

THE STUMBLING BLOCKS TO IVF

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Many couples who might successfully utilize IVF techniques to build their families fail to benefit from these technologies. Although roughly half of the three million infertile couples in this country seek medical intervention to have a child, the overwhelming majority stop short of IVF. This is true even when their chances of achieving a live birth through that technology are good.

What are the barriers that cause so many people to stumble on their way to IVF? The answer to that question is complex, because what is a stumbling block to one person may provide no hindrance to another. It is fair to say, however, that there are general issues that cause concern to all would-be IVF patients. First is the fear that IVF will not be successful, or that there will be bad outcomes for the mother or baby. Secondly, IVF may be perceived as an expensive and unaffordable option. Thirdly, the techniques employed may be seen to be inconsistent with a couple's religious or moral beliefs. And finally, many patients are concerned that they will not be able to meet their current professional and personal obligations while undergoing a rigorous course of treatment that includes IVF. None of these concerns is insignificant. In my years of practice in the field, however, I have come to recognize the many ways that these issues can successfully be addressed and the barriers overcome.

Specifically, I would suggest that couples who want to try IVF but are finding the task daunting look at using decision-making approaches and cost-benefit analysis to review their options. I would also suggest that patients develop treatment plans with an endpoint in mind, and that they begin to research the range of family building options available to them while they are still in treatment. Finally, I have found that patients who consciously and constructively integrate IVF treatment into other life activities are better able to complete their chosen course of care. This is not to say that IVF is for everyone, because it isn't. The intent of this article is to help couples who want IVF to overcome their personal stumbling blocks and achieve that goal.

Decision-Making

It is important to recognize that decision-making regarding a course of treatment is difficult and can easily be done poorly. Reliable information can be difficult to obtain or understand, and most of us lack experience in this type of decision-making until circumstances require us to do it. At that point, it may feel like decisions have to be made within an extremely short time frame. Additionally, different people make decisions in different ways, some intuitively, some based on experience, and others based on a straightforward analysis of the facts. Much depends on what types of decisions we have had to make in other areas of our lives and on our personal experience. Sometimes, our values and beliefs inform our choices in ways that are difficult to explain to others. Often a bias towards securing benefits and avoiding harm in the present and near future enters our thinking. We may say we are making a conscious choice, but perhaps in reality, we are more concerned with protecting the status quo. We may develop fears or anxieties that greatly exceed actual risks. At the other extreme, there are those who feel that "it won't happen to me" and are prepared to make choices by discounting risks substantially, whether they are highly unlikely, or even, significant. Distinguishing between a reasonable and unreasonable exaggeration of concern is often difficult. "Framing" decisions so that either benefits or risks are over-emphasized is a pitfall that can be difficult to avoid.

Usually, the best approach is to evaluate available choices in alternative ways looking at the various options from different perspectives.

The first step in decision-making in infertility care is to determine your individual religious, moral and ethical values. IVF can present some unique and complex issues. Your views must then be openly discussed with your partner because it is imperative that both of you reach agreement on how to start or expand your family. Your physician must also agree with your intentions. Ethical dilemmas can arise when options for care are seen to conflict with the couple's autonomy, quality of life, or their perception of socially responsible behavior. Should there be significant differences of opinion between the physician and the couple, alternative sources of infertility treatment should be identified. At no time should a couple or a physician feel that they are pursuing a course of treatment against their best judgment or personal beliefs.

The issue of the quality of infertility care needs to be addressed. Since infertility management can be a complicated process, it is important that your physician have the requisite level of expertise. The American Society for Reproductive Medicine has established guidelines for the provision of infertility services, with three levels of care. Some patients will have initial diagnostic tests and/or treatment performed by providers with only basic capabilities. This can be appropriate if patients are referred to the more experienced providers when indicated by the guidelines. Most IVF programs provide very good care, but you should ensure that the IVF clinic you choose belongs to the Society for Assisted Reproductive Technology (SART), and be comfortable that the clinic's laboratory quality, medical care and financial services meet your needs. You should complete a comprehensive medical evaluation and acquire information about treatment alternatives other than IVF from the clinic. You should then determine a plan of action that sets out specifics of your medical treatment; financial management, time limits, lifestyle modifications and utilization of family building options that are acceptable to you. These many decisions are often facilitated by use of a modified cost-benefit analysis.

