

AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE

INFERTILITY:
AN OVERVIEW

A Guide for Patients



PATIENT INFORMATION SERIES

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INFERTILITY: AN OVERVIEW

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A glossary of italicized words is located at the end of this booklet.

INTRODUCTION

Infertility is typically defined as the inability to achieve pregnancy after one year of unprotected intercourse. If you have been trying to conceive for a year or more, you may need to have an infertility evaluation. However, if you are in your 30s or older, you should begin the infertility evaluation after about six months of unprotected intercourse rather than a year, so as not to delay treatment in this age group. Also, if you have very irregular menstrual cycles (suggesting that you are not ovulating), or if you or your partner has a known fertility problem, you probably should not wait an entire year before seeking treatment.

If you and your partner have been unable to have a baby, you're not alone. One out of seven couples has trouble conceiving. During this time, it is normal to experience feelings of frustration, jealousy and anger. However, once you begin to explore your medical options, you'll find that fertility treatments offer more hope for a successful pregnancy than ever before.

THE INITIAL VISIT

Your regular gynecologist may perform the initial fertility evaluation, or you may choose to be evaluated by an infertility specialist. It is important to find a doctor who you trust and with whom you feel comfortable. Some general obstetricians/gynecologists (ob/gyns) have a special interest in the treatment of infertility. Reproductive endocrinologists are specialized ob/gyns who, after completing the full ob/gyn residency, complete at least two additional years of specialized training in reproductive endocrinology and infertility at an approved fellowship program. Some urologists also specialize in the area of male infertility. To locate physicians in your area who specialize in infertility, go to the ASRM Web site at www.asrm.org and click on "Find a Doctor."

Once you decide upon a qualified physician, you and your partner will undergo a series of tests requiring significant time, money, and physical and emotional energy. Before these tests are performed, your physician will ask questions and review any records that you and your partner may have from a previous infertility evaluation. Ensuring that your physician has access to previous medical records is critical in minimizing wasted time and money for repeated diagnostic evaluation and therapy. Both you and your partner should attend the first meeting since infertility is a shared experience and is best dealt with as a couple. During this visit, you'll begin to understand the degree of commitment and cooperation that an infertility investigation requires.

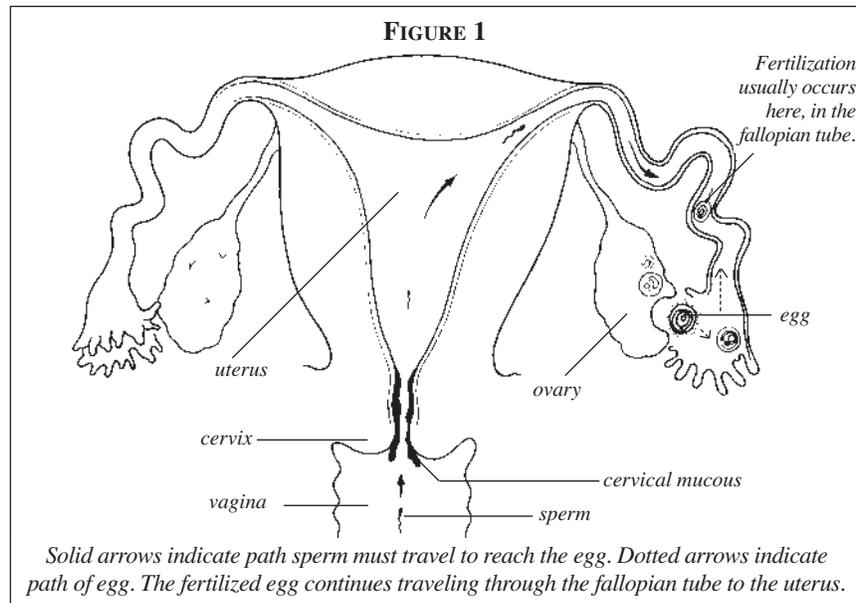
Your physician will review your history and ask you and your partner questions that will help clarify or explain potential causes for your difficulty in conceiving. In a typical initial visit, the physician will ask about the frequency and regularity of your menstrual period, pelvic pain, abnormal vaginal bleeding or discharge, history of pelvic infection, and medical illnesses. Expect questions concerning prior conceptions, miscarriages, operations, and methods of contraception. Your partner will be asked questions concerning prior genital injury, operations, infections, drug and/or medication usage, history of prior paternity, and medical illnesses. You'll be asked how long you've been trying to conceive, how often you have sexual intercourse, if you use lubricants during intercourse, and if anyone in either family has birth defects. Your physician will need to know the complete sexual and reproductive histories of you and your partner, including any former relationships. Since at least 25% of infertile couples have more than one factor causing infertility, it is very important to evaluate all factors that may affect both you and your partner.

