AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE
Formerly The American Fertility Society

ASSISTED REPRODUCTIVE TECHNOLOGIES

A Guide for Patients

PATIENT INFORMATION SERIES

Published by the American Society for Reproductive Medicine under the direction of the Patient Education Committee and the Publications Committee. This booklet is in no way intended to replace, dictate, or fully define evaluation and treatment by a qualified physician. It is intended solely as an aid for patients seeking general information on issues in reproductive medicine.

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

INTRODUCTION

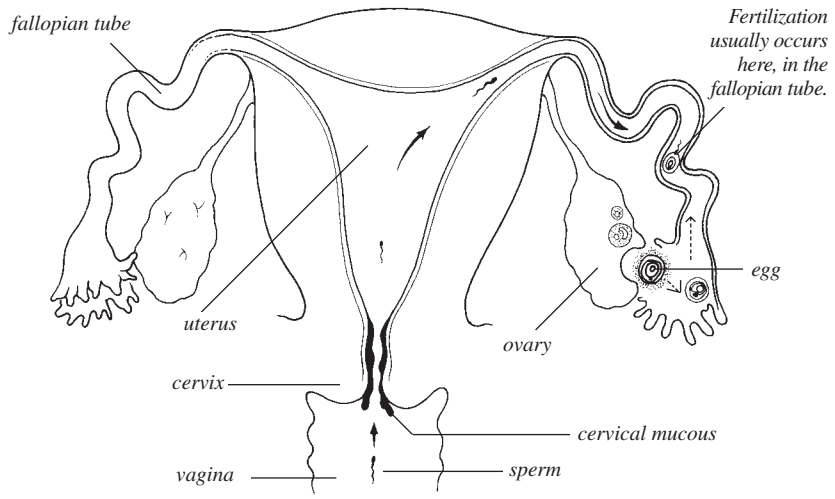
This booklet will help you understand *in vitro fertilization (IVF)* and other *assisted reproductive technologies (ART)* that have become accepted medical treatments for infertility. Through these procedures, many couples with otherwise untreatable infertility have given birth to healthy babies.

Un-Assisted Reproduction

In order to understand assisted reproduction and how it can help infertile couples, it is important to understand how conception takes place naturally. In order for traditional conception to occur, the man must ejaculate his semen, the fluid containing the *sperm*, into the woman's *vagina* near the time of *ovulation*, when her *ovary* releases an *egg*. Ovulation is a complex event controlled by the *pituitary gland*, which is located at the base of the brain. The pituitary gland releases *follicle stimulating hormone (FSH)*, which stimulates a *follicle* in one of the ovaries to begin growing. The follicle produces the hormone *estrogen* and contains a maturing egg. When the egg is mature, the pituitary gland sends a surge of *luteinizing hormone (LH)* that causes the follicle to rupture and release (ovulate) the egg (Figure 1).

Following ovulation, the egg is picked up by one of the *fallopian tubes*. Since fertilization usually takes place inside the fallopian tube, the man's sperm must be capable of swimming through the vagina and *cervical mucus*, up the *cervical canal* into the uterus, and up into the fallopian tube, where it must attach to and penetrate the egg in order to fertilize it. The fertilized egg continues traveling to the *uterus* and implants in the uterine lining, where it grows and matures. If all goes well, a child is born approximately nine months later.

Figure 1



Solid arrows indicate path sperm must travel to reach the egg. Dotted arrow indicates path of egg. The fertilized egg continues traveling through the fallopian tube to the uterus.

IN VITRO FERTILIZATION (IVF)

There are many factors that can prevent the union of sperm and egg, and these are discussed in the ASRM patient information booklet titled *Infertility, An Overview*. Fortunately, assisted reproductive techniques such as IVF can help. IVF is a method of assisted reproduction in which a man's sperm and a woman's eggs are combined outside of the body in a laboratory dish. If *fertilization* occurs, the resulting *embryos* are transferred to the woman's uterus, where one or more may implant in the uterine lining and develop. Initially, IVF was used to treat women with blocked, damaged, or absent fallopian tubes. For more information on this type of infertility, refer to the ASRM patient information booklet titled *Tubal Factor Infertility*. Today, IVF is used to treat many causes of infertility, such as *endometriosis* and *male factor*, or when a couple's infertility is unexplained.

The basic steps in an IVF treatment cycle are *ovarian stimulation*, *egg retrieval*, *insemination*, fertilization, *embryo culture*, and *embryo transfer*.

Ovarian Stimulation

During ovarian stimulation, also known as *ovulation induction*, ovulation drugs, or "fertility drugs," are used to stimulate the ovaries to produce multiple eggs rather than the single egg that normally develops each month. Multiple eggs are needed because some eggs will not fertilize or develop normally after egg retrieval. Pregnancy rates are higher when more than one egg is fertilized and transferred to the uterus during an IVF treatment cycle. At present, IVF is rarely performed without the use of ovulation drugs (Table 1).

Table 1

Medications for Ovarian Stimulation

• human menopausal gonadotropins (hMG) (Pergonal®, Humegon™, Repronex™)
• follicle stimulating hormone (FSH) (Follistim™, Gonal-F®, Bravelle™)
• human chorionic gonadotropin (hCG) (Profasi®, APL®, Pregnyl®, Novarel™, Ovidrel®)
• clomiphene citrate (Clomid®, Serophene®)

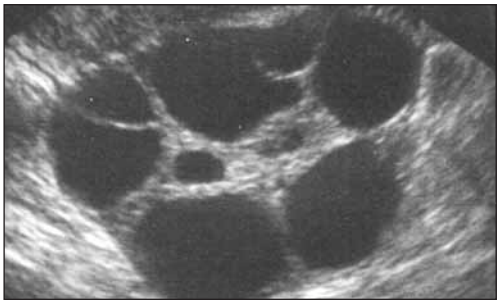
Medications to Prevent Premature Ovulation

• GnRH agonists (Lupron® and Synarel®)
• GnRH antagonists (Antagon® and Cetrotide®)

Drug type and dosage vary depending on the program and the patient. Most often, ovulation drugs are given over a period of eight to 14 days. Ovulation drugs include *clomiphene citrate*, *human menopausal gonadotropins (hMG)*, follicle stimulating hormone (FSH), *recombinant FSH and LH*, and *human chorionic gonadotropin (hCG)*. *Gonadotropin releasing hormone (GnRH) agonists* or *GnRH antagonists* are used in conjunction with these medications to prevent premature ovulation.