Cost-benefit Analysis

In regards to infertility, a cost-benefit analysis is designed to compare and evaluate the eight options available to expand or start a family. These options are:

1. No treatment,
2. Standard infertility testing and treatment involving surgery,
3. Controlled ovarian hyperstimulation with "fertility drugs",
4. Treatment of the male partner and/or intrauterine insemination,
5. IVF
6. Third party reproduction involving donor eggs, donor sperm or surrogate (host uterus or gestational carrier),
7. Adoption,
8. Child-free living.

The benefit of any of these choices depends on the value that one places on the outcome. Clearly, the outcomes of the choices are not all the same, ranging from one's own genetic baby, to an egg donor or sperm donor baby, an adopted baby, or no baby at all. With IVF, there are many "values" that must be considered. It is important to ask the hard questions at the time a treatment plan is being developed. How do you feel about intracytoplasmic sperm injection (ICSI), which is considered by some to be less "natural" than IVF? Do you want to

cryopreserve (freeze) embryos? How many embryos do you want to replace in each cycle? To maximize your chances for pregnancy, you may want to replace several, but fewer will limit the chances of multiple pregnancy. How do you feel about induced reduction if you had triplet or higher order pregnancy? How do you feel about the advantages and disadvantages of raising twins or even triplets? What are your feelings about amniocentesis, congenital anomalies, and pregnancy complications? How do you feel about donor sperm, donor eggs, host uterus, embryo donation and stem cell research? These are all issues that require thoughtful decisions.

In addition to determining the value of various outcomes, one must accurately assess the probability that each outcome may occur. In the case of IVF, this requires that a knowledgeable physician complete a comprehensive evaluation of both the male and female, and assess their likelihood of achieving a live birth in light of those findings. To determine the benefit of any outcome, the relative value of each choice must be multiplied by the probability that the outcome will occur: $\text{Benefit} = \text{Value} \times \text{Chances of Success}$. You decide the relative value to you of the different outcomes, and your physician tells you what the chances are of achieving each outcome. It is evident that if either you don't value a choice very much or if the chances for success are low, the benefit of the choice is also low. Each potential choice is then prioritized according to the one that has the highest benefit, the second highest benefit, the third highest benefit, and so on. The next step will be to evaluate the "cost" of each choice, since the cost will reduce the benefit. In this way, the order of your choices might change.

There are four kinds of costs. The first is financial. IVF costs an average of \$12,000 to \$15,000 per cycle, and this is often not covered by employee health plans. It is important to find out exactly what is and is not covered by your insurance, so that the amount of personal expense may be determined. You can then decide how much money, if any, you are prepared to spend from medical savings accounts, retirement funds, or savings. Many couples defer major purchases while seeking treatment, but this is not always possible. IVF costs can be quite high, and they may appear to be more than some patients, especially younger ones, can afford. However, it's better for a couple to make the sacrifices to get the appropriate care when they are younger because their chances for success are better. Because the cost of care is such a major stumbling block, some practices are now beginning to offer affordable financing for treatment packages and a refund guarantee or if your treatment does not result in a live birth. You should ask your physician about the availability of these financial tools.

The second major cost is time. If you are younger, time is not as critical. Once the woman's age is over age 35, however, time begins to play a more important role, affecting how quickly one needs to move to more intensive treatment such as IVF. Women often feel that a barrier to IVF is the amount of time required for office visits and procedures, time that must be taken away from one's job. It is important to identify in advance the best way to manage this problem, often by discussing this with your employer and physician. Time for infertility treatment can also detract from time with your partner, family, friends and personal commitments. Again, the best approach is to discuss these issues with those involved, make a plan to minimize the impact of infertility treatments, and minimize unnecessary personal, family, work and social commitments.