During the first visit, you may discuss the emotional stress of infertility, a subject that is often difficult for you to share with family and friends. Physicians know that the procedures and intimate questions involved in an infertility workup can be difficult. You should always feel free to make your physician aware of your concerns and frustrations.

A complete physical examination of you and your partner usually follows the initial review. The extent of the examinations will depend upon whether or not any factors impacting your fertility are found early in the evaluation.

THE PROCESS OF CONCEPTION

In order to understand the fertility tests and treatments you may be offered, it is important to understand how conception naturally occurs. First, your *ovary* must release (ovulate) an egg, which must be picked up by the *fallopian tube*. Sperm must travel through the vagina, into the uterus, and up into the fallopian tube in order to fertilize the egg. Fertilization usually takes place in the fallopian tube. Then, the fertilized egg, or embryo, travels down to the uterus, where it implants in the uterine lining and develops (Figure 1). Infertility results when a problem develops in any part of this process.



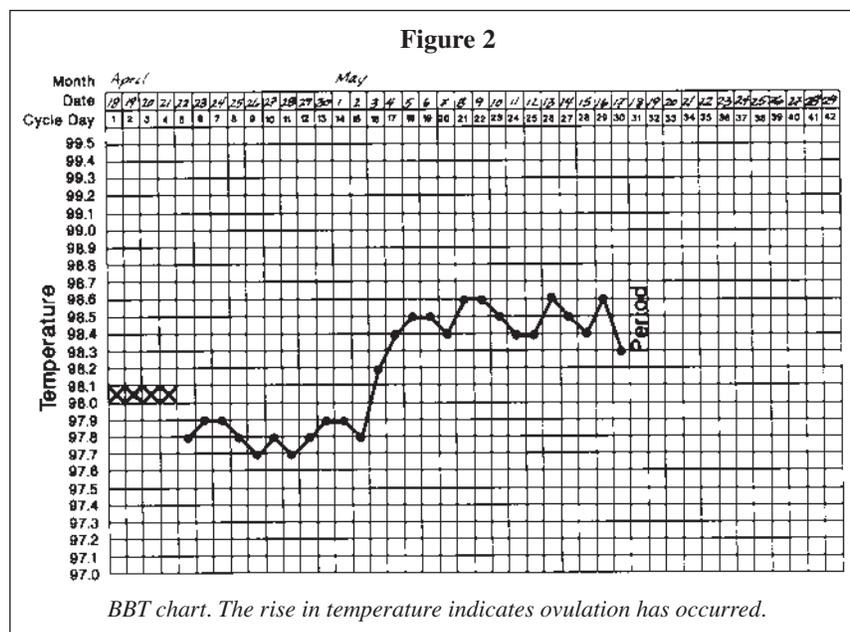
FERTILITY FACTORS

The Ovulation Factor

Problems with *ovulation* are common causes of infertility, accounting for approximately 25% of all infertility cases. Ovulation involves the release of a mature egg from one of your ovaries. After ovulation, the ovary produces the hormone *progesterone*. During the 12 to 16 days before the onset of menstruation, progesterone transforms the lining of your uterus into a receptive environment for implantation and nurturing of the fertilized egg. If you have regular menstrual cycles, you are probably ovulating. Cycle lengths of approximately 24 to 34 days are usually ovulatory. If you only have a period every few months or not at all, you are probably not ovulating or are ovulating infrequently.

Charting your *basal body temperature* (BBT) is a simple, inexpensive way to see if you are ovulating. To complete a BBT chart (Figure 2), you must take your temperature orally each morning the moment you awaken for at least one month and record the temperature daily under the appropriate date. Normally, the release of progesterone due to ovulation causes a mid-cycle temperature rise of 0.5 to 1.0 degrees Fahrenheit, indicating that ovulation has occurred. However, some women who ovulate normally may not have a rise in temperature, and many factors unrelated to the reproductive cycle, such as a cold or fatigue, can affect the BBT. At best, the BBT chart helps determine when and if ovulation is taking place, but only after it has happened.

