



Infertility:

From a Personal Public Health

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Anne T. Fidler, ScD,
Judith Bernstein, PhD, RNC

THE DESIRE TO HAVE CHILDREN is virtually universal, and the right to reproduce is recognized by the Supreme Court as a basic civil right. Whether driven by biology, emotional needs, or social pressure, at some point in their lives most adults seek to have a child, generally taking for granted that they will be able to do so by the usual biologic route whenever they choose. Infertility, or the inability to conceive a child, is a condition that affects millions of Americans each year and has a profound impact on a person's self-esteem, personal relationships, sense of value, and sense of purpose—not to mention health and pocketbook.

SYNOPSIS

The inability to conceive a child is most often viewed as a private matter, but public health perspectives and skills can contribute greatly to our knowledge about infertility, and the development of effective and rational public policy for prevention, access to health care, and regulation of new technologies. We offer a primer of public health aspects of infertility in an effort to encourage the broad spectrum of public health professionals to become more knowledgeable about these topics and join in the national debate about preventive strategies, cost-benefit assessment, resource allocation, and ethics.

to a
Problem

Over the past decade, infertility has been the subject of significant media attention and public discussion, particularly in light of new technologic advances in treatment. Nevertheless, the inability to conceive a child is still viewed as essentially a private matter to be resolved in the medical arena, in the case of treatment, or within the social work domain, in the case of adoption. However, issues related to infertility have a significant impact not only on the health and well-being of the individual or couple affected but on society as a whole. Public health researchers and practitioners are rightly beginning to see infertility as a public concern, not just as a private health matter.

The public health sub-disciplines of epidemiology, environmental and occupational health, social and behavioral sciences, health services research, health law and ethics, and maternal and child health all encompass aspects of infertility—assessment, prevention, treatment, and policy—that unite its private and public domains. Epidemiologists from many fields of study are involved in research to quantify the extent of the problem, identify preventable causes, and measure the effectiveness and potential risks of therapies. Health services investigators are beginning the difficult process of establishing risk-benefit and cost-

benefit ratios for a variety of infertility treatments. Public health ethicists and legal scholars are making major contributions to the development of policies related to infertility research and are opening up a much-needed dialogue about the ethical, moral, and legal implications of new developments in infertility treatments.

We present here a hypothetical case study, a narrative of one couple's journey through the experience of infertility, to illustrate how public health perspectives apply at each decision step.

THE OCCURRENCE OF INFERTILITY

Roberta and Bob M. are fairly typical infertility patients. They have been married for five years and attempting pregnancy without success for eight months. She is a 37-year-old woman who has never been pregnant and was a faithful user of contraception until eight months ago. Bob is 40 years old, with no children. Concerned about the possibility of infertility and mindful of Roberta's "biological clock," they make an appointment with Roberta's gynecologist. The physician recommends a work-up and refers the couple to the infertility advocacy organization Resolve for information and support.

Prevalence. Bob and Roberta may be typical infertility patients, but do they represent the typical infertile couple? Much of what is known about the prevalence of and risk factors for infertility is learned from the National Survey of Family Growth (NSFG), conducted periodically since 1973 by the National Center for Health Statistics (NCHS) of the Centers for Disease Control and Prevention. Based on personal interviews with a national sample of women 15–44 years of age, the NSFG is a multipurpose study to collect data on factors affecting women the health of US women. The NSFG provides information not only on the prevalence of infertility but also on adoption¹ and the use of infertility health services.

The most recent NSFG, conducted in 1995, reveals that approximately 7% of married couples (more than two million couples) in the United States reported experiencing difficulty in achieving a pregnancy ("relative infertility").² In 1995 alone, more than six million women (10% of all women ages 15–44 years) in the US reported reproductive difficulty defined more broadly as impaired fecundity, or the inability to get pregnant or carry a child to term.² Of those, almost half (2.8 million) had no children. The prevalence of infertility rises significantly with increasing age, among women without children. No such effect of age was observed among women

WOMEN'S HEALTH DATA AVAILABLE

An invaluable but underutilized resource for anyone interested in women's health is the National Survey of Family Growth (NSFG), conducted by NCHS. Based on personal interviews with thousands of women in the US ages 15–44, its main function is to collect data on factors affecting pregnancy and women's health in the US. It is the only dataset that provides information on some of these issues. NSFG surveys have been conducted in 1973, 1976, 1982, 1988, 1990, and 1995.