The third major cost is the risk of IVF. Recent articles and media attention have focused on IVF outcomes that appear to be less favorable than that with non-IVF pregnancies. However, several earlier, larger studies have shown equivalent outcomes. But all these studies have

design problems. Additionally, the adverse outcomes cited in some studies occur in very low frequency. Generally, IVF treatment is safe and outcomes for both women and babies are good. Certain subgroups of IVF patients are at higher risk than others, and further well-designed studies are needed to answer some important questions. However, the risk of death or serious illness from any pregnancy, regardless of whether or not IVF is used, is several times higher than the risk of the drugs or procedures used in IVF.

Physical risks can include short-term complications of the actual treatment. Some women worry that the fertility drugs will use up more eggs than normal ovulation, but this does not occur. Ovarian hyperstimulation syndrome (OHSS) with some bloating and pelvic discomfort occurs in a small percentage of patients, but is serious enough to require hospitalization in only one per 300 cycles. Complications such as bleeding or infection from egg retrieval occur only once per several hundred cycles, and almost never require transfusion. Obstetrical complications are mostly related to age of the mother and her underlying medical condition, as well as the presence of multiple pregnancy, but are not substantially different with or without IVF when controlled for the number of babies being carried. It is possible that infertility patients are at a slightly higher risk for obstetrical complications unrelated to type of treatment. Obtaining high quality obstetrical care and bed rest during the pregnancy can reduce many of these potential problems. Spontaneous abortion and ectopic pregnancy rates are about the same with or without IVF, although IVF reduces the risk of ectopic pregnancy in women with fallopian tube disease. In the past, concerns were raised about the risk of ovarian cancer following use of fertility drugs. Multiple well-designed studies have demonstrated no increased risk of ovarian cancer, and a possible small increase in risk of borderline ovarian tumors. Indeed, pregnancy itself significantly reduces the risk of both ovarian and breast cancer. After almost a quarter century of IVF, there are no other known long term problems for women who have had babies through IVF.

Some patients are concerned about the risks of laboratory procedures. Intracytoplasmic sperm injection (ICSI), which is used for male factor infertility, has the same live birth rates as non-ICSI IVF. A few men who otherwise would have no chance of becoming fathers carry genetic conditions that can be passed on to their male offspring. Hypospadias, or an abnormally located opening of the urethra in the penis, also occurs more frequently, but still rarely, in baby boys born after ICSI. This problem is often minor and can be surgically repaired. Assisted hatching, often used for older women or those with prior failed IVF cycles, is associated with a higher risk of monozygotic twins, which have higher risks of complications than a singleton pregnancy. Cryopreservation of embryos is associated with a lower live birth rate after thawing, but the babies are just as healthy as those born from fresh IVF embryos. Donor sperm and donor egg babies also have the same outcome as IVF with the patient and her own partner's genetic material. Others are concerned about the potential loss or mix-up of sperm, eggs or embryos in the laboratory. Of course, mistakes can happen, but they are very rare. Laboratories that belong to SART undergo rigorous inspection every two years of their personnel, equipment and systems to ensure that the highest quality care can be delivered. Great emphasis is placed on correct identification of sperm, eggs and embryos, so that these types of problems are most unusual.

A major exception to the safety of any fertility treatment, however, is the risk of multiple pregnancy, twins occurring with about 30% of deliveries and triplets with just under 5%. While many infertile couples consider twins to be the ideal outcome, multiple pregnancy has a higher risk of premature delivery and low birth babies. Even twins carry about twice the risk of death

or severe disability to each baby compared to a singleton pregnancy, and triplets face about 4 times the risk of death or serious disability for each baby. However, a healthy baby is the result well over 95% of the time with IVF.

