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Infertility

*A guide to help couples build
healthy families[®]*



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For couples who are having difficulties conceiving a child, infertility can be a challenging time. Fortunately, there are many tests and tools physicians can use to identify and overcome reproductive barriers.

This guide is intended to help explain infertility and the latest treatment options available.

How is infertility defined?

An infertile couple is one that has been unable to become pregnant after one year of trying. About 20% of couples who are trying to become pregnant will be successful in the first month; 50% after 3 months of trying; 75% after 6 months of trying; and 85-90% after 12 months of trying. About 10-13% of couples do not get pregnant even after a year of trying. With more and more women delaying child-bearing because of careers and other life choices, infertility is on the rise.

Effects of the Mother's Age on Pregnancy Rates

Age Group	Pregnancy Rate (within 12 Months of trying)
20-24	86 percent
25-29	78 percent
30-34	63 percent
35-39	52 percent

How should you decide when to go for an evaluation for infertility?

This depends on your age. Although infertility is defined as not becoming pregnant after a year of trying, some couples should be evaluated before one year of trying has passed. If you are less than 35 years old, it is reasonable to try for one year before getting a medical evaluation. However, as a woman ages, her chances of getting pregnant decrease, and an earlier evaluation is recommended.

Age of Woman	When to seek evaluation by an infertility specialist
Less than 35 years old	After one year of trying
35-40 years old	After six months of trying
Over 40 years old	Begin evaluation immediately



Causes of Infertility

There are many different causes of infertility, and often there are several causes in one couple. These include:

- **Male factor.** In about 25-40 percent of couples, a problem with the sperm is the cause of the infertility. The problem may be the number of sperm, the shape of the sperm, or their ability to move effectively.
- **Ovulation.** In 25-30 percent of couples, there are problems with the production of the woman's egg, or ovulation. This may be the result of an abnormality in the woman's ovary (such as polycystic ovary syndrome), or other hormonal causes. These defects are treated by giving medications to stimulate ovulation.
- **Tubal defect.** Infertility is caused by an abnormality of the Fallopian tubes, the tubes that connect the ovaries to the uterus, in 20-30 percent of couples. Tubal defects can be caused by scarring from previous surgery, infection, or a previous tubal ligation ("tying of the tubes").
- **Unexplained.** There is no obvious cause of infertility in about 10-20 percent of couples.
- **Endometriosis.** This is a disorder in which pieces of the lining of the uterus implant themselves onto pelvic organs, including the Fallopian tubes, the ovaries, and sometimes even the intestines. This is the cause of infertility in 5-10 percent of couples.

Evaluation of the Infertile Couple

The goal of the initial evaluation of the couple is to determine the likely cause of the infertility, and to determine the most logical approach to treatment. Your doctor will take a careful history and order various tests.

History

Questions for the male partner	Questions for the female partner
How long have you been infertile?	How long have you been trying to get pregnant?
Have you ever fathered a child with your current or previous partners?	Have you had any prior pregnancies in this or in other relationships?
Have you had any medical problems? Any surgeries?	Have you ever had pelvic infections, endometriosis, fibroids, cervical diseases, pelvic or abdominal surgery, or used an IUD? Do you smoke cigarettes?
Are you taking any medications?	Are you taking any medications?
Do you drink alcohol, smoke marijuana or cigarettes? (Note: excessive alcohol and/or marijuana use can lead to lower testosterone levels and can decrease sperm production.)	How old were you when you got your period? Is it regular? How long are your cycles? Have you had any hot flashes?
Have you had any significant environmental exposures? For example, excessive heat exposure (saunas, hot tubs), chemical or radiation exposure?	Did your mother use DES when she was pregnant with you? (Note: DES, or diethylstilbestrol, is a medication given in the 1940s-1960s to prevent miscarriage; women whose mothers took this medication can have abnormalities of the cervix and uterus.)
Do you have any problems with your sexual function? Do you have trouble getting erections or maintaining them? Do you have problems with ejaculation?	What have you used for contraception in the past? IUDs? Oral contraceptive pills? Tubal ligation?
How frequently do you have intercourse?	How frequently do you have intercourse?
Have you had any previous infertility testing and/or treatments?	Have you had any previous infertility testing and/or treatments?