Clomiphene citrate is administered orally while the other medications are given by injection. Clomiphene citrate is less potent than injectable medications and is not as commonly used in ART cycles. There is no evidence that one injectable medication is superior to any other. For further information, consult another booklet in the ASRM patient information series titled *Ovulation Drugs*. Timing is crucial in an IVF cycle. The ovaries are evaluated during treatment with vaginal *ultrasound* examinations to monitor the development of ovarian follicles (Figure 2). Blood samples may be drawn to measure response to ovulation drugs. Normally, estrogen levels increase as the follicles develop, and *progesterone* levels are low until after ovulation.

Figure 2



Ovarian follicles, stimulated by ovulation drugs, visible on ultrasound. The dark, circular areas are the follicles.

Using ultrasound examinations and blood testing, the physician can determine when the follicles are appropriate for egg retrieval. Generally, eight to 14 days of FSH and/or HMG injections are required. When the ovaries are ready, hCG or other medications are given. The hCG replaces the woman's natural LH surge and helps the eggs to mature so they may be capable of being fertilized. The eggs are retrieved before ovulation occurs, usually 34 to 36 hours after the hCG injection is given. However, 10% to 20% of cycles are cancelled prior to the hCG injection.

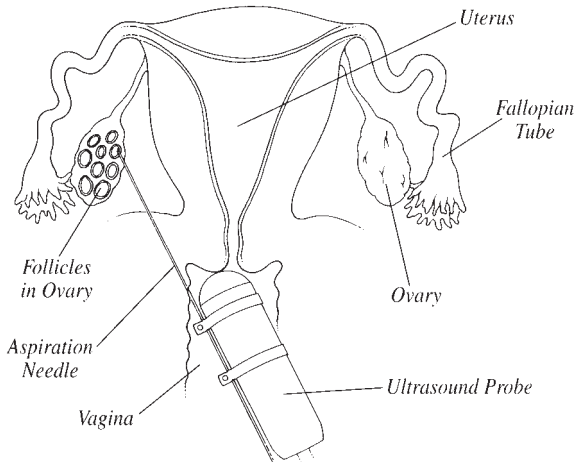
IVF cycles may be cancelled for a variety of reasons, usually due to an inadequate number of follicles developing. Cancellation rates due to low response to the ovulation drugs increase with age, especially after age 35. When cycles are cancelled due to a poor response, alternate drug strategies may be helpful to promote a better response in a future attempt. Occasionally, a cycle may be cancelled to reduce the risk of severe *ovarian hyperstimulation syndrome (OHSS)*.

Treatment with a GnRH agonist or antagonist prevents the release of LH and FSH from the pituitary gland, and thereby reduces the risk of premature ovulation. These medications are modified forms of natural GnRH. However, ovulation occurs spontaneously in a small percentage of ART stimulation cycles, despite the use of these drugs. When this occurs, the eggs may be lost in the pelvic cavity, and the cycle is usually cancelled.

Egg Retrieval

Egg retrieval is usually accomplished by *transvaginal ultrasound aspiration*, a minor surgical procedure that can be performed in the physician's office or outpatient center. Some form of anesthesia is generally administered. An ultrasound probe is inserted into the vagina to identify the mature follicles, and a needle is guided through the vagina and into the follicles (Figure 3). The eggs are

Figure 3



Egg retrieval is usually performed through the vagina with an ultrasound-guided needle.

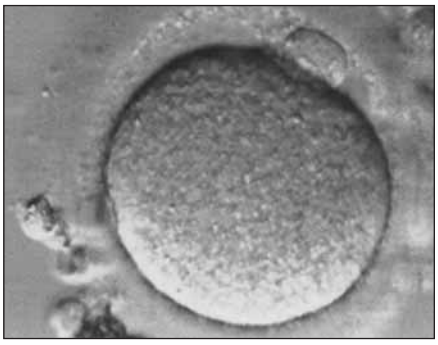
aspirated (removed) from the follicles through the needle connected to a suction device. The egg retrieval is usually completed within 30 minutes. Some women experience cramping on the day of the retrieval, but this sensation usually subsides by the next day. Feelings of fullness and/or pressure may last for several weeks following the procedure because the ovaries remain enlarged.

In some circumstances, one or both ovaries may not be accessible by transvaginal ultrasound. *Laparoscopy* may then be used to retrieve the eggs. For more information on laparoscopy, consult the ASRM patient information booklet titled *Laparoscopy and Hysteroscopy*.

Insemination, Fertilization, and Embryo Culture

After the eggs are retrieved, they are examined in the laboratory. The best quality, mature eggs (Figure 4) are placed in *IVF culture medium* and transferred to an incubator to await fertilization by the sperm.

Figure 4



A mature, unfertilized egg.

Sperm, obtained by ejaculation or a special condom used during intercourse, are separated from the semen in a process known as *sperm preparation*. *Motile* sperm are then placed together with the eggs, in a process called insemination, and stored in an incubator. Fertilization occurs in the laboratory when the sperm cell penetrates the egg, usually within hours after insemination.