Importantly, there are ways to reduce the risk of multiple birth. The Society for Assisted Reproductive Technology (SART) initiated national guidelines regarding the number of embryos to transfer so that live birth rates are maximized and multiple births are minimized. Triplet rates have been coming down for the past few years. Furthermore, every patient has the option of specifying that fewer embryos should be replaced if she wishes, including a decision to replace only one embryo. Extra embryos can be cryopreserved for subsequent cycles if the woman does not conceive, or to try for a second baby later if she does. Every patient can and should discuss this issue with their physician and make a decision with which she is comfortable regarding the number of embryos to transfer. If multiple pregnancy does occur, spontaneous reduction or loss of a fetus from a triplet to twin or twin to singleton pregnancy occurs 25% to 50% of the time. In some additional cases, patients may elect to undergo induced reduction (pregnancy reduction, selective reduction, multifetal reduction) from triplets or more to twins. This procedure is physically safe and effective approximately 90% to 95% of the time, and can improve the chances of delivering fewer, but healthier babies. However emotional and personal value issues are important in the decision to undergo this procedure.

The final cost is often the most important, and that is the psychological or emotional cost of infertility. Infertility can be a real life crisis for many people, affecting how they feel about ourselves as women and men, wives and husbands, and potential mothers and fathers. Frequently patients have to suffer in silence because infertility is so poorly understood by society. Patients may have concerns about financial issues, the "unnatural" conception that occurs outside the body, the impact of infertility on themselves and their partner, or the effect on their marriage and sex life. They may find it difficult to deal with friends and family, to change from their gynecologist to a reproductive endocrinologist, to take fertility drugs, or to lose time at work. The science and the language that describes IVF are new and intimidating. Suddenly one is supposed to know about IVF procedures, cryopreservation, ICSI, assisted hatching, multiple births, induced reduction, and the use of donor gametes. Additionally, adoption, with all of its complexity, may be an issue that is just over the horizon. It is normal to be anxious and concerned about these many aspects of infertility and IVF! There is a lot to think about.

But there are some things you can do to deal with this problem. The first is for both partners to communicate to each other clearly how they feel about these issues and how they want to approach it, what choices are acceptable and which are not. It is also important to look after yourself with a healthy diet, exercise and sleep. Meditation or yoga can be very helpful for people dealing with the stresses of infertility. It is important get as much information as possible, although one should remember that not all information is reliable. Check your source, and be cautious on the Internet. RESOLVE and the American Society for Reproductive Medicine are particular good places to get information. Your physician should also give you information about their evaluation of your specific situation. Write down questions at home so you can remember them when you see your physician, and if it is urgent, call your physician. If you are not getting the answers you want, you don't understand what your chances are and what the plan is for your care, if you feel the infertility investigation and treatment are taking too long, or if you are not feeling supported by your physician's office, it may be time to look around. You should ask for a referral to another reproductive endocrinologist or IVF clinic. Finally, some

situations warrant the assistance of trained counselors in this field. They might be helpful, for example, if you are considering the use of donor eggs or sperm, if there are difficult choices to make, or if you are overly anxious, depressed or not managing the infertility situation well. RESOLVE may be able to give you a list of infertility counselors. Of course, joining a RESOLVE support group is also an excellent idea.

Once you have this information from your physician, discuss in detail and come to decisions with your partner how you would like to proceed. You might be able to do this using the "20 minute rule" where you discuss infertility for just 20 minutes (or whatever time you agree upon) daily until you reach resolution, or you might take a weekend away somewhere quiet to review your situation. Once you have determined what is acceptable to you, know the prognosis and planned treatment with timelines, have decided how to afford treatment, and how to manage your personal, family and work time, you can make a written plan to deal with the many aspects of IVF. Patients should proceed at their own pace, with options acceptable to them, within medically appropriate guidelines. Some will decide not to pursue IVF, and that is perfectly appropriate for those patients. For others, the approach described above can help overcome the stumbling blocks to IVF, allowing them to build their families through this very successful medical technology.