Tests

Most couples are very anxious to get started on their evaluations and treatment. Ask your primary care physician or general gynecologist to perform as many preliminary tests as soon as possible before your visit to the infertility specialist.

Male Partner

- **Semen analysis to determine sperm count**

At the beginning of the evaluation, the male partner should have a semen analysis. He should avoid ejaculation for 48 hours (but no more than six days) before providing the sample on the day of the test. The sample can either be produced at the Brigham and Women's Hospital Reproductive Endocrine Laboratory in a private lounge or he may bring in the specimen from home in a sterile plastic container. If the sample is brought from home, it cannot be more than one and a half hours old, should not have been exposed to soaps, lubricants, or condoms and must be kept warm (held against the body) until delivery. In either case, the sample should be delivered to the Brigham and Women's Hospital Reproductive Endocrine Laboratory, which is open Mondays through Fridays, 8:00 a.m. to 10:00 a.m. The results are usually available the next day. Semen that contains over 10 million normal sperm is considered adequate.

Female Partner

- **Testing for ovulation**

Several tests can be done to prove that the woman is producing an egg in her cycle. In a 28-day cycle, ovulation usually occurs on day 14 (day one is the first day of menstruation), but may occur later in women with longer cycles. Usually, ovulation occurs 14 days before the first day of menstruation, so that if a woman has 32 day cycles, ovulation would occur on day 18. In women who are over 40, cycles are often shorter, and sometimes ovulation occurs less than 14 days from the end of the cycle.

An easy way to test ovulation is with over-the-counter ovulation kits. These often cost around \$20, and contain four test strips. About two days before the predicted day of ovulation (day 12 for a 28 day cycle), you should test your urine first thing in the morning. Repeat the test for four days in a row. The day of ovulation, the color of the test strip changes from light blue to dark blue if ovulation has occurred.

- **Progesterone level.**

Another way to test for ovulation is with a blood test (serum progesterone level), which can be measured in the second half of the cycle (day 20-22 in a 28 day cycle).

- **Day Three Follicle Stimulating Hormone (FSH) level.**

This is done by testing the blood for FSH on day three of the menstrual cycle. The majority of fertile women have levels less than 10.

- **Clomiphene citrate challenge test (CCCT).**

This test is recommended for couples with unexplained infertility, and for women over age 35. This is a more sensitive ovulation test than the day three FSH test. An oral medication, clomiphene citrate (Clomid™), is taken on days five to nine of the menstrual cycle. A blood test is performed on day three and day 10 to measure FSH levels. An abnormal test is an elevated level of FSH greater than 15 on either day three or day 10. Abnormal CCCTs are more common in older women.

- **Progestin challenge test.**

This involves giving a progestin (such as medroxyprogesterone acetate), 10 mg daily for five days, after making sure that the pregnancy test is negative. The test is positive if the woman experiences vaginal bleeding within 14 days of stopping the progestin, indicating that she does have adequate estrogen secretion. If she does not have vaginal bleeding, she has low estrogen secretion from either decreased hormonal secretion by the reproductive portion of the brain (hypothalamus) or premature ovarian failure. Testing the follicle stimulating hormone (FSH) level in the blood can distinguish between these two possible diagnoses (low or normal for pituitary problem; high in premature ovarian failure).

- **Testing for thyroid function.**

Women with over- or underactive thyroids may have irregularities in their menstrual cycles. Fortunately, it is easy to test for thyroid problems by measuring the blood level of the thyroid stimulating hormone (TSH). A low level suggests an overactive thyroid, and a high level suggests that the thyroid is underactive. Both conditions are easily treated.