To predict ovulation before it takes place, in order to schedule intercourse or insemination for example, you may use an over-the-counter ovulation prediction



kit. These urine test kits are designed to detect the surge of *luteinizing hormone (LH)* that occurs just before you ovulate. The LH surge stimulates one of the ovaries to release an egg and produce progesterone. Ovulation prediction kits usually detect the LH surge about a day or a day and a half before ovulation, giving you and your partner advance notice of impending ovulation. However, not all women who ovulate will have an LH surge that will be detected using these kits.

In a normal cycle, progesterone levels peak about seven days after ovulation. Your physician may perform a blood test to measure the level of progesterone in your blood at this time. Generally, blood progesterone is tested on day 19 to 23 of a 28-day menstrual cycle. An elevated progesterone level helps to confirm ovulation and the adequacy of ovarian hormone production.

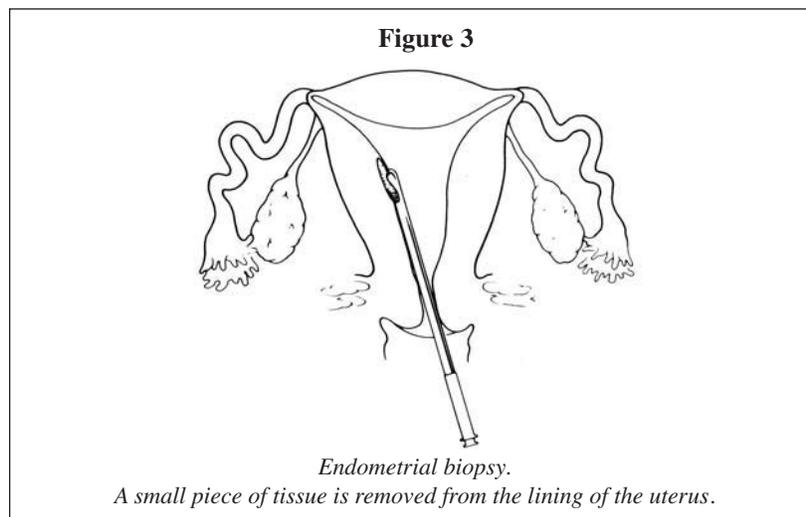
Your physician may perform a pelvic ultrasound examination to evaluate ovulation, but this is not done routinely. This examination may indicate whether your ovaries are producing *follicles*. These follicles are fluid filled sacs (cysts) located just beneath the ovary's surface that contain the immature eggs. Ultrasound may also help to document the follicle's collapse, implying release of the egg.

Another procedure, the *endometrial biopsy*, may be advised in a few cases to evaluate the uterine lining. Just before your period begins, your physician takes a small sample of tissue from your endometrium, which is the inner lining of your uterus (Figure 3). This test may produce painful cramping and your physician may prescribe medication for pain relief prior to the procedure. A pregnancy test is performed prior to the biopsy to make sure that you are not pregnant. The removed tissue is specially prepared by a pathologist and examined under a microscope to

determine if it has responded adequately to circulating progesterone. The endometrial biopsy is usually obtained one to three days before menstruation is expected, typically day 26 of a 28-day cycle, which is when progesterone-induced changes in the endometrium are at their maximum. The endometrial biopsy can also be scheduled 12 to 13 days after the LH surge. Your physician must know the ovulation date or the starting date of your next period to interpret the biopsy.