When rates of fertilization are expected to be poor, fertilization may be achieved in the IVF laboratory using specialized *micromanipulation* techniques. *Intracytoplasmic sperm injection (ICSI)*, the most commonly used method, is a procedure in which a single sperm is injected directly into the egg in an attempt to achieve fertilization (Figure 5). In the United States, ICSI is performed in approximately 40% of all ART cycles.

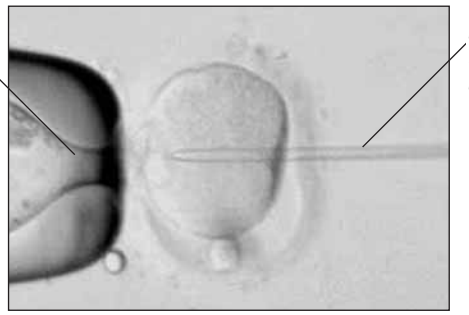
Overall, pregnancy and delivery rates with ICSI are similar to the rates seen with traditional IVF. Genetic counseling is advisable before ICSI if inherited abnormalities are identified that may be passed from father to son. For more information, see the ASRM Fact Sheet titled *Intracytoplasmic Sperm Injection*.

Visualization of two *pronuclei* the following day confirms fertilization of the egg. One pronuclei is derived from the egg and one from the sperm. Approximately 40% to 70% of the mature eggs will fertilize after insemination or ICSI. Lower rates may occur if the sperm and/or egg quality are poor. Occasionally, fertilization does not occur at all.

Two days after the egg retrieval, the fertilized egg has divided to become a 2-to 4-cell embryo (Figure 6). By the third day, the embryo will contain approximately six to 10 cells. By the fifth day, a fluid cavity forms in the embryo, and the placenta and fetal tissues begin to develop. An embryo at this stage is called a *blastocyst*.

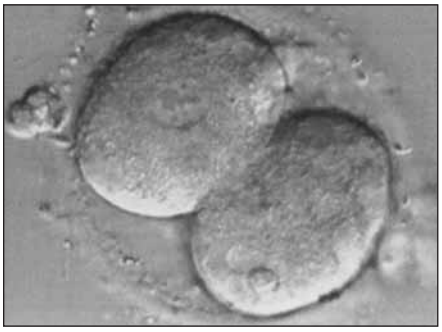
Embryos may be transferred to the uterus at any time between one to six days after the egg retrieval. If successful development continues in the uterus, the embryo hatches from the surrounding *zona pellucida* and implants into the lining of the uterus approximately six to 10 days after the egg retrieval.

Figure 5



Intracytoplasmic sperm injection (ICSI), in which a sperm is injected directly into an egg to facilitate fertilization.

Figure 6



A fertilized egg that has divided once and is now a two-cell embryo.

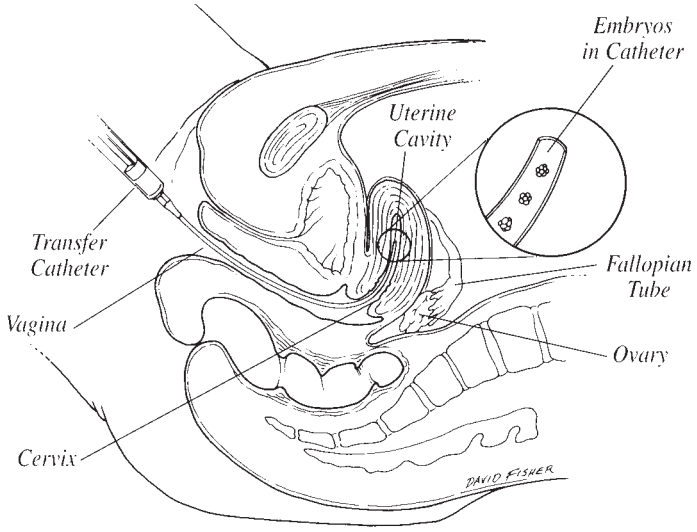
Assisted hatching (AH) is a micromanipulation procedure in which a hole is made in the zona pellucida just prior to embryo transfer to facilitate hatching of the embryo. AH may improve pregnancy rates for older women or couples who have failed prior IVF attempts. Although AH may improve embryo implantation and pregnancy rates in these circumstances, there is no clear benefit in younger IVF patients.

Preimplantation genetic diagnosis (PGD) is performed at some centers to screen for inherited diseases. In PGD, one or two cells are removed from the developing embryo and tested for a specific genetic disease. Embryos that do not have the gene associated with the disease are selected for transfer to the uterus. These procedures require specialized equipment and experience, but may be an alternative to *amniocentesis* and pregnancy termination for genetic disorders.

Embryo Transfer

The next step in the IVF process is the embryo transfer. No anesthesia is necessary, although some women may wish to have a mild sedative. The physician identifies the *cervix* using a vaginal speculum. One or more embryos suspended in a drop of culture medium are drawn into a transfer catheter, a long, thin sterile tube with a syringe on one end. The physician gently guides the tip of the transfer catheter through the cervix and places the fluid containing the embryos into the uterine cavity (Figure 7). The procedure is usually painless, although some women experience mild cramping.

Figure 7



Embryo transfer is performed through the cervix.

Cryopreservation

Extra embryos remaining after the embryo transfer may be cryopreserved (frozen) for future transfer. *Cryopreservation* makes future ART cycles simpler, less expensive, and less invasive than the initial IVF cycle, since the woman does not require ovarian stimulation or egg retrieval. Once frozen, embryos may be stored for several years. However, not all embryos survive the freezing and thawing process, and the live birth rate is lower with cryopreserved embryo transfer. Couples should decide if they are going to *cryopreserve* extra embryos before undergoing IVF.

