

Preconceptional Considerations and Counseling for the Infertile Couple

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Approximately 15% to 20% of couples of reproductive age have difficulty conceiving or maintaining a spontaneous pregnancy. In 2002, 1.2 million (2%) women of reproductive age reported having an infertility-related medical appointment within the previous year, and approximately 9% of women ages 18 to 44 reported receiving an infertility service at some point that included advice on infertility and/or testing and services for infertility.¹ Infertility impacts every racial and ethnic group and can cause significant emotional distress in a couple's relationship when an anticipated pregnancy does not occur in the time period in which they expected to start a family.

A period of one year of unprotected intercourse without a spontaneous conception typically defines infertility.² There are a number of factors that can lead to infertility. Approximately 20% of infertility is related to male factors. Female factors account for 40%, and 30% can be related to both male and female factors. Unfortunately, in 15% of cases the etiology of infertility cannot be traced to any specific cause.

For healthy reproductive age couples, spontaneous pregnancy is usually achieved within six months of unprotected intercourse during the female's fertile period. For couples less

than 30 years of age, failure to achieve spontaneous pregnancy after six cycles of unprotected intercourse is classified as subfertile.^{3,4} However, 50% of these couples will become pregnant within the next six cycles on their own. Being patient, eliminating stressors in professional and personal lives, and using timed intercourse and ovulation predictors will likely lead to successful conception for these couples. For the infertile couple, the cumulative probability of spontaneous conception is age-dependent and declines particularly for females in their mid-30s to early 40s.

Unlike the typical pregnancy in the US that is unplanned in nearly 50% of couples, the infertile couple has made a conscious decision that they desire pregnancy and, for the most part, are thoroughly invested in optimizing the chances for a successful outcome. However, the financial and emotional burden for evaluation and treatment of the infertile couple is significant. As such, preconceptional counseling about all aspects of preconceptional and pregnancy care, including ramifications and potential outcomes, should be discussed with both partners prior to embarking upon infertility treatment.

The age of the couple (the woman in particular), family history, and past and current history of medical conditions can have a direct impact on pregnancy complications and a healthy pregnancy outcome. The inability to become pregnant spontaneously is associated with many emotions including shame, guilt, anxiety, and depression. Studies suggest that as many as 40% of infertility patients suffer anxiety that may lead to major depression.⁵ It is critical that both the woman and her partner understand that these diagnoses can have negative impacts on family life, employment status, household finances, and can increase the severity of any underlying health conditions, such as diabetes or hypertension.

Evaluation

In the process of the infertility evaluation the etiology for the couple's inability to conceive is likely to be revealed. Male factors are usually ruled out early with a normal semen analysis. Many men do not anticipate that the couple's infertility is a problem directly related to them and learning that they have the problem sometimes requires some adjustment and reassurance. The man's past medical, surgical, and social

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history is important. Alcohol and drug use can potentially impact male fertility. If the male has an abnormal semen analysis, options will be discussed and outlined for the couple. An abnormal semen analysis warrants a thorough physical examination and possibly a laboratory investigation to determine the etiology. For example, genetic conditions such as cystic fibrosis can be discovered in the course of the infertility evaluation as a number of men with this condition have a congenital absence of the vas deferens which leads to an absence of sperm in the ejaculate. Abnormal male genitalia should prompt a genetic evaluation for chromosomes to rule out conditions such as Klinefelter's syndrome which is the presence of an additional X chromosome (XXY compared to the normal XY). If the sperm concentration is low (oligospermia) the evaluation could include a hormonal blood test to measure total testosterone and other pituitary hormones. Treatment depends on the etiology of the problem. In cases of low or no sperm, a testicular biopsy might be recommended to determine if sperm is present or being produced. Treatment of infertility as a result of decreased sperm may include in vitro fertilization (IVF) techniques, including a procedure called intracytoplasmic sperm injection (ICSI) where the sperm is injected directly into the egg. This requires significant preparation including harvesting the eggs from the female partner.

The female infertility workup is laborious, expensive, and stressful. The workup should begin with a thorough medical, surgical, and gynecologic history. The menstrual history and pattern of bleeding is important in diagnosis of ovulatory disorders such as polycystic ovary syndrome (PCOS). Approximately 20% of female infertility is related to problems of ovulation, with 70% of ovulatory dysfunction due to PCOS.⁶⁷ Over-the-counter ovulation prediction kits which monitor the surge in luteinizing hormone (LH) are widely used by couples who are attempting to conceive and can be very useful for women with irregular ovulation. LH levels rise approximately 40 hours before ovulation. A blood test measuring progesterone level in the second half (18-24 days) of the woman's menstrual cycle is an accurate predictor that ovulation has occurred. Ovulation disorders such as PCOS may be treated with drugs such as clomiphene citrate (Clomid), which improves ovulation. Most Clomid-induced ovulation leads to pregnancy within three cycles of administration. The use of gonadotropin injections to enhance ovulation increases the risk for ovarian hyperstimulation and higher order multiple gestations (triplets, quadruplets, etc.).⁸ The state of the ovary should be carefully monitored with ultrasound when using gonadotropin injections. Some women with PCOS have insulin resistance as part of the syndrome. These women may be treated with metformin, an oral hypoglycemic agent.

Past history of a sexually transmitted infections (STI) such as Chlamydia *trachomatis* or gonorrhea pelvic infections can lead to tubal damage, scarring, and blockage. Chlamydia has a high prevalence in women less than 24 years of age. If left untreated, chlamydia can lead to tubal damage and subsequent infertility. All women and particularly adolescents should be

educated on the potential infertility consequences of STIs and be promptly treated for this condition. Chlamydia testing should be included in the annual gynecologic examination for women under age 24 years.