Topics women are asked about in the survey include:

- Children ever born and total births expected
- "Intended," "mistimed," and "unwanted" births
- Sexual intercourse
- Marriage and cohabitation
- Contraceptive use
- Fecundity, infertility, and sterilization operations
- Breastfeeding, maternity leave, and child care
- Adoption, stepchildren, and foster children

- Health insurance coverage
- Family planning and other medical services
- Cigarette smoking
- HIV testing
- Pelvic inflammatory disease
- Sex education

The next NSFG will be conducted by NCHS in 2001. The 2001 survey will use a national sample of about 12,000 women ages 15–44 and an independent national sample of 7000 men ages 15–49. For both males and females, three groups will be oversampled: blacks, Hispanics, and 15–24 year-olds. New questions will be asked on attitudes toward marriage, children, and the family.

The report of summary findings from the 1995 NSFG contains 91 tables of data on a wide variety of topics. NSFG reports can be downloaded without charge from the NSFG home page at www.cdc.gov/nchs/about/major/nsfg/nsfg.htm. For a copy of the NSFG dataset and documentation, call 301-458-4222.

with children. There were no significant differences in prevalence of infertility across education level or racial or ethnic categories.²

Problems in assessing the occurrence of infertility.

Assessing the occurrence of infertility in a population is hampered by several features that distinguish it from other health concerns. First, infertility is typically experienced not by an individual, but by a couple. Though infertility is still too often seen primarily as a woman's problem, the underlying cause may be a male factor (abnormal sperm or low sperm count), a female factor (tubal or ovulatory dysfunction), a combination of problems, or a couple factor (with both partners experiencing reproductive problems). In addition, there is a significant social basis to the condition; one usually requires the desire or opportunity for conception to be considered infertile. Two women with blocked fallopian tubes and therefore with a similarly impaired ability to become pregnant will be viewed differently in an epidemiologic study of infertility if one woman wants to become pregnant and the other does not. The latter may never even know of her physical disability unless and until she wishes to have a child.

As for many diseases or disorders, there is no single objective test of infertility and no universally accepted definition, though typically it is defined in clinical practice as the inability to become pregnant after more than one year of unprotected intercourse. Various definitions have been used in epidemiologic studies. A comparison of several of these definitions demonstrated, not surprisingly, that the different definitions yielded very different estimates of prevalence and pregnancy success rates.³ Each of the definitions considered by Marchbanks et al.³ categorized infertility as the inability to become pregnant based on the length of time in which conception fails to occur. Defining a health outcome not as a structural or physiologic abnormality but as the lack of the ability to do something is problematic. Suppose, for example, if one were to study the inability to climb stairs without considering whether the failure to reach the top were the result of cardiac insufficiency, respiratory disease, or a broken leg. Such a construct would obscure the ability to understand the distribution of the condition in the population and would cloud the identification of risk factors and preventive strategies for the underlying disorders. Defining infertility without considering its underlying physical, structural, or hormonal bases may be the best that can be achieved by most population studies since the underlying cause of the functional difficulties is often not known. However, doing so may not lead to an adequate understanding of causes, preventive strategies, or the effectiveness of various therapies.

