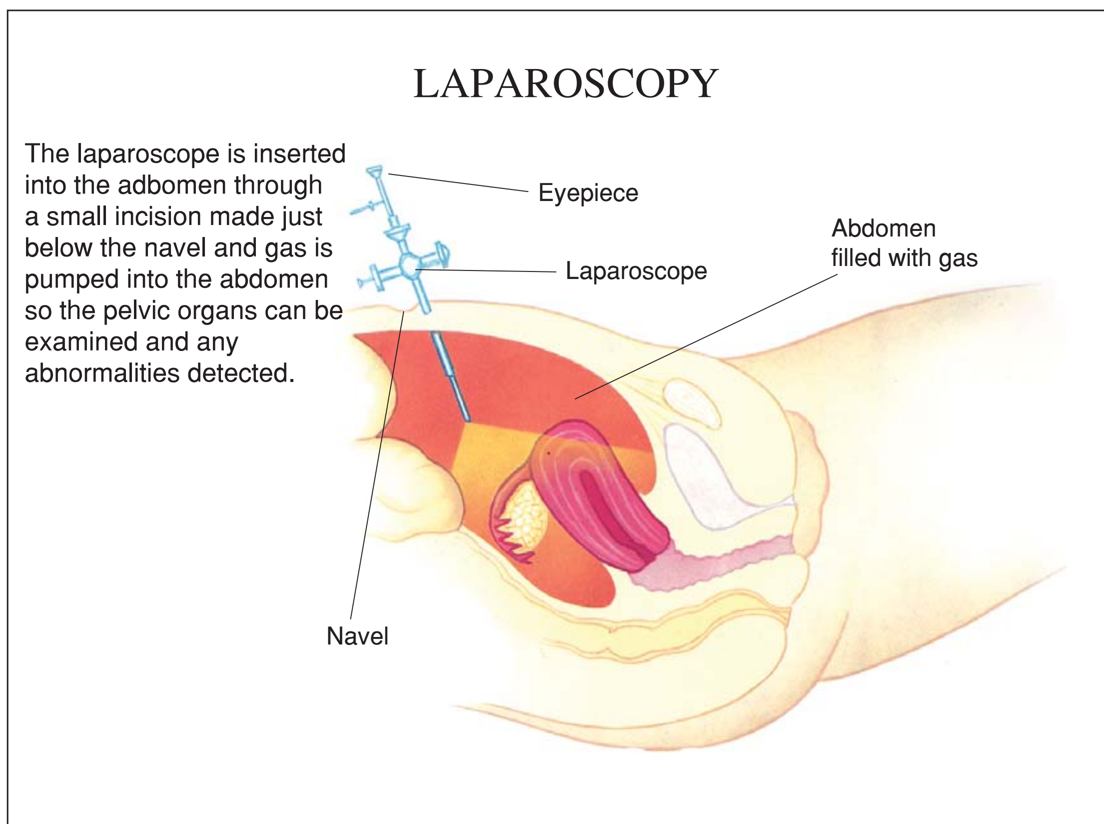
Day 21 - progesterone - If facilities are available and the cost is affordable by measuring the level of progesterone in blood on the 21-st day of the 28 day cycle ovulation can be checked.

Ultrasonography (Transvaginal) - This can be used to monitor the growth of the graphian follicle and ovulation. It is the most objective repetitive test. It also provides an opportunity to assess the endometrial preparation, which is necessary for implantation.

CHECK FOR TUBAL PATENCY

Laparoscopy and dye test -This surgical procedure is done by inserting the laparoscope into the abdomen through a small incision below the umbilicus. Methylene blue is injected through the cervix and can be seen to flow via the fimbrial end if the tubes are patent. In addition to the patency of the tubes conditions such as endometriosis, fibroids, polycystic ovaries and adhesions are also diagnosed at laparoscopic examination and may be treated at the same time.

Figure 11 - Laporoscopic Procedure



Hysterosalpingogram

For this test a radioopque dye is introduced through the cervix and X-ray pictures are obtained to check whether the dye emerges from the fimbrial end.