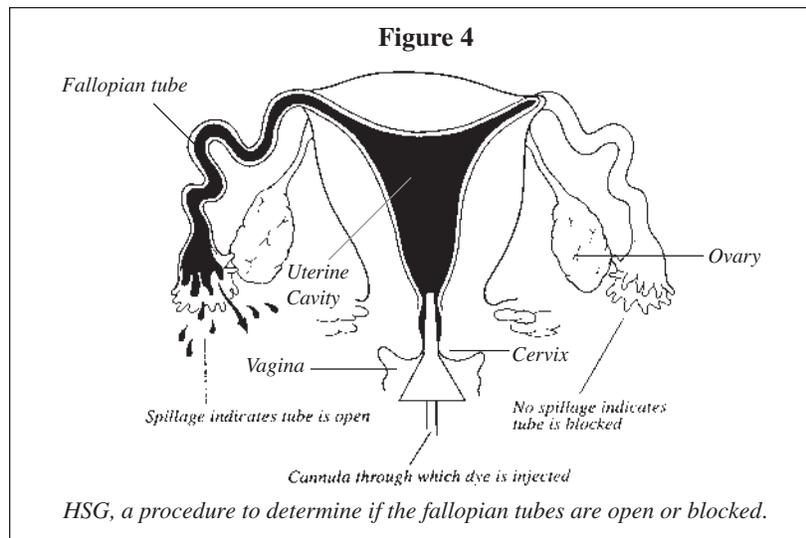
The biopsied tissue's appearance under the microscope may indicate a *luteal phase defect*, which means that it has not responded properly to the progesterone secreted by the ovary after ovulation. Treatment may consist of administering progesterone or ovulation drugs. Endometrial biopsy to look for luteal phase defects is not routinely done by most infertility specialists because the information has not usually been helpful in improving pregnancy rates.

If you are not ovulating, your physician may prescribe ovulation drugs to induce ovulation as well as order special tests to determine the reason. Your medical history and physical exam will help determine which tests are appropriate. More potent fertility drugs given by injection may be prescribed if oral therapy fails.



The Tubal Factor

Because open and functional fallopian tubes are necessary for conception, tests to determine tubal openness (patency) are important. Tubal factors, as well as factors affecting the *peritoneum* (lining of the pelvis and abdomen), account for about 35% of all infertility problems. A special x-ray called a *hysterosalpingogram (HSG)* (Figure 4) can be performed to evaluate the fallopian tubes and uterus. During an HSG, a special fluid (dye) is injected through your cervix, fills your uterus, and travels into your fallopian tubes. If the fluid spills out the ends of the tubes, they are open. If the fluid does not spill out the ends, then the tubes are blocked.



If the HSG shows blocked fallopian tubes, your physician may perform a *laparoscopy* to assess the degree of tubal damage. If the tubes are found to be blocked, scarred, or damaged, surgery can sometimes correct the problem. Although some tubal problems are correctable by surgery, women with severely damaged tubes are so unlikely to become pregnant that *in vitro fertilization (IVF)* offers them the best hope for a successful pregnancy. Because very badly damaged tubes may fill with fluid and lower IVF success rates, your physician may recommend removal of the tubes prior to IVF. More information on tubal disease can be found in the ASRM Patient Information booklet titled *Tubal Factor Infertility*.

The Male Factor

In approximately 40% of infertile couples, the male partner is either the sole or a contributing cause of infertility. Therefore, a *semen analysis* is important in the initial evaluation. To prepare for a semen analysis, your partner will be asked to abstain from ejaculating for at least 48 hours. He then will collect a semen sample in a cup by masturbating at home or in the physician's office. In some instances, a semen sample may be obtained during sexual intercourse using a special condom provided by the physician. The semen specimen is examined under a microscope to determine the volume (amount), motility (movement), and morphology (appearance and shape) of the sperm. In general, two or three semen analyses are recommended over two to six months, since sperm quality can vary over time. Other tests may be recommended as well.

If your partner's semen analysis reveals abnormalities, he may need to consult a urologist or other physician who specializes in male infertility. Treatment for male factor infertility may include antibiotic therapy for infection,

surgical correction of *varicocele* (dilated or varicose veins in the scrotum) or duct obstruction, or medications to improve sperm production. In some cases, no obvious cause of poor sperm quality can be found. *Intrauterine insemination (IUI)* or IVF may then be recommended. Direct injection of a single sperm into an egg (*intracytoplasmic sperm injection [ICSI]*) may be recommended as well. For more information, refer to the ASRM Patient Information booklets titled *Male Infertility and Vasectomy Reversal* and *Husband Insemination*.

If no sperm are present, your physician may discuss using a sperm donor. Insemination with donor sperm may also be considered if IUI is not successful or if you and your partner do not choose to undergo IVF. For more information about this topic, please refer to the ASRM Patient Information booklet titled *Donor Insemination*.