Additional testing that may be ordered by the fertility specialist

- **Hysterosalpingogram (HSG, or tubogram)**
This is a test to assess if the Fallopian tubes (the tubes connecting the ovaries to the uterus) are open. The test is performed under x-ray and involves injecting dye into the cervix to see if the tubes are open and whether the dye can flow freely through them. The size and the shape of the uterine cavity are also examined in this test. This test is done in the first half of the cycle, immediately after the woman's period has ended, but before ovulation. Antibiotics are routinely given for three days starting the day before the test. The test may be uncomfortable, so taking ibuprofen or Tylenol® before the test is recommended. Occasionally, the flushing of the tubes is enough to remove debris and allow a pregnancy to occur in that cycle.
- **Laparoscopy**
This is an outpatient surgery in which a magnifying scope is used to look inside the abdominal and pelvic cavity. This test is performed if endometriosis or adhesions are suspected. During the laparoscopy, the scar tissue associated with mild to moderate endometriosis can be broken up to allow for passage of eggs and sperm through the tubes.
- **Hysteroscopy**
In this procedure, a small scope is inserted into the uterus through the vagina and cervix to look at the inside of the uterus. This test is done if uterine abnormalities are seen during the HSG (tubogram) or if scar tissue or polyps are suspected.
- **Pelvic ultrasound**
An ultrasound may be ordered if enlarged uterine size or ovarian masses are noted on an exam.

Treatment Options

Intrauterine insemination (IUI).

The male partner's sperm is collected and is then injected into the female partner's cervix usually on two consecutive days at the time of ovulation. An oral medication, Clomid™, is often taken on days five to nine increasing the success rate of this treatment. IUI is most appropriate for couples with mild male factor, minimal endometriosis, or unexplained infertility with success rates ranging 2-20 percent per cycle.

Therapeutic Donor Insemination (TDI).

This treatment involves injecting sperm from an anonymous or a known donor into a woman's cervix at the time that she is ovulating. This treatment is undertaken in couples in whom the male partner has a low sperm count; in women without partners; and in lesbian couples. The use of frozen semen to prevent sexually transmitted disease is recommended by the Food and Drug Administration and the Center for Disease Control. At sperm banks, donors are tested for sexually transmitted diseases, including HIV, chlamydia, gonorrhea, syphilis, hepatitis, and others.

Commercial sperm banks are the source of donor sperm in the majority of cases. The sperm banks provide information about the physical characteristics, medical history, education, and ethnic or racial background of the donors. More recently, some donors have given permission to sperm banks to reveal their identities if requested by the child at some point in the future. Since success rates for cycles with frozen sperm are slightly less than with fresh sperm, this treatment should be continued for three to six cycles before trying another treatment.

Ovulation induction

In this process, medications are taken (oral or injectable) to stimulate the ovaries to make eggs. Women with ovulation problems caused by polycystic ovary disease (PCOD), elevated prolactin levels, absence of periods due to abnormal hormonal secretion by the reproductive portion of the brain (hypothalamus), and premature ovarian failure have good results with this treatment method. When ovulation induction is successful, pregnancy rates per cycle are close to those of normally ovulating women in their age group.