VARIATIONS OF IVF

Gamete intrafallopian transfer (GIFT) is similar to IVF, but the gametes (egg and sperm) are transferred to the woman's fallopian tubes rather than her uterus, and fertilization takes place in the tubes rather than in the lab. Another difference is that laparoscopy, a surgical procedure, is necessary to transfer the sperm and egg to the tubes. GIFT is an option only for women who have normal fallopian tubes. Some couples may consider GIFT for religious reasons because eggs are not fertilized outside the body. One limitation of GIFT is that fertilization cannot be confirmed as with IVF. Today, GIFT comprises less than 2% of ART procedures performed in the United States.

Another ART procedure is *zygote intrafallopian transfer (ZIFT)*. This technique differs from GIFT in that fertilization takes place in the lab rather than the fallopian tube, but is similar in that the fertilized egg is transferred to the tube rather than the uterus. This procedure also requires a laparoscopy. Today, ZIFT comprises less than 1.5% of ART cases performed in the United States.

SUCCESS RATES

The most recent rates for individual IVF programs in the United States are available on the Internet from the Centers for Disease Control and Prevention: cdc.gov/nccdphp/drh/arts/index.htm. Although this information is readily available, the results should be interpreted carefully. The success rates of an IVF center depend upon a number of factors, and a comparison of clinic success rates may not be meaningful because patient characteristics and treatment approaches vary from clinic to clinic. For example, the type of patients accepted into the program and the numbers of embryos transferred per cycle affects the program's statistics. Statistics calculated on small numbers of cycles may not be accurate. An IVF center's rates may change dramatically over time, and the CDC's compiled statistics may not represent a program's current success.

It is important to understand the definitions of pregnancy rates and live birth rates. For example, a pregnancy rate of 40% does not mean that 40% of women took babies home. Pregnancy does not always result in live birth, and even the word "pregnancy" has more than one meaning. A *biochemical pregnancy* is common after IVF. This is a pregnancy confirmed by blood or urine tests but not

by ultrasound, because the pregnancy miscarries before it is far enough along to show up on ultrasound. A *clinical pregnancy* is one in which the pregnancy is seen with ultrasound, but miscarriage may still occur. Therefore, when comparing the "pregnancy" rates of different clinics, it is important to know which type of pregnancy is being compared.

Most couples are more concerned with a clinic's live birth rate, which is the probability of delivering a live baby per IVF cycle started. Pregnancy rates, and more importantly live birth rates, are influenced by a number of factors, especially the woman's age. In the United States, the live birth rate for each IVF cycle started is approximately 30% to 35% for women under age 35; 25% for women ages 35 to 37; 15% to 20% for women ages 38 to 40; and 6% to 10% for women over 40. Live birth rates for GIFT and ZIFT are comparable to IVF.

Donor Sperm, Eggs, and Embryos

IVF may be done with a couple's own eggs and sperm or with donor eggs, sperm, or embryos. A couple may choose to use a donor if there is a problem with their own sperm or eggs, or if they have a genetic disease that could be passed on to a child. Donors may be known or anonymous.

In most cases, donor sperm is obtained from a sperm bank, and sperm donors undergo extensive medical and genetic screening. The sperm are frozen and quarantined for six months, the donor is tested for sexually transmitted diseases including the AIDS virus, and sperm are only released for use if all tests are negative. Donor sperm may be used for insemination or in an ART cycle. Overall, the use of frozen sperm rather than fresh sperm does not lower success rates.

Donor eggs are an option for women with a uterus who are unlikely or unable to conceive with their own eggs. Egg donors undergo the same medical and genetic screening as sperm donors, although it is not currently possible to freeze and quarantine eggs like sperm. The egg donor may be chosen by the infertile couple or the ART program. Egg donors assume more risk and inconvenience than sperm donors. In the United States, egg donors selected by ART programs generally receive monetary compensation for their participation.

Egg donation is more complex that sperm donation and is done as part of an IVF procedure. The egg donor must undergo ovarian stimulation and egg retrieval. During this time, the recipient (the woman who will receive the eggs after they are fertilized) receives hormone medications to prepare her uterus for pregnancy. After the retrieval, the donor's eggs are fertilized by sperm from the recipient's partner and transferred to the recipient's uterus. The recipient will not be genetically related to the child, but she will carry the pregnancy and give birth.

Egg donation is expensive because donor selection, screening, and treatment add additional costs to the IVF procedure. However, the relatively high live birth rate for egg donation, between 40% to 45% nationally, provides many couples with their best chance for success. Overall, donor eggs are used in nearly 10% of all ART cycles.

In some cases, when both the man and woman are infertile, both donor sperm and eggs have been used. Donor embryos may also be used in these cases. Some IVF programs allow couples to donate their unused frozen embryos to other infertile couples.

The use of donor sperm, eggs, or embryos is a complicated issue that has lifelong implications. Talking with a trained counselor who understands donor issues can be very helpful in the decision-making process. Many programs have a mental health professional on staff or the physician may recommend one. If a couple knows the donor, their physician may suggest that both the couple and the donor speak with a counselor and an attorney. Some states require an attorney to file paperwork for the couple with the court when donor gametes or embryos are used.

Surrogacy/Gestational Carrier

A pregnancy may be carried by the egg donor (*surrogate*) or by another woman (*gestational carrier*). If the embryo is to be carried by a surrogate, pregnancy may be achieved through insemination alone or through ART. The surrogate will be biologically related to the child. If the embryo is to be carried by a gestational carrier, the eggs are removed from the infertile woman, fertilized with her partner's sperm, and transferred into the gestational carrier's uterus. The gestational carrier will not be genetically related to the child. All parties benefit from psychological and legal counseling before pursuing surrogacy or a gestational carrier.

Risks of ART

The medical risks of ART depend upon each specific step of the procedure. The following are some of the primary risks of ART procedures.