The Age Factor

Delaying pregnancy is a common choice for women in today's society. The number of women in their late 30s and 40s attempting pregnancy and having babies has increased in recent years. If you've chosen to delay pregnancy, due to college or career for example, you may not realize that your fertility begins to decline significantly in your mid 30s and accelerates in your late 30s. Some women even begin to experience a decline in their fertility in their late 20s and early 30s.

Fertility declines with age because fewer eggs remain in your ovaries, and the quality of the eggs remaining is lower than when you were younger. Blood tests are now available to determine your *ovarian reserve*, which reflects your age-related fertility potential. In the simplest of these tests, the hormones *FSH* and *estradiol* are tested in your blood on the second, third, or fourth day of your menstrual period. An elevated FSH level indicates that your chances for pregnancy may be slim, especially if you are age 35 or older, but does not mean that you have no chance of successful conception.

Older women tend to have a lower response to fertility medications and a higher miscarriage rate than younger women. The chance of having a chromosomally deformed embryo, such as one with Down syndrome, also increases with age. Because of the marked effect of age on pregnancy and birth rates, it is common for older couples to begin fertility treatment sooner and, in some cases, to consider more aggressive treatment than younger couples.

Possible treatments for age-related infertility in women include fertility drugs plus IUI or IVF. In cases where the treatments fail or are predicted to have a low chance of success, *egg donation* is an option. Egg donation has a high chance of success, regardless of your FSH level. For couples who have not succeeded with fertility treatments or who choose to forgo treatment, adoption is an important option. For more information about these options, please consult the ASRM Patient Information booklets titled *Age-Related Infertility and Adoption*.

The Cervical/Uterine Factor

Conditions within the *cervix*, which is the lower part of the uterus, may impact your fertility, but they are rarely the sole cause of infertility. It is important for your physician to know if you have had prior biopsies, surgery, “freezing” and/or laser treatment of the cervix, abnormal pap smears, or if your mother took DES (diethylstilbestrol) while she was pregnant. In order to determine if there is a problem with your cervix, your physician may recommend a *postcoital test (PCT)* which evaluates cervical mucus, sperm, and the interaction between the two. However, many physicians are not currently recommending this test because it has not been shown to be of value in increasing pregnancy rates. Cervical problems are generally treated with antibiotics, hormones, or by IUI.

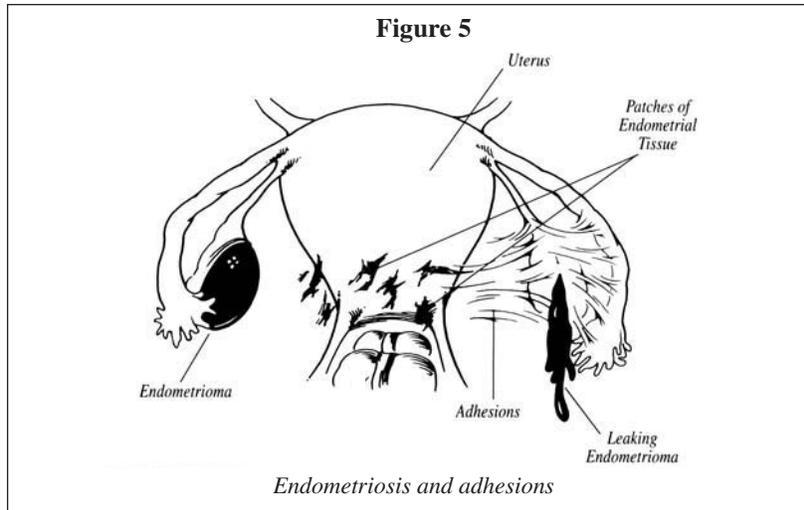
The HSG test, which is used to investigate the fallopian tubes, can also reveal defects inside the uterine cavity, which is the hollow space inside your uterus where an embryo would implant and develop. An HSG is sometimes conducted after your period stops and before ovulation. Possible uterine abnormalities that may be identified include uterine scar tissue, polyps (bunched-up pieces of the endometrial lining), *fibroids*, or an abnormally shaped uterine cavity. Problems within your uterus may interfere with implantation of the embryo or may increase the incidence of miscarriage. Surgery (*hysteroscopy*) may be required to further evaluate and possibly correct uterine structural problems.