Medications to Stimulate Ovulation

Drug	Dosage	Cost	Comments
Clomiphene citrate (Clomid™)	50 to 150 mg by mouth on days 5-9 of cycle	\$5/pill, or \$15-45 per cycle	Appropriate initial treatment for patients with unexplained infertility or polycystic ovary disease. Cervical mucous can become thick on this medication, and therefore IUI is often recommended if the woman does not conceive within three cycles. There is approximately a 20-25 percent pregnancy rate per cycle. If no pregnancy occurs after 3-6 cycles, other causes of infertility should be considered. About 1 percent of women will have overstimulation of the ovaries, in which they experience pain and abdominal swelling. Multiple births (twins, triplets) occur at a rate of about 5-10 percent.
Gonadotropin therapy with human menopausal gonadotropin (Pergonal™) or purified FSH (Metrodin™, Follistim™, or Gonal-F™)	1-2 ampules injected into the muscle (administered at home by patient or partner) starting day three of cycle	Pergonal™: \$66.50/ampule Follistim™: \$85/ampule Gonal-F™: \$50/ampule \$88/ampule \$169/ampule	Requires frequent visits approximately every other day starting day seven of cycle for ultrasound measurement of follicle size and estradiol levels. When the appropriate follicle size and estrogen level are reached, a medication called hCG is administered intramuscularly and 12-36 hours later, timed intercourse or insemination should occur. Success rates: Extremely high for women with absence of periods due to hypothalamic problem (pregnancy rates of 90 percent over the course of six cycles), but slightly lower rates for women with polycystic ovaries or unexplained infertility. Not recommended for women with premature menopause due to low success rates. Complications include overstimulation of the ovaries (10-20 percent) and multiple births (25 percent, with 20 percent twins, 5 percent triplets or quadruplets).
Agents to treat elevated prolactin levels (Bromocriptine™ or Dostinex™)	Bromocriptine™: 2.5-7.5 mg tablets daily by mouth Dostinex™ 0.25-1 mg 2x/week by mouth	Bromocriptine™: \$51-154/mo. Dostinex™: \$141-\$562/mo	Causes periods to resume in 90 percent of women with elevated prolactin levels.
Metformin (Glucophage™)	500 mg po qd	\$14/mo.	Resumes ovulation in 90 percent of patients with polycystic ovary syndrome.

Assisted Reproductive Therapy

	Patients for Whom Recommended	Procedure
In vitro fertilization (IVF)	<ul style="list-style-type: none"> • Women with blocked tubes • Women with severe endometriosis • Couples with unexplained infertility • Men with low sperm counts or abnormal sperm 	Involves giving medications to increase the number of follicles. Once the eggs are mature, a hormone, hCG, is administered and 34 to 36 hours later, the woman is taken to the operating room, where the eggs are removed from her ovaries and combined with sperm in a dish. Once the eggs have fertilized, they are placed in an incubator, and then placed back in the woman's uterus three to five days later.
Cryoembryo Transfer	This is done for patients who have undergone a cycle of IVF in which excess eggs were frozen and stored.	In this procedure, the excess frozen fertilized embryos from the previous IVF may be transferred at a later time. The advantage of this procedure is that a repeat ovarian stimulation can be avoided. In addition, this procedure allows a woman who is older to use embryos that were fertilized with oocytes from when she was younger.
IVF with Donor Oocytes	<ul style="list-style-type: none"> • Women with premature ovarian failure • Women with perimenopause, or menopause • Couples who failed IVF due to problems with the egg (accounts for 50 percent of IVF failures) 	The donor may either be anonymous or selected by the couple. A legal contract is needed between the donor and the recipient couple prior to initiation of the procedure. Insurers do not cover the payment to the donor and screening of the donor.
Intracytoplasmic Sperm Injection (ICSI)	<ul style="list-style-type: none"> • Men with congenital abnormalities of the outflow tract for sperm • Men with no sperm or very low sperm counts • Men with previous vasectomy 	ICSI involves direct injection of a single sperm into the cytoplasm of an egg. Success has been reported even with non-motile and immature sperm. Success rates are the same as those reported for IVF, or about 35 percent per embryo transfer.
Gestational Carrier	<ul style="list-style-type: none"> • Women without a uterus • Women with a medical condition that preclude carrying a pregnancy to term • Male homosexual couples 	Involves IVF (see above) with transfer of the embryos to a gestational carrier, which is a woman with a uterus who will carry the pregnancy to term. To avoid custody lawsuits, when eggs are needed, use of a separate egg donor, (an individual who is different than the gestational carrier) is recommended. This is particularly important for male homosexuals or for women who lack functional ovaries or uterus, or who have a medical contraindication to pregnancy. At Brigham and Women's Hospital, surrogate carriers (women who are inseminated with the male partner's sperm, and who carry the pregnancy) are not used.