Ovarian stimulation carries with it a risk of hyperstimulation, where the ovaries become swollen and painful. Fluid may accumulate in the abdominal cavity and chest, and the patient may feel bloated, nauseated, and experience vomiting or lack of appetite. At least 30% of patients undergoing ovarian stimulation have a mild case of OHSS that can be managed with over-the-counter painkillers and a reduction in activity. In moderate OHSS, patients develop or accumulate fluid within the abdominal cavity, and gastrointestinal symptoms may occur. These women are monitored closely, but generally do very well with simple outpatient management. The condition tends to resolve without intervention unless pregnancy occurs, in which case recovery may be delayed for several weeks. One or two percent of patients develop severe OHSS characterized by excessive weight gain, fluid accumulation in the abdomen and chest, electrolyte abnormalities, over concentration of the blood, and rarely the development of blood clots or kidney failure. It may be medically necessary to drain fluid from the abdomen with a needle if breathing becomes difficult. Patients with severe OHSS require hospitalization until the symptoms improve.

Although initial reports suggested that women who use fertility drugs have an increased risk for ovarian cancer, numerous recent studies support the conclusion that fertility drugs are not linked to ovarian cancer. Nevertheless, there is still uncertainty whether a risk exists and research continues to address this question. An annual gynecologic visit is recommended for all women, with examination of the ovaries, regardless of prior use of ovulation medications.

There are risks related to the egg retrieval procedure. Laparoscopy carries with it the risks of any surgery that requires anesthesia. Removing eggs through an aspirating needle entails a slight risk of bleeding, infection, and damage to the bowel, bladder, or a blood vessel. This is true whether the physician uses laparoscopy or ultrasound to guide the needle. Less than one patient in 1,000 will require major surgery to repair damage from complications of the egg retrieval procedure. In rare cases, the uterus may be punctured during embryo transfer, or an infection may occur after the embryo has been transferred.

The chance of multiple pregnancy is increased in all assisted reproductive technologies when more than one embryo is transferred. Although some would consider twins a happy result, there are many problems associated with multiple births, and problems become progressively more severe and common with triplets and each additional fetus thereafter. Women carrying a multiple pregnancy may need to spend weeks or even months in bed or in the hospital in an attempt to delay premature delivery. The risk of premature delivery in multiple pregnancies is high, and babies may be born too early to survive. Premature babies require prolonged and intensive care and risk lifelong handicaps due to premature birth. Some couples may consider *multifetal pregnancy reduction* to decrease the risks due to multiple pregnancy, but this is likely to be a difficult decision. For more information on this topic, refer to the ASRM Patient Information Booklet titled *Multiple Gestation* and the ASRM Fact Patient Sheet *Complications of Multiple Gestation*. Data also suggest that IVF conceptions, even singletons, have a slightly increased risk of premature delivery or low birth weight.

First trimester bleeding may signal a possible miscarriage or *ectopic pregnancy*. If bleeding occurs, a medical evaluation is needed to determine the cause. Some evidence suggests that early bleeding is more common in women who undergo IVF and GIFT and is not associated with the same poor prognosis as it is in women who conceive spontaneously.

Miscarriage may occur after ART, even after ultrasound identifies a pregnancy in the uterus. Miscarriage occurs after ultrasound in nearly 15% of women younger than age 35, in 25% at age 40, and in 35% at age 42 after ART procedures. In addition, there is approximately a 5% chance of ectopic pregnancy with ART.

It is not clear whether the risk of birth defects is increased with IVF. Most studies do not show an increased risk, but several studies do. Research is ongoing to determine the magnitude, if any, of this risk. Furthermore, when ICSI is used in cases of severe male factor infertility, the genetic cause of male infertility may be passed on to the offspring.

Assisted reproductive technologies involve a significant physical, financial, and emotional commitment on the part of the couple. Psychological stress is common, and some couples describe the experience as an emotional roller coaster. The treatments are involved and costly. Patients have high expectations, yet failure is common in any given cycle. Couples may feel frustrated, angry, isolated, and resentful. At times, this feeling of frustration leads to depression and feelings of low self-esteem, especially in the immediate period following a failed ART attempt. The support of friends and family members is very important at this time. Couples are encouraged to consider psychological counseling as an additional means of support and stress management. Many programs have a mental health professional on staff to help couples deal with the grief, tension, or anxieties associated with infertility and its treatment.

Preparation For ART

Preliminary preparation for an ART procedure may be as important as the procedure itself. Testing for *ovarian reserve* may be recommended in order to predict how the ovaries will respond to fertility medication. The chance of success may be poor, for example, if blood tests demonstrate diminished ovarian reserve or fertility potential. Ovarian reserve may be determined by measuring FSH and estradiol levels at the beginning of the menstrual cycle or performing a *clomiphene challenge test*. An elevated FSH and/or estradiol level is associated with reduced pregnancy rates. Uterine cavity abnormalities such as *fibroids*, *polyps*, or a *septum* may need to be corrected before IVF or GIFT. A *hydrosalpinx*, a fluid-filled, blocked fallopian tube, reduces IVF success, and some physicians advise opening or removing the affected tube prior to IVF. For more information, see the ASRM Patient Fact Sheet titled *Hydrosalpinx*.

Semen is tested before ART. If semen abnormalities are identified, consultation with a specialist in male infertility should determine if there are correctable problems or underlying health concerns. For example, genetic abnormalities in the Y chromosome have been linked to some cases of male infertility, and men born without a *vas deferens*, a tube that transports sperm from the testicle, are often carriers of a gene that causes cystic fibrosis. In these circumstances, genetic testing may be advisable.

Major advances have been made in the treatment of male infertility, and IVF may help some men who were previously considered sterile. Detailed consultation with a specialist in male infertility who works directly with an IVF program is essential. When sperm cannot be collected by masturbation, *electroejaculation (EEJ)*, *microepididymal sperm aspiration (MESA)*, *percutaneous epididymal sperm aspiration (PESA)*, or *testicular sperm extraction (TESE)* may be effective methods to collect sperm for IVF. EEJ may be an effective way to collect sperm from men with spinal cord injuries. During EEJ, electrical impulses from a probe placed in the rectum near the prostate often accomplish ejaculation. MESA can be performed to recover sperm after vasectomy or failed

vasectomy reversal and in some men with absence of the vas deferens. TESE involves testicular biopsy and recovery of sperm directly from testicular tissue and may be performed in an office setting with local anesthesia. Sperm obtained by these methods may be frozen, stored, and thawed later for ART.