Use of infertility services. Unlike Roberta, most women who experience infertility or impaired fecundity do *not* seek medical help. Of the 6.2 million women estimated to have impaired infertility in 1995, about 2.7 million (44%) had ever sought infertility services in their lives, and about 700,000 (11%) had done so in the previous year.⁴ Not surprisingly, women with impaired fecundity who sought medical services differed in several respects from those who did not. They were more likely to be older (particularly among women with no children) and have a higher income. They were also more likely to be married. Though there were no significant differences in the rate of impaired fecundity across racial or ethnic categories in the 1995 NSFG,² women who reported using "specialized services" were more likely to be white than non-white and were of higher socioeconomic status than women who did not report using such services.⁴ This is not surprising given the high cost of these procedures and the fact that in most states they are not covered by medical insurance.

The *percentage* of women with impaired fecundity who had ever received medical help for their problem was 44% in both the 1988 and 1995 surveys; however, the *absolute number* of such women rose from 2.1 million in 1988 to 2.7 million in 1995, due primarily to the larger size of the fecundity-impaired population.⁴ The absolute number of women being treated with assisted reproductive technologies (ARTS, defined as treatments or procedures that involve the handling of human eggs and sperm for the purpose of helping a woman become pregnant) rose dramatically in that period.⁵

The emotional toll. A true understanding of the condition of infertility cannot be achieved by exploring only the physical causes and consequences. For many couples, infertility is as much an emotional and spiritual crisis as it is a physical challenge. The gynecologist's referral of Bob and Roberta for emotional support is important and based not only on clinical intuition but on substantial scientific evidence. Infertility interferes with one of the most fundamental and highly valued human activities, and thus presents a major life challenge.⁶ In a June 1998 decision in the case of *Bragdon v. Abbot*, the US Supreme Court ruled that reproduction is a major life activity and that individuals with physical or mental impairments that substantially limit reproduction now qualify for protection under the Americans with Disabilities Act.

There is evidence that the psychological effects are similar to those of cancer and heart disease.⁷ For many individuals and couples, the inability to have a desired child results in social isolation, clinical depression, and reduced job performance and life satisfaction. Infertility thus has a social as well as an individual impact.⁸⁻¹⁰

Bob and Roberta have been referred to Resolve, Inc., a nationwide education, advocacy, and support network. This organization provides critical services, particularly information and support groups, for people facing infertility. The support groups it has fostered have served as an impetus for the inclusion of mental health services in infertility programs and for the development of multidisciplinary teams that include psychologists and psychiatrists who specialize in the emotional effects of infertility. The legislative advocacy activities of Resolve were instrumental in the passage of a federal law to regulate success rate reporting for *in vitro* fertilization (IVF) and other ARTs and state laws to promote insurance coverage for infertility treatment.

PREVENTION OF INFERTILITY

Before we begin the discussion of the public health ramifications of Bob and Roberta's diagnosis and treatment, we should rightly begin with a discussion of the prevention of infertility. In its review of the medical and social aspects of infertility, the Office of Technology Assessment concluded, "With the personal, familial, and societal losses caused by infertility inestimable and the economic costs so great, it is clear that infertility is better prevented than treated."¹¹ Certainly, one of the principal goals of public health is health promotion through disease prevention. A clear understanding of possible risk factors for infertility is essential to designing and implementing effective strategies to protect the fertility of both men and women. Though in a large percentage of cases, the causes of infertility are unknown, several preventable causes have been identified.

Chlamydia trachomatis. The most common preventable cause of infertility is infection with *Chlamydia trachomatis*, a sexually transmitted bacterial infection. The exact prevalence of chlamydia infection is unknown, but estimates are generally higher than 10% among sexually active girls and higher than 5% among young adult women.¹² Chlamydia infections are surely underreported, since the infection is asymptomatic in approximately 50% of men and 75% of women.¹³ In 1998 alone, more than 600,000 cases were reported to the Centers for Disease Control and Prevention (CDC), reflecting the tip of the iceberg. It is estimated that approximately three million cases occur annually.¹⁴ Adolescents and young adults are at the greatest risk for infection with *Chlamydia trachomatis*, with the vast majority of reported cases occurring in people younger than age 25. This may be due to both a higher level of exposure among young people and the fact that young women are biologically more susceptible to the effects of *Chlamydia* than are older women. In addition to

young age, the principal risk factor for infection with *Chlamydia trachomatis* is multiple sex partners.¹⁵ Chlamydia infections, if undiagnosed or inadequately treated, can lead to pelvic inflammatory disease (PID), with serious reproductive sequelae. An estimated 40% of women with inadequately treated cervical chlamydia infections develop PID. Of those, 20% go on to experience infertility due to tubal scarring, and another 9% have ectopic pregnancies.^{16,17}