Uterine abnormalities can also be seen by a saline hysteroqram (SHG). This test may also be called a sono-hysteroqram or water ultrasound. An SHG is a pelvic ultrasound performed while saline is injected through your cervix to outline the uterine cavity. Unlike the HSG, the SHG allows visualization of the wall of the uterus as well as the cavity at the same time, a difference which may be helpful in some cases.

Peritoneal Factor Infertility

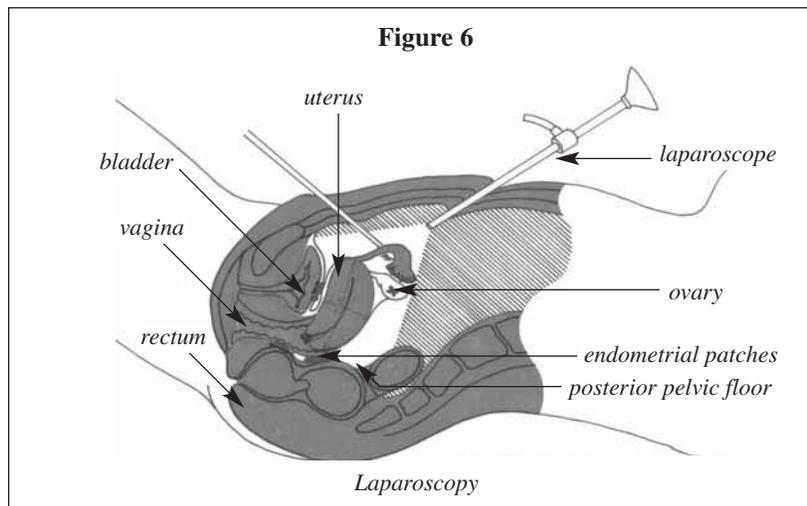
Peritoneal factor infertility refers to abnormalities involving the peritoneum such as scar tissue (*adhesions*) or *endometriosis* (Figure 5). Endometriosis is a condition where tissue that normally lines the uterus begins to grow outside the uterus. This tissue may grow on any structure within the pelvis including the ovaries and is found in about 35% of infertile women who have no other diagnosable infertility problem. Endometriosis is found more commonly in women with infertility. For further information concerning this problem, see the ASRM Patient Information booklet titled *Endometriosis*.

Laparoscopy is a surgical procedure which is performed to diagnosis and treat adhesions or endometriosis. Laparoscopy is usually performed under general anesthesia, often in a hospital’s same-day surgery unit. During the procedure, a narrow, lighted telescopic instrument called a *laparoscope* is inserted through a small incision within or just below your navel (Figure 6). The physician then looks directly into your abdominal cavity and inspects the ovaries, fallopian tubes, and uterus. A dye is usually injected through the cervix to determine if the



passage to the uterus and tubes is open. One or more additional smaller cuts may be made above your pubic area in order for the physician to insert additional instruments to better examine your pelvic organs and treat any disease if found.

A variety of specialized surgical instruments, including lasers, may now be used laparoscopically to treat such conditions as endometriosis, adhesions, and ovarian cysts such as endometriomas (fluid-filled cysts on the ovaries). In many cases, laparotomy, which involves a larger abdominal incision than laparoscopy and an approximately six-week recovery, is no longer necessary since many problems can now be treated laparoscopically. Although it is reasonable and sometimes advisable to perform laparoscopy to identify and treat pelvic disease,



this procedure is not routinely performed in an infertility evaluation. Laparo-scropy is expensive and involves some surgical risk. You and your physician should discuss whether not or laparoscopy is recommended in your particular case.

Unexplained Infertility

In approximately 5% to 10% of couples trying to conceive, all of the above tests are normal and there is no apparent cause for infertility. In a much higher percentage of couples, only minor abnormalities are found that are not severe enough to result in infertility. In these cases, the infertility is referred to as unexplained. Couples with unexplained infertility may have problems with egg quality, tubal function, or sperm function that are difficult to diagnose and/or treat. Fertility drugs and IUI have been used in couples with unexplained infertility with some success. If no pregnancy occurs within three to six treatment cycles, IVF may be recommended.