Figure 12 - Hysterosalpingogram showing patent tubes

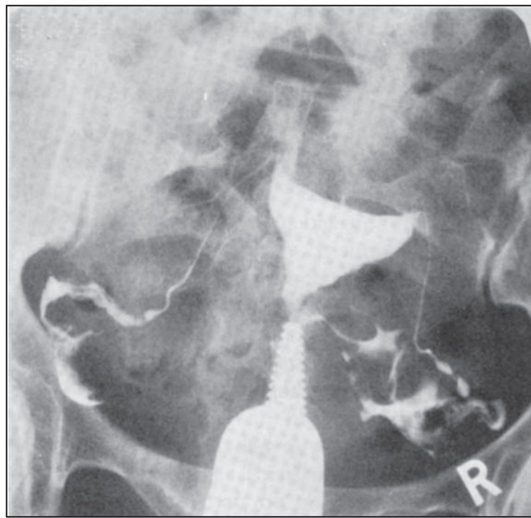
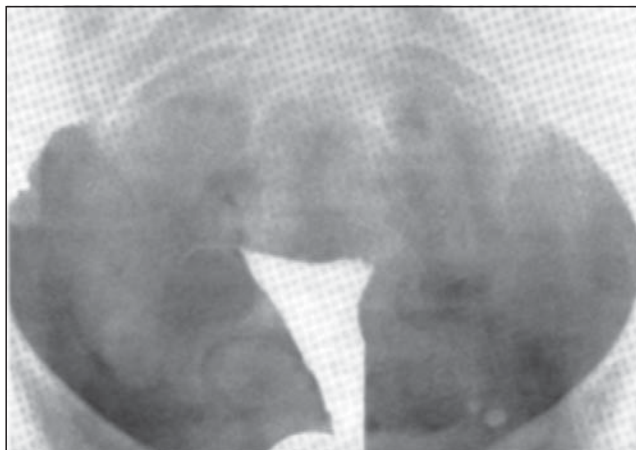


Figure 13 - Hysterosalpingogram showing blocked tubes



Hydrotubation

This due to its inaccuracy has been largely replaced by the above tests.

SPECIAL INVESTIGATIONS - these are done only when indicated

Female

Serum levels of gonadotrophins and prolactin, thyroid function tests,U/S scan of abdoman and pelvis, post coital test.

Male

Serum level of FSH, U/S Scan of testis, Testicular biopsy.

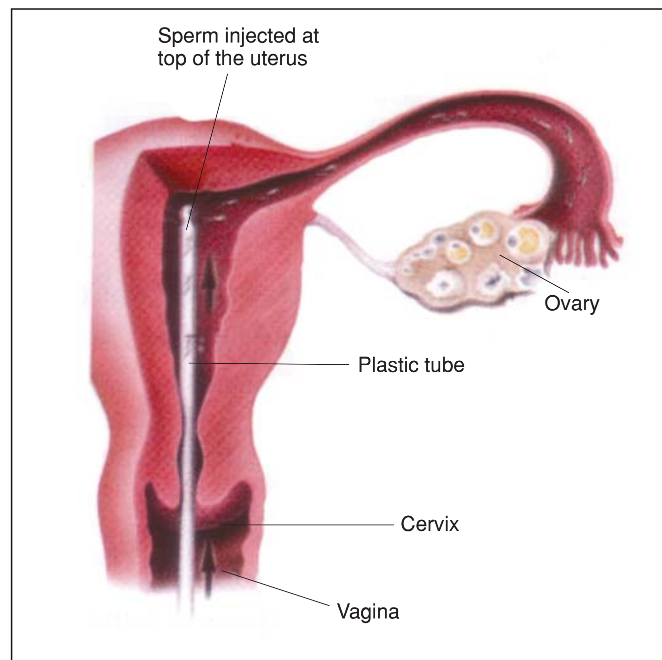
TREATMENT OF A SUBFERTILE COUPLE

Prior to management always ensure that the above steps of history, examination and investigation have been completed.

Main causes and their treatment

SEMINAL FLUID ANAMOLIES - The commonest treatment modality is preparation of the seminal fluid in order to separate the best sperms into a small volume of about 0.3 ml for artificial insertion into the uterus using a special catheter. This process is called Intra Uterine Insemination (IUI).

Figure 14 - Intra Uterine Insemination



Note: Unprepared seminal fluid should not be used as the success rate is very low and can cause serious problems due to infection and anaphylaxis. When using donor sperms the possibility of HIV infection and problems regarding custody of the child need to be borne in mind.

If a significant varicoele is present it can be treated surgically. Occasionally the anomalies are amenable to drug treatment.

ANOVULATION - Depending on the cause there are very effective drugs.

Clomiphene citrate - Acts by blocking the negative feed back of oestrogen on the pituitary and thereby increasing the release of gonadotrophins. The risk of multiple pregnancy is 10%. This drug should not be used as a placebo when there is no clear indication.

Gonadotrophins - Follicular stimulating and Leutinising hormone like drugs. These are usually administered in the form of injections. They can cause more serious side effects such as the ovarian hyper stimulation syndrome (OHSS) and carry a higher risk of multiple pregnancy.

In anovulation due to polycystic ovarian syndrome in addition to the above drugs diathermy puncture of ovaries and metformin are also used as methods of treatment.

Bromocriptine and thyroxine are used in the treatement of anovulation due to hyperprolactinaemia and hypothyroidism respectively.