Testing for tubal blockage is typically done with a hysterosalpingogram (HSG). The test involves injecting contrast media into the uterine cavity and taking an X-ray to determine the internal anatomy of the uterus and spillage of the dye from the tubes. Ultrasound can also be used to determine uterine and tubal anatomy (hysterosonography). Women with proven tubal damage may be best treated with assisted reproduction through IVF and embryo transfer to optimize chances for conception and viable pregnancy.

Endometriosis is also associated with infertility. Endometriosis can lead to adhesions which limit tubal motility or damage and obstruct the fallopian tubes. A history of pelvic pain around the time of the menses or painful intercourse is suspicious for endometriosis in the infertile couple. Endometriosis is confirmed with laparoscopy and can be treated surgically or medically. Infertile women with severe endometriosis are often treated with IVF.

Prepregnancy Counseling for the Infertile Couple

Pregnancy planning for the infertile couple provides a unique opportunity for the clinician to optimize the health of the patient in anticipation of pregnancy. All women should be counseled to take a vitamin that contains at least 400 μ g of folic acid at least one month prior to conception and to continue the vitamin during critical embryogenesis to decrease the risk for birth defects such as neural tube defects (spina bifida). For women with medical conditions such as diabetes or hypertension, optimization of glucose and/or blood pressure control is crucial before becoming pregnant. Certain medications are contraindicated during pregnancy such as ACE inhibitors for hypertension, and alternative medications should be offered before conception. Overweight and obesity increase the risk for decreased fertility, pregnancy loss, and birth defects. Weight loss is typically recommended prior to undergoing infertility treatment because it improves the chances for conception. Overweight and obesity are not uncommon for women with ovulatory dysfunction from PCOS. Unfortunately, weight problems cannot be corrected overnight and realistically the woman most often will not achieve an optimal weight loss before proceeding with treatment. For some women with PCOS and obesity, the combination of Clomid and Metformin may increase the chances of ovulation and the ability to conceive. The couple must be counseled about the pregnancy risks of overweight and obesity, including gestational diabetes, preeclampsia, and cesarean delivery. Medication history is important especially if the drugs present a risk to the developing embryo and are associated with an increased risk for birth defects.

As mentioned previously, many infertile women become anxious or depressed and might be on medications for these

disorders. They should be reassured that most currently prescribed anti-anxiety medications are safe during conception, embryogenesis, pregnancy, and breastfeeding. Women with a history of anxiety and depression are at greater risk for postpartum depression disorders and should not discontinue medications unless recommended by their clinician. The risk of depression disorders increases if pregnancy complications, such as a preterm birth, occur.

Older women should also make sure they have age-appropriate screenings, such as mammography if age 40 or older, before proceeding with pregnancy. Women over 35 years should receive genetic counseling to discuss risk of fetal chromosomal abnormalities. Couples should be screened for hereditary genetic disorders such as cystic fibrosis, Tay Sachs, and sickle cell disease depending on racial/ethnic prevalence of these conditions.

All ovulation enhancing drugs increase the risk for multiple gestations as do assisted reproductive techniques including IVF with embryo transfer. The couple must be made aware that a multiple gestation is associated with pregnancy loss, preterm delivery, and an increased risk for obstetric and medical complications such as diabetes, hypertension, and cesarean delivery. They must be prepared to decrease physical activity or be off work with a multiple gestation if the pregnancy becomes complicated by preterm labor or cervical shortening. This may further tax an already limited family budget that has been challenged by the expenses of the infertility treatment. In most instances, IVF is not covered by insurance, and each IVF cycle costs several thousand dollars (approximately \$13,000 including medications). Success rates for IVF for women under 35 year are approximately 30%-35% per cycle, and success rates decline with maternal age and underlying causes of infertility. For example, women older than 40 years have IVF success rates of only 6%-10% per cycle. Women in their early to mid-40s seeking pregnancy may not be able to produce sufficient eggs through ovulation induction as the reserve of eggs has been depleted. These women will likely

require donor eggs that are fertilized by the partner's sperm and the embryos transferred to the uterus. IVF with donor eggs costs on average approximately \$20,000 per cycle, including medications.

Conclusions

The number of couples seeking infertility services has increased over the past decade. For some, the impetus is impatience that pregnancy has not occurred within the time of their personal expectations. For others, a true cause for infertility exists and can be overcome in most instances with etiology-appropriate treatment. Depending on history and age of the couple it is important to time the investigation somewhere between a period of subfertility (six months of trying) to infertility (one year of trying) to avoid the potential for undertreatment, when significant factors are apparent, or overtreatment that can lead to unnecessary expense.⁹ Earlier evaluation and treatment may be justified after six months in women over 35 years. The workup and treatment for infertility can lead to distress for both the woman and the man. They must view their desire to become parents as a team effort and must support each other throughout the process. Certainly decreasing stress and optimizing personal health increases the chances of success for infertility treatment, healthy conception, and pregnancy outcome. With most techniques for ovulation induction and IVF the risk for multiple births is increased, and the couple should recognize this as a potential complication of treatment. Improvement in drug dosing and monitoring decreases the risk for higher order multiple gestation, which in turn increases the risk for pregnancy loss. Selective reduction for multiple gestation is an option, depending on the beliefs and desires of the couple.

Unfortunately, for some couples a pregnancy is not possible in spite of exhausting all methods of infertility treatment. These couples should be counseled toward adoption options to fulfill their goal of parenthood. **NCMJ**

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