CHANCES OF SUCCESS WITH IVF

Each couple has a unique set of circumstances, and the chances of treatment success vary widely. The success of IVF depends on many factors, especially your age. For more information on IVF, refer to the ASRM Patient Information booklet titled *Assisted Reproductive Technologies*. National and regional *assisted reproductive technologies (ART)* success rates are available on the Internet at www.cdc.gov.

PSYCHOLOGICAL IMPLICATIONS

Infertility is a medical condition that has many emotional aspects. Feelings such as anger, sadness, guilt, and anxiety are common and may affect your self-esteem and self-image. You may find it difficult to share your feelings with family and friends, which can lead to isolation. It is important to know that these feelings are normal responses to infertility and are experienced by many couples. Although a physician will describe various treatments and realistic odds of success with treatments, you must decide how far you will go in your attempts to conceive. Coming to a joint decision with your partner about goals and acceptable therapies is important. Setting endpoints for therapy may also be advisable. For more information, refer to the ASRM Patient Information booklet titled *Infertility: Coping and Decision Making*. You may also go to the ASRM Web site at www.asrm.org and click on "Find a Doctor" to locate counselors in your area who specialize in infertility issues.

SUMMARY

Sometimes the factors affecting your fertility are easy to detect and treat, but in many cases a specific reason for infertility may be difficult to identify. After a full evaluation, your physician can give you a reasonable idea of your chances of achieving pregnancy with various treatment options. The choice of which treatment to pursue, if any, is strictly a personal one. Side effects, costs, the risk of multiple births, which is increased with some infertility treatments, and expected success rates are important factors to consider when choosing a treatment plan. It is helpful when beginning fertility treatment to develop a long-term plan with your physician so that you will have an idea of how long to pursue a particular treatment before considering moving on to more aggressive therapy or stopping treatment. It may be necessary at times to temporarily cease therapy and begin again at a later date. Thanks to the many options existing today, including advanced reproductive technologies and adoption, most infertile couples will be able to experience the joy of parenthood.

Let Us Know What You Think

Email your comments on this booklet to asrm@asrm.org. In the subject line, type “Attention: Patient Education Committee.”

GLOSSARY

Adhesions. Bands of fibrous scar tissue that may bind the pelvic organs and/or loops of bowel together. Adhesions can result from previous infections, endometriosis, or surgeries.

Assisted Reproductive Technologies (ART). All treatments which include laboratory handling of eggs, sperm, and/or embryos. Some examples of ART are in vitro fertilization (IVF), gamete intrafallopian transfer (GIFT), pronuclear stage tubal transfer (PROST), tubal embryo transfer (TET), and zygote intrafallopian transfer (ZIFT).

Basal body temperature (BBT). The body temperature at rest. It is taken orally each morning immediately upon awakening and recorded on a BBT chart. The readings are studied to help identify ovulation, which usually occurs at approximately the same time as the rise in BBT.

Cervix. The narrow, lower part of the uterus that opens into the vagina. The cervical canal runs through the cervix and connects the vagina with the uterine cavity. The cervix produces mucus through which sperm must swim before entering the uterine cavity and then the fallopian tubes.

Corpus luteum. A mature follicle that has collapsed after releasing its egg at ovulation. The corpus luteum secretes progesterone and estrogen during the second half of a normal menstrual cycle. The secreted progesterone prepares the lining of the uterus (endometrium) to support a pregnancy.

Egg Donation. The process of fertilizing eggs from a donor with the male partner's sperm in a laboratory dish and transferring the resulting embryos to the female partner's uterus. The female partner will not be biologically related to the child, although she will be the birth mother on record. The male partner will be biologically related to the child.

Endometrial biopsy. The extraction of a small piece of tissue from the endometrium (lining of the uterus) for microscopic examination. The results indicate whether or not the endometrium is at the appropriate stage for implantation of a fertilized egg.

Endometriosis. A condition where endometrial-like tissue (the tissue that lines the uterus) develops outside of the uterine cavity in abnormal locations such as the ovaries, fallopian tubes, and abdominal cavity. This tissue can grow with hormonal stimulation and cause pain, inflammation, and scar tissue. It may also be associated with infertility.

Estradiol. The predominant estrogen (hormone) produced by the follicular cells of the ovary.

Fallopian Tubes. A pair of hollow tubes attached one on each side of the uterus through which the egg travels from the ovary to the uterus. Fertilization with the man's sperm usually occurs in the fallopian tube. The fallopian tube is the most common site of ectopic pregnancy.