Recent technical advances have improved the ability to detect, diagnose, and treat chlamydia infections. Relying on these advances, large-scale regional screening and treatment programs, beginning with one in US Public Health Service Region X (Washington, Oregon, Alaska, and Idaho), have been successful in reducing the prevalence of chlamydia infections.¹⁸ In its first nine years, Region X's program resulted in a 67% decline in chlamydia positivity (from 9.3% of those tested in 1988 to 3.1% in 1997). The National Infertility Prevention Program currently funds chlamydia screening and treatment services in all 10 PHS regions. There is evidence that supports that these centers have contributed to a decline in the incidence of chlamydia cases nationally.¹⁴

CDC estimates that *Chlamydia trachomatis* infections and their consequences cost approximately \$2.6 billion (in 1997 US dollars) each year.¹⁹ Based on a conservative CDC estimate of 6.6% prevalence of chlamydia infection, universal screening and treatment for chlamydia of women ages 15–20 in STD and family planning clinics would save approximately \$900 to \$1000 (1993 dollars) for each case of chlamydia successfully treated, compared with a no-screening strategy.²⁰

Other lifestyle factors. Many other preventable causes of both male and female infertility have been identified, including lifestyle factors such as obesity and weight gain; weight loss and eating disorders; excessive exercise; and use of nicotine, alcohol, or caffeine.²¹ Although these causes are important to consider both clinically and epidemiologically, the magnitude of their effect is dramatically less than that of complications resulting from chlamydia infection.

While it is important to educate couples about factors that have been shown to be associated with infertility, it is difficult to predict the likelihood that changing behavior will result in a pregnancy. Many people may choose to change their behavior simply because it is something over which they have control. That, in and of itself, may be psychologically desirable, since the feeling of powerlessness experienced by infertile couples is sometimes overwhelming. In addition, changes in health-related behaviors, such as moderating diet, reducing caffeine intake, and stopping smoking, may result in two other positive outcomes—an improved



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overall health status and a reduced likelihood of harm to the fetus should a pregnancy occur.

Maternal age. Bob and Roberta, as an “older” couple wishing to conceive a child, represent a growing subset of the population reporting infertility. An increasingly common cause of infertility is advancing age of the woman. The effects of aging on egg quality and ovulatory function as well as an increased risk of disorders such as endometriosis, result in decreased fertility as a woman proceeds from her 20s through her 30s and into her 40s. In addition to a lower ability to conceive, older women are also at greater risk of early pregnancy loss. According to 1995 NSFG data,² 11.7% of women ages 15–24 experience impaired fecundity, while in the 35–44 age group, almost four times as many women (42.1%) have difficulty becoming pregnant or carrying a baby to term.

The current generation of women in their late 30s and early 40s has exercised an unprecedented degree of control over childbearing with the birth control pill, legalization of abortion, delayed marriage, and the increasing choice to pursue a career prior to starting a family. The rise in the prevalence of infertility since 1988 has been due largely to the rise in the number of women entering the older reproductive age range (ages 35–44 years)—the “baby boomers” coming of age—and the markedly high percentage of these

women who have delayed childbearing.⁴

A possible negative side effect of the extensive media coverage of technologic advances in the treatment of infertility is that it may provide many couples false expectations about the ability of technology to help them should they have difficulty achieving a pregnancy. Couples should be counseled about the increased risks of infertility and impaired fecundity associated with advancing maternal age and provided with a realistic estimate of success rates for various therapies. Though many factors, including emotional and financial security, must rightfully be considered in the decision to have a child, it is clear that the decision cannot be postponed indefinitely.