Emotional Aspects of Infertility Treatments

Infertility treatment is a physically and emotionally bewildering experience for most people and it is common to feel depression, grief, anxiety, and stress throughout the process. The frequent office visits, insurance issues, the need to juggle work with doctors' appointments, and the strain on the couple's relationship all make infertility treatments among the most stressful experiences that people can face.

Many couples and individuals experience stress, sadness, and even shame, as a result of their infertility. You and your partner may have different responses to infertility diagnosis and treatment. People have different attitudes toward letting family and friends know about the infertility, or that they are going for treatment. Support groups can be a valuable option for individuals and couples with infertility because they may help alleviate feelings of isolation, though people have different attitudes about sharing their experiences in a group. Depression is common in couples with infertility. If you or your partner is feeling depressed, or unable to carry out your normal activities because of feelings of being overwhelmed, you should speak with your physician about how you are feeling.

There are mental health providers (such as psychiatrists, social workers, and psychologists) who specialize in infertility. These therapists see individuals alone, or as a couple, and can help not only with the emotional aspects of treatment, but also offer strategies for dealing with work or home conflicts that come up because of the need for frequent testing and treatments.

Resources

There are a number of resources available to help you through this stressful process.

RESOLVE: Founded in Massachusetts, this is a self-help organization that provides support and information to couples undergoing infertility evaluation and treatment. www.resolve.org

PO Box 541553
Waltham, MA
02454-1553
Telephone: (781) 647-1614
Website: www.resolveofthebaystate.org
Email: admin@resolveofthebaystate.org

Internet sites: There is a wealth of information, and misinformation, on the web. It is important for you to review with your doctors any information gathered on the web.

Mind/Body programs: These programs focus on the feelings couples have about their infertility, and not on their treatment success or failure.

If you need a gynecologist, primary care physician, specialist, or more information on services at Brigham and Women's Hospital, call our Physician Referral Service at **1-800-BWH-9999**, Monday - Friday, 8:00 a.m. to 5:00 p.m. or visit our web site at www.brighamandwomens.org.



Adoption Issues and Resources

Adoption is a reasonable option for single individuals or couples who have been unsuccessful with or do not wish to undergo fertility treatments. There are many issues for the prospective parents to consider: the age, ethnic background, or race of the child they wish to adopt, domestic vs. foreign adoption, and whether the couple would be willing to adopt a child with special needs.

Many couples disagree about adoption and it can take some time and effort to arrive at a plan that is satisfying to both members of the couple. The costs of adoption can be high, approximately \$30,000, for either domestic or foreign adoption, and are not covered by insurance.

There are many resources available to those who are considering adoption. Many couples find consultation with an adoption counselor to be very helpful in sorting through all the options that are available to them.

Two resources available to couples considering adoption include:

- **The Open Door Society:** <http://www.odsma.org>
- **RESOLVE:** <http://www.resolve.org>

Domestic Adoption

Domestic adoption (adoption within the United States) can be either public (through the Department of Social Services) or private (through an agency or lawyer). Most private domestic adoptions in Massachusetts are semi-open, meaning that couples will have some contact with the birth family before the birth and sometimes afterwards. The advantage of domestic adoption is that babies are very young, often right out of the hospital. Disadvantages include the expense and uncertainty around waiting and being “matched” with a birth mother.

Foreign Adoption

Many organizations in Massachusetts and nationwide help families adopt children from other countries. The children are slightly older in most cases, but are legally (in most countries) considered orphaned or abandoned, so some adoptive parents find this more “certain.” The international adoption process varies a great deal by country, so it is important to work with a good agency that can help work with the systems both in this country and in the country of adoption. Children of all ages and races from many different countries—most commonly in Asia, Latin America, and the former Soviet Union—are waiting to be adopted.