TUBAL BLOCKAGE - Surgery is done but success depends on the cause and site.

UNEXPLAINED INFERTILITY - Superovulation using the above mentioned drugs and Intra Uterine Insemination is the first line of treatment.

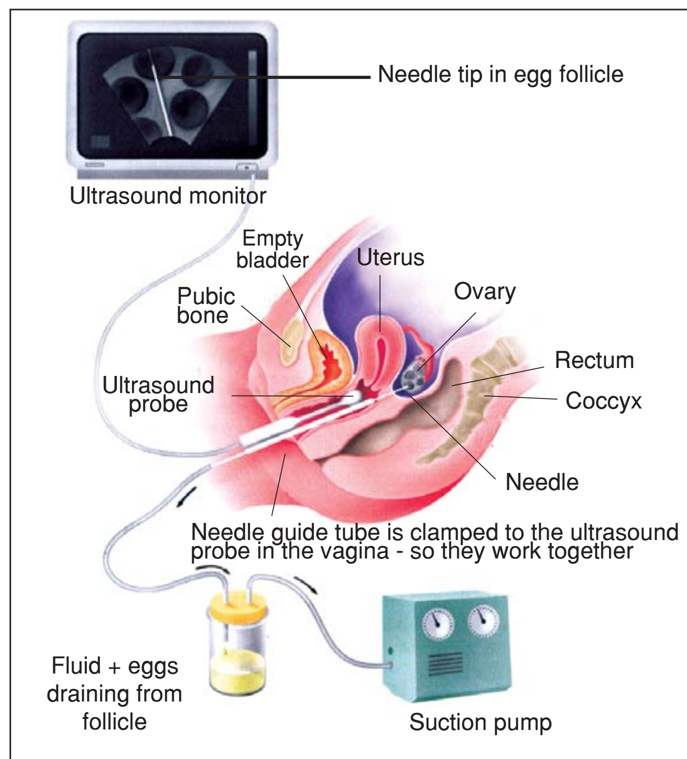
What are Assisted Reproductive Techniques (ART)?

Commonly referred to as test tube baby this consists of a large number of techniques with new additions being introduced constantly. In all these the ova taken out of the female body and sperms from the ejaculate are helped to undergo fertilization using various methods. Eg.

- In Vitro Fertilisation and Embryo Transfer - IVF /ET
- Gamete Intra Fallopian Transfer - GIFT
- Intra Cytoplasmic Sperm Injection – ICSI

The first step in these techniques is the administration of ovulation induction drugs to cause the development of multiple ova (superovulation), which are then monitored using ultra sound scanning. When the graffian follicles are fullygrown the fluid in them are extracted using an ultrasound-guided needle as shown below. This fluid is examined under a microscope and the ova are identified.

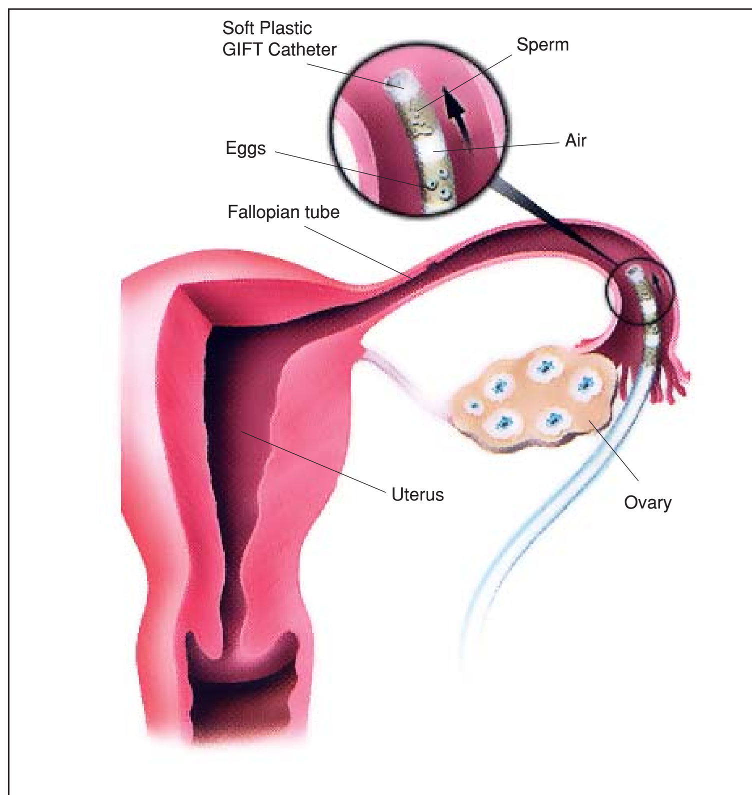
Figure 15 - Ovum Recovery



In IVF these ova are surrounded by 50 to 200,000 sperms in a special culture medium contained in a petri dish and once fertilization takes place the embryo (around 4 cell stage) is transferred back to the uterus transcervically using a special catheter as in IUI.