Lifestyle issues should be addressed before ART. Smoking, for example, may lower a woman's chance of success by as much as 50%. All medications, including over-the-counter supplements, should be reviewed since some may have detrimental effects. Alcohol and drugs may be harmful, and excessive caffeine consumption should be avoided. Because folic acid taken prior to pregnancy reduces the risk of neural tube defects such as *spina bifida*, women should take prenatal vitamins containing at least 400 micrograms of folic acid before beginning an ART cycle. A complete exam and Pap smear may identify problems that should be treated before pregnancy.

A detailed examination of ART insurance benefits is helpful. Even if ART is excluded from a policy, coverage may be available for some aspects of these procedures. Couples should consult their companies' benefits director in advance, since options such as a medical savings account may be available. It is also important to determine the costs for the ART treatment cycle. Keep in mind that fees for initial consultation, screening tests, medications, and special procedures such as ICSI and cryopreservation may not be included in the estimate. Other expenses to consider include travel, lodging, and time missed from work.

Selecting an ART Program

When selecting an ART program, information is crucial. Important points for consideration include the qualifications and experience of personnel, types of patients being treated, support services available, cost, convenience, live birth rates per ART cycle started, and multiple pregnancy rates. Older programs have established live birth rates based on years of experience. Small and new programs may still be determining their live birth rates, although their personnel may be equally well qualified.

Every couple wants to use the most successful ART program, but many factors contribute to the overall success of a program. For example, some clinics may be willing to accept patients with a low chance of success. A clinic may specialize in certain types of infertility treatment. Costs may vary between programs. A couple may prefer a program based upon interpersonal interactions with the ART team or may feel more confident in the recommended treatment plan. Consequently, it may not always be appropriate to compare programs based only on the published pregnancy rates.

Credibility is important too. Does the program adhere to the guidelines set forth by the *American Society for Reproductive Medicine (ASRM)*? Is the program a member of the *Society for Assisted Reproductive Technology (SART)*, a society affiliated with the ASRM? Is the IVF lab accredited by the College of American Pathologists and SART or by the Joint Commission on Accreditation of Healthcare

Organizations? These organizations require ART programs to have personnel on their staff who have been trained in reproductive endocrinology, laparoscopic surgery, sonography, hormone measurement, tissue culture technique, and sperm/egg interaction. Are the physicians board certified in reproductive endocrinology and infertility? Does the program report its results to the *SART Registry* and the *Centers for Disease Control and Prevention*? The compiled results from the registry are published annually in *Fertility and Sterility*, the ASRM journal, and results are available on the CDC's Web site at www.cdc.gov/nccdphp/drh/art.htm.

The above considerations and answers to the following questions, which may be asked of the program, will help you make an informed decision when choosing an IVF/GIFT program.

Cost and Convenience

- What pre-cycle screening tests are required, how much do they cost, and will my insurance provide coverage for these tests?
- How much does the ART procedure cost, including drugs per treatment cycle?
- Do I pay in advance? How much? What are the methods of payment?
- If applicable, will you submit any bills to my insurance company?
- How much do I pay if my treatment cycle is canceled before egg recovery? Before embryo transfer?
- What are the costs for embryo freezing, storage, and transfer?
- How much work will I miss? How much will my partner miss?
- Do you help arrange low-cost lodging, if needed?

Details About the Program

- Does the program meet and follow ASRM guidelines?
- Does the program report its results to the SART Registry and the CDC?
- Is the program a member of the Society for Assisted Reproductive Technology?
- How many physicians will be involved in my care?
- Are one or more physicians board certified in reproductive endocrinology?
- To what degree can my own physician participate in my care?
- What types of counseling and support services are available?
- Whom do I call day or night if I have a problem?
- Do you freeze embryos (cryopreservation)?
- Is donor sperm available in your program? Donor eggs? Donor embryos?
- Do you have an age or basal FSH limit?
- Do you do ICSI? If so, when? Cost?
- Do you do assisted hatching? If so, when? Cost?
- How many eggs/embryos are transferred?

Success of the Program

The CDC is a very good source of information to obtain ART outcomes for each reporting program in the United States. This information is two to three years old, so it is important to find out if there have been any significant changes in the program since the most recent report including:

- Personnel changes.
- Changes in the approach to ovarian stimulation, egg retrieval, embryo culture, or embryo transfer.
- Change in the number of cycles.
- Change in the miscarriage rate, live birth rate per cycle started, or the multiple pregnancy rate.

If a program cites a live birth rate for each procedure, be sure that the program representative counts twins as one successful pregnancy, not two. When discussing recent ART program outcomes, keep in mind that the live birth rate may vary depending on the denominator used – i.e., per cycle started, per retrieval, or per embryo transfer. For example, live birth rates per egg retrieval do not consider cancelled cycles, and rates based per embryo transfer do not include cancelled cycles or fertilization failures. Therefore, live birth rates per cycle are higher per egg retrieval and are highest per embryo transfer.

When to End Treatment

Studies indicate that the chance for pregnancy in consecutive IVF cycles remains similar in up to four cycles. However, many other factors should be considered when determining the appropriate endpoint in therapy, including financial and psychological reserves. Members of the IVF team can help couples decide when to stop treatment and discuss other options such as egg and/or sperm donation or adoption, if appropriate. The physician, support groups, and other couples undergoing infertility treatment can provide valuable support and guidance.