Fibroids. Benign (non-cancerous) tumors of the uterine muscle wall that can cause abnormal uterine bleeding.

Follicle. A fluid-filled sac located just beneath the surface of the ovary, containing an egg (oocyte) and cells that produce hormones. The sac increases in size and volume during the first half of the menstrual cycle and at ovulation, the follicle matures and ruptures, releasing the egg. As the follicle matures, it can be visualized by ultrasound.

Follicle Stimulating Hormone (FSH). In women, FSH is the pituitary hormone responsible for stimulating follicular cells in the ovary to grow, stimulating egg development and the production of the female hormone estrogen. In the male, FSH is the pituitary hormone which travels through the bloodstream to the testes and helps stimulate them to manufacture sperm. FSH can also be given as a medication.

Hysteroscopy. A procedure in which a lighted scope (hysteroscope) is inserted through the cervix into the uterus to enable the physician to view the inside of the uterus to diagnose and treat problems within the uterine cavity.

Hysterosalpingogram (HSG). An x-ray procedure in which a special media (dye) is injected into the uterus to demonstrate the inner contour of the uterus and degree of openness (patency) of the fallopian tubes.

Intracytoplasmic sperm injection (ICSI). A micromanipulation technique used in conjunction with IVF that involves injecting a sperm directly into an egg in order to facilitate fertilization. The fertilized egg is then transferred to the uterus.

Intrauterine insemination (IUI). The process whereby sperm are injected directly into the uterine cavity in order to bypass the cervix and place the sperm closer to the egg. The sperm are usually washed first in order to remove chemicals that can irritate the uterine lining and to increase sperm motility and concentration.

In vitro fertilization (IVF). A method of assisted reproduction that involves surgically removing eggs from the woman's ovaries, combining them with sperm in the laboratory and, if fertilized, replacing the resulting embryo into the woman's uterus.

Laparoscope. A narrow, lighted viewing instrument with a telescopic lens.

Laparoscopy. A diagnostic procedure in which a surgeon inserts a laparoscope through a small incision below the navel and visually inspects the uterus, uterine ligaments, fallopian tubes, ovaries, and abdominal organs. Other incisions may also be made through which additional instruments can be inserted to facilitate diagnosis and treatment of pelvic disease.

Luteal phase defect. A condition present when the lining of the uterus does not mature properly in response to the progesterone secreted by the ovary after ovulation.

Luteinizing hormone (LH). The hormone that triggers ovulation and stimulates the corpus luteum to secrete progesterone.

Ovary. One of the two female sex glands in the pelvis, located one on each side of the uterus. The ovaries produce eggs and hormones including estrogen, progesterone, and androgens.

Ovarian reserve. Refers to a woman's fertility potential in the absence of any problems in the reproductive tract (fallopian tubes, uterus, vagina). It mainly depends on the number and quality of eggs in the ovaries and how well the ovarian follicles are responding to the hormonal signals from the brain.

Ovulation. The release of a ripened egg from its follicle in the outer portion of the ovary. Ovulation usually occurs on day 14 or 15 of a 28-day cycle or 14 days prior to the first day of the next period.

Peritoneum. The lining of the abdominal cavity.

Postcoital test (PCT). The microscopic analysis of a cervical mucus sample, usually collected within 18 hours after intercourse. This test determines the quality of cervical mucus and the ability of sperm to enter and penetrate the mucus.

Progesterone. A female hormone secreted by the ovary during the second half of the menstrual cycle. Progesterone prepares the lining of the uterus for implantation of the fertilized egg.

Semen analysis. The microscopic examination of semen to determine the number of sperm, their shapes, and their ability to move.

Uterus (Womb). The hollow, muscular organ in the pelvis where an embryo implants and grows during pregnancy. The lining of the uterus, called the endometrium, produces the monthly menstrual blood flow when there is no pregnancy.

Vagina. The genital canal in the female that leads from the vulva (external genitalia) to the cervix and uterus.

Varicocele. A varicose or dilated vein within the scrotum that can cause infertility in some men.

For a list of additional reading materials, contact the ASRM administrative office at 1209 Montgomery Highway, Birmingham, Alabama 35216-2809; (205) 978-5000.

NOTES

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