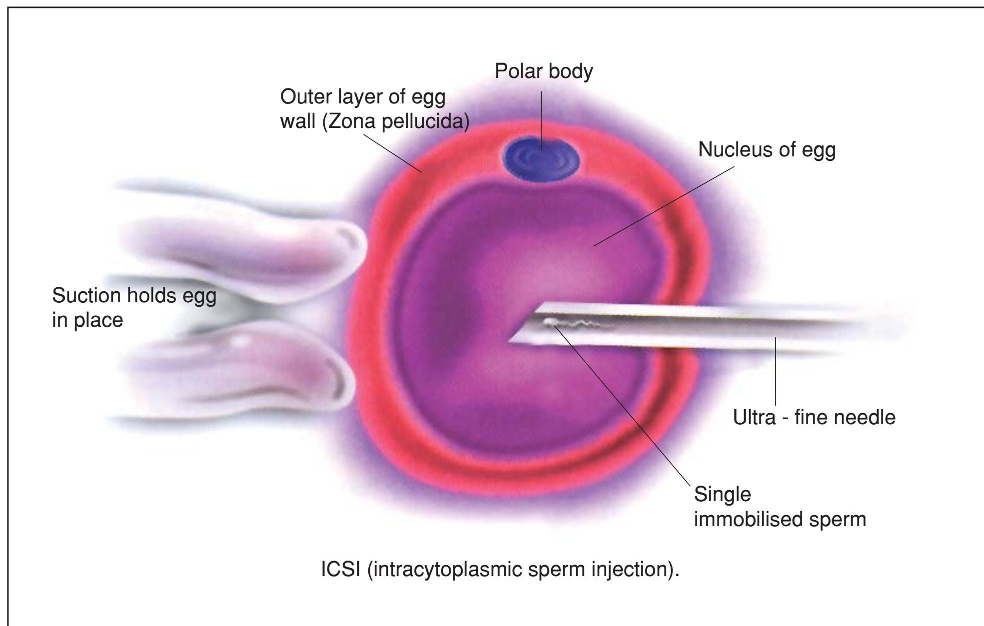
In GIFT the recovered ova together with about 40,000 sperms is placed in the lateral part of the fallopian tube with the aid of a laparoscopically guided catheter.

Figure 16 - Gamate Intrafallopian Transfer



In ICSI the sperm head containing the male nucleus is directly injected into the recovered ovum under the microscope and the fertilized embryo is transferred back to the uterus as in IVF/ET.

Figure 17 - Intra cytoplasmic Sperm Injection



ICSI (intracytoplasmic sperm injection).

These methods can be used for the treatment of unexplained infertility, male factor problems, tubal blockage and endometriosis.

THE ROLE OF THE PRIMARY HEALTH CARE PROVIDER IN THE MANAGEMENT OF SUBFERTILITY

The field staff can identify subfertile couples using information in the eligible couples register and the definition given in the introduction and direct them to obtain treatment. They can also identify clients with risk factors and emphasise to them the need for early intervention.

Educate the public on

a) Deleterious effects of alcoholism, smoking and obesity
b) Knowledge about the fertile period
c) The importance of preventing and treating pelvic infection
d) The need for vaccination against rubella
e) Benefits of commencing preconceptual Folic Acid

Helping to dispel some commonly believed myths regarding subfertility & providing the correct information

a) The cause of Subfertility may lie in either partner and is not always in the female
b) Subfertility is a common problem and therefore there is no necessity to be shy to divulge it.
c) Many causes of subfertility are now treatable and therefore seeking medical help is beneficial.
d) Subfertility is a medical disorder as any other disease and should not be associated with general misfortune.
d) Temporary contraception does not cause subfertiliy

Obtain a detail history and do a thorough examination of both partners keeping in mind the important factors mentioned previously & thereby try to identify the possible cause for their subfertility.

Directing couples to the appropriate center for investigations and treatment i.e. initially to the closest base hospital for preliminary investigations and management but in the event of that being unsuccessful they need to be sent to more specialized centers.

Explaining the importance of remaining with a center for a sufficient length of time enabling them to carry out a proper course of management provided their plan of management is explained and is acceptable to the couple. Providing necessary advice and explanations in order to encourage the couple to continue with treatment.

Helping to accept and cope with a situation of no success when all attempts at treatment have failed. At this stage it would be beneficial to counsel them regarding adoption. It would also be useful to make them realize that there are many other important aspects in marriage and life which bring happiness apart from having a baby.