Conclusion

The decision to seek treatment for infertility is a viable one due to the assisted reproductive technologies available today. With patience, a positive attitude, and the appropriate treatment, many infertile couples will eventually experience the joys 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

American Society for Reproductive Medicine (ASRM). A professional medical organization of more than 10,000 health care professionals dedicated to reproductive medicine.

Amniocentesis. A procedure in which a small amount of amniotic fluid is removed through a needle from the fetal sac at about 16 weeks into a pregnancy. The fluid is studied for chromosomal abnormalities which may affect fetal development.

Assisted hatching (AH). A procedure in which the zona pellucida (outer covering) of the embryo is partially opened, usually by application of an acid, to facilitate embryo implantation and pregnancy.

Assisted reproductive technology (ART). All treatments which include the handling of eggs 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).

Biochemical pregnancy. When a patient's pregnancy test is initially positive but becomes negative before a fetus is visible on ultrasound.

Blastocyst. An embryo that has formed a fluid-filled cavity, and the cells begin to form the early placenta and embryo, usually 5 days after ovulation or egg retrieval.

Centers for Disease Control and Prevention. Federal agency for protecting the health and safety of people at home and abroad, providing credible information to enhance health decisions, and promoting health through strong partnerships.

Cervical canal. The passageway leading from the vagina into the uterus.

Cervical mucus. The substance in the cervix through which sperm must swim in order to enter the uterus.

Cervix. The narrow, lower end of the uterus that connects the uterine cavity to the vagina.

Clinical pregnancy. A pregnancy confirmed by an increasing level of human chorionic gonadotropin (hCG) and the presence of a gestational sac detected by ultrasound.

Clomiphene challenge test (CCCT). A test of ovarian reserve in which serum FSH is checked on days three and 10 of the menstrual cycle and clomiphene citrate is taken on days five through nine.

Clomiphene citrate. An oral antiestrogen drug used to induce ovulation. Clomid® and Serophene® are brand names.

Cryopreservation. Freezing at a very low temperature, such as in liquid nitrogen (-196°C) to keep embryos, eggs, or sperm viable.

Croypreserved. Frozen.

Ectopic pregnancy. A pregnancy in the fallopian tube or elsewhere outside the lining of the uterus.

Egg (oocyte). The female sex cell (ovum) produced by the ovary, which, when

fertilized by a male's sperm, produce embryos.
Egg retrieval. The procedure in which eggs are obtained by inserting a needle into the ovarian follicle and removing the fluid and the egg by suction. Also called oocyte aspiration.
Electroejaculation (EEJ). Procedure to cause ejaculation of sperm, performed by electrical stimulation of tissue in the region of the prostate.
Embryo. A fertilized egg that has begun cell division.
Embryo culture. Growth of the embryo in a laboratory (culture) dish.
Embryo transfer. Placement of an embryo into the uterus or, in the case of ZIFT and TET, into the fallopian tube.
Endometriosis. A disease in which tissue resembling endometrium (the lining of the uterus) grows outside the uterus. It is often associated with infertility.
Estradiol. The predominant estrogen (hormone) produced by the follicular cells of the ovary.
Estrogen. The female hormone largely responsible for thickening the uterine lining during the first half of the menstrual cycle in preparation for ovulation and possible pregnancy. Estradiol is the main estrogen.
Fallopian tubes. A pair of tubes attached to the uterus, one on each side, where sperm and egg meet in normal conception.
Fertilization. The fusion of sperm and egg.
Fibroids. Benign (non-cancerous) tumors of the uterine muscle wall that can cause abnormal uterine bleeding.
Follicle. A fluid-filled sac in the ovary containing an egg and the surrounding cells that produce hormones. As the follicle matures, the fluid can be visualized by ultrasound.
Follicle stimulating hormone (FSH). The pituitary hormone responsible for stimulating the growth of the follicle that surrounds the egg. In addition, the hormone in injectable ovulation drugs that promotes growth of the follicles.
Gamete intrafallopian transfer (GIFT). The direct transfer of sperm and eggs into the fallopian tube. Fertilization takes place inside the tube.
Gestational carrier. A woman who carries a pregnancy for another couple. The pregnancy is derived from the egg and sperm of the couple. Although she carries the pregnancy to term she has neither a genetic relationship nor rearing rights or responsibilities to the resulting child.
Gonadotropin releasing hormone (GnRH). Hormone secreted by the hypothalamus, a control center in the brain, that prompts the pituitary gland to release FSH and LH into the bloodstream.
GnRH agonists. A GnRH analog that initially stimulates the pituitary gland to release LH and FSH, followed by a delayed suppressive effect. They are also used to help stimulate follicle growth when started at the beginning of an IVF cycle.
GnRH analogs. Synthetic hormones similar to the naturally occurring gonadotropin releasing hormone used to prevent premature ovulation. There are two types of GnRH analogs: GnRH agonists and GnRH antagonists.