Although most clinical definitions of infertility rely on the magical cut-off of one year of unprotected, well-timed intercourse, it is important that couples and clinicians alike be mindful that the timetable for women in their mid- to late 30s should be shortened. Jansen, a leading researcher, argues that the two best predictors of the chance of achieving pregnancy naturally in circumstances of relative infertility are the duration of infertility and the estimated time left for conception.²² It is clear that, at 37, Roberta’s chances of a successful pregnancy are considerably slimmer than they might have been even a few years earlier.²³ Therefore, after only eight months (or even sooner), she is an appropriate candidate for medical work-up.

Occupational and environmental exposures. In addition to chlamydia infection and the lifestyle factors that have been implicated as causative agents in infertility, more than 50 chemicals found in the workplace and the environment are known to be associated with adverse reproductive outcomes in both men and women.²⁴ Several studies have demonstrated an association between exposures to chemicals, most notably solvents and pesticides, and adverse outcomes such as spontaneous abortions and birth defects.²⁵ Less clear has been the link between workplace and environmental hazards and decreased fertility, perhaps partly due to the difficulty of studying that outcome, particularly among women.

Workplace chemicals and infertility. Despite methodologic problems, significantly higher rates of infertility have been observed in women employed in several occupations, including dental assistants exposed to nitrous oxide,²⁶ women exposed to glycol ethers in the production of silicon wafers in the semiconductor industry,²⁷ and women exposed to organic solvents in a variety of occupations.²⁸

One of the most notorious chemicals implicated in male infertility is 1,2-dibromo-3-chloropropane (DBCP), a soil fumigant (nematocide) used widely in the United States from the early 1950s until 1977. After several men employed at a chemical company in California were noted to be experiencing significant difficulties in starting families, a study of 36 workers engaged in the manufacture of DBCP revealed that 14 (39%) had low sperm counts.²⁹ Further studies documented a dose-response relationship between exposure to DBCP and sperm count, apparently due to damage to the seminiferous tubules, as seen on testicular biopsy.³⁰ Within one month of workers at the chemical company reporting their problem to their union, the Occupational Safety and Health Administration (OSHA) issued an emergency temporary standard, and six months later a permanent standard of one part per billion (eight-hour time weighted average) was promulgated. Two years later, the Environmental Protection Agency banned the use (with one exception that has since been eliminated) of DBCP in the US.

The history of DBCP is considered a public health success story. Alert workers and an alert clinician worked together to document a problem, which led to the establishment of policies geared to reducing and eliminating exposure to the offending agent. It must be noted, however, that there are numerous other pesticides still in use worldwide that have been associated with male infertility or other adverse reproductive outcomes.³¹⁻³³ In addition, of the approximately 60,000 chemicals and four million chemical mixtures in commercial use, only a small fraction have been tested for reproductive effects.^{34,35} While more than 1000 workplace chemicals have shown reproductive effects in animals, physical and biological agents in the

workplace that may affect fertility and pregnancy outcomes are practically unstudied in humans.³⁵ A true public health success story would be one in which adverse health effects were prevented in the first place by more rigorous strategies to evaluate the toxicant properties of chemicals currently in use.

Environmental exposure. In addition to potentially harmful exposures experienced on the job, larger populations may be affected by exposures occurring in the environment. There is concern that environmental toxicants may be contributing to a more widespread lessening of fertility, in particular a decline in sperm count over time. One of the most troubling and controversial findings in recent years has been an apparent decline in semen quality worldwide over a 50-year period. In an analysis of 61 studies published from 1938 through 1990, Carlsen et al.³⁶ found a significant decline in mean sperm concentration and volume. Their study suffered from several methodologic limitations, including simplistic statistical modeling, possible selection biases, and numerous uncontrolled potential confounders. However, a recent re-analysis that attempted to account for many of these limitations still found evidence of reduced sperm quality over time.³⁷ Importantly, however, the decline did not appear to be geographically uniform across regions. Recent studies also provide evidence of geographic variation, documenting a decline in France and Scotland but not in the United States.³⁸⁻⁴⁰ Geographic differences are marked and need further exploration to shed light on population and environmental factors that contribute to these differences.

The proliferation of chemicals that disrupt the functioning of the endocrine or hormonal system is a principal suspect in the apparent decline in sperm quality in parts of the world. Humans are exposed to a number of such "endocrine disruptors"—synthetic, fat soluble, long-lived compounds, including chlorinated pesticides such as DDT and kepone and industrial compounds such as polychlorinated biphenyls (PCBs), phenols, and dioxins. Exposure to these chemicals may occur through a variety of pathways, including exposure to pesticides or industrial emissions and/or ingestion of animal fat or contaminated drinking water. Evidence from animal studies implicating these chemicals in causing adverse reproductive effects is convincing across a large number of species,⁴¹ but human evidence is less clear-cut. Further research is clearly needed.

THE INFERTILITY WORK-UP

After their work-up, Roberta and Bob meet with the physician to discuss their findings, which include partial obstruction of one fallopian tube on X-ray, an abnormal post-coital test (a measure of the ability of sperm to move through a woman's cervical mucus at

the time of ovulation), and lower than "normal" motility on semen analysis. The couple is referred to an infertility specialist, who recommends a course of antibiotics for both partners to treat a presumptive male genital infection and three months of intrauterine insemination with controlled ovarian stimulation. If no pregnancy ensues, they will move on to IVF.

Regardless of the etiology or etiologies of their reproductive difficulties, whether related to some previous infection or advancing age or due to some suspected or unknown personal or environmental factor or a combination of causes, Bob and Roberta now have to deal with having been told by their physician that they have abnormal test findings. What do their test findings mean? The accuracy of common diagnostic tests and the effectiveness of common treatments for infertility have not been well established. Although post-coital testing and semen analysis are standard elements of the infertility work-up, a correlation of the findings of these routinely used tests with the post-treatment conception rate has not been established.^{42,43} Variations in standards and test performance are common for both of these tests, and current testing standards may be inadequate to control inter-rater reliability, consistency of results from method to method and laboratory to laboratory,⁴⁴ and an acceptable level of sensitivity and specificity.⁴⁵

TREATING INFERTILITY

After antibiotic therapy and three months of intrauterine insemination without success, our couple attempts IVF. In the first two tries, Roberta does not respond well to ovulation induction, and no mature oocytes can be recovered with which to attempt fertilization. The physician meets with Roberta and Bob, summarizes their results so far, presents them with a list of options, and discusses in detail the expected prognosis and potential problems associated with each course of action.

Informed consent. Bob and Roberta are well served by their physician if they receive high quality care based on knowledge of and expertise in the most recent technologic advances, with consideration of the most appropriate therapies that suit them individually and as a couple. However, they are only served well if that care comes with their full understanding of and consent to treatment options; with full disclosure of the probability of success and possible adverse effects of each option; and with full disclosure of non-medical options to achieving parenthood such as adoption.

The issues surrounding informed consent for infertility treatment are complex and challenging. Concerns arise within the realm of infertility treatment that simply do not occur in other forms of medical care. These include the

ethical and legal issues related to embryo storage and third-party (surrogate mother or gamete donor) reproduction. In addition to protecting the autonomy of the adults involved in decision-making, the informed consent process must safeguard the interests of the child who may be born as a result of these procedures. In fact, the amount of information to be presented to infertility patients is so extensive that two states (New Hampshire and Virginia) have enacted laws to govern the content of discussions and one state (New York) has developed an extensive set of recommended guidelines for the use of ARTS, including the informed consent process.⁴⁶

In addition to the features that distinguish infertility therapies from treatments for other conditions, there are, of course, an obvious set of issues that are common to informed consent for all types of medical interventions. Paramount among these is disclosure about effectiveness and safety. Calculation of risk-benefit ratios for infertility treatments has been