GnRH antagonists. Synthetic hormones similar to the naturally occurring gonadotropin releasing hormone used to prevent premature ovulation. These medications have an immediate suppressive effect on the pituitary gland.
Human chorionic gonadotropin (hCG). A hormone produced by the placenta; its detection is the basis for most pregnancy tests. Also refers to the medication used during ovulation induction to cause ovulation and the final stages of egg maturation.
Human menopausal gonadotropin (hMG). An ovulation drug that contains follicle stimulating hormone (FSH) and luteinizing hormone (LH) derived from the urine of postmenopausal women. hMG is used to stimulate the growth of multiple follicles.
Hydrosalpinx. A blocked, dilated, fluid-filled fallopian tube.
Intracytoplasmic sperm injection (ICSI). A micromanipulation procedure in which a single sperm is injected directly into an egg to attempt fertilization, used with male infertility or couples with prior IVF fertilization failure.
Insemination. Placement of sperm into the uterus or cervix for producing a pregnancy, or adding sperm to eggs in IVF procedures.
In vitro fertilization (IVF). A process in which an egg and sperm are combined in a laboratory dish to facilitate fertilization. If fertilized, the resulting embryo is transferred to the woman's uterus.
IVF culture medium. A special fluid into which sperm, eggs, and embryos are placed when outside the human body.
Laparoscopy. A surgical procedure that allows viewing of the internal pelvic organs. During the procedure, a long narrow fiberoptic instrument, called a laparoscope, is inserted through an incision in or below the woman's navel. One or two other incisions may be made for inserting additional instruments.
Luteinizing hormone (LH). The pituitary hormone that normally causes ovulation and maturation of the egg.
Male factor. Infertility caused by a problem in the male, for example, inability of ejaculate or insufficient number of sperm.
Microepididymal sperm aspiration (MESA). Outpatient microsurgical procedure used to collect sperm in men with blockage of the male reproductive ducts such as prior vasectomy or absence of the vas deferens. Used in IVF-ICSI procedures.
Micromanipulation. The IVF laboratory process whereby the egg or embryo is held with special instruments and surgically altered by procedures such as intracytoplasmic sperm injection (ICSI), assisted hatching, or embryo biopsy.
Motile. Moving.
Multifetal pregnancy reduction. Also known as selective reduction. A procedure to reduce the number of fetuses in the uterus. This procedure is sometimes performed on women who are pregnant with multiple fetuses who are at an increased risk of late miscarriage or premature labor. These risks increase with the number of fetuses.
Oocyte. Medical term for egg, the female gamete. Also called ova.
Ovarian hyperstimulation syndrome (OHSS). A condition that may result from

ovulation induction characterized by enlargement of the ovaries, fluid retention, and weight gain.

Ovarian reserve. A woman's fertility potential in the absence of specific pathophysiologic changes in her reproductive system. Diminished ovarian reserve is associated with depletion in the number of eggs and worsening of oocyte quality.

Ovarian stimulation. See Ovulation induction.

Ovary (Ovaries). 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.

Ovulation. Release of an egg from the ovary.

Ovulation induction. The administration of hormone medications (ovulation drugs) that stimulate the ovaries to produce multiple eggs. Sometimes called enhanced follicular recruitment or controlled ovarian hyperstimulation.

Percutaneous epididymal sperm aspiration (PESA). A sperm aspiration procedure in which a needle is inserted into the epididymis (gland that carries sperm from testicle to vas deferens) in order to retrieve sperm for use in an IVF procedure.

Pituitary gland. A small gland just beneath the hypothalamus in the brain that secretes follicle stimulating hormone (FSH) and luteinizing hormone (LH).

Polyps. A general term that describes any mass of tissue which bulges or projects outward or upward from the normal surface level.

Preimplantation genetic diagnosis (PGD). A test performed by an embryologist in which one or two cells are removed from an embryo. The removed cells are then screened for genetic abnormalities. PGD may be performed in conjunction with IVF.

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

Pronuclei. The nucleus of a male or female gamete (egg or sperm) seen in the one cell embryo (zygote).

SART Registry. An ongoing collection of IVF results from participating clinics developed and maintained by SART, a society affiliated with the ASRM.

Septum, uterine. A band of fibrous tissue present from birth that forms a wall extending from the top of the uterine cavity. A septum may increase the risk of miscarriage and other pregnancy complications.

Semen. The fluid in which sperm are located.

Society for Assisted Reproductive Technology (SART). A society affiliated with the ASRM and comprised of representatives from assisted reproductive technology programs who have demonstrated their ability to perform IVF.

Sperm. The male reproductive cells that fertilize a woman's egg. The sperm head carries genetic material (chromosomes), the midpiece produces energy for movement, and the long, thin tail wiggles to propel the sperm.

Sperm preparation. A procedure to remove seminal fluid from sperm cells.

Spina bifida. A birth defect of the spinal column. Spina bifida is the failure of the spine to close properly during development.
Surrogate. A woman who carries a pregnancy intended for another family.
Testicular sperm extraction (TESE). Operative removal of testicular tissue in an attempt to collect living sperm for use in an IVF-ICSI procedure.
Transvaginal ultrasound aspiration. An ultrasound guided technique for egg retrieval whereby a long, thin needle is passed through the vagina into the ovarian follicle and suction is applied to accomplish retrieval.
Tubal embryo transfer (TET). A process where an early stage embryo is transferred to the fallopian tube.
Ultrasound. A technology that uses high-frequency sound waves to form an image of internal organs on a monitor screen; used by fertility specialists to monitor the growth of ovarian follicles and to retrieve the eggs from the follicles and evaluate a pregnancy.
Uterus (womb). The hollow, muscular female reproductive 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 canal in the female that leads to the cervix, which leads to the uterus.
Vas deferens. The two muscular tubes that carry sperm from the epididymis to the urethra.
Zona pellucida. The egg's outer layer that a sperm must penetrate in order to fertilize the egg.
Zygote. A fertilized egg before cell division (cleavage) begins.
Zygote intrafallopian transfer (ZIFT). An egg is fertilized in the laboratory and the zygote is transferred to the fallopian tube at the pronuclear stage before cell division takes place. The eggs are retrieved and fertilized on one day and the embryo is transferred the following day.

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

Booklets available for purchase through the
American Society for Reproductive Medicine Patient Information Series:

____*Abnormal Uterine Bleeding (1996)*
____*Adoption (1996)*
____*Age and Fertility (2003)*
____*Assisted Reproductive Technologies (2003)*
____*Birth Defects of the Female Reproductive System (1993)*
____*Donor Insemination (1996)*
____*Ectopic Pregnancy (1996)*
____*Endometriosis (1995)*
____*Endometriosis (Spanish Translation) (2003)*
____*Fertility After Cancer Treatment (1995)*
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For copies, ask your physician or contact the ASRM at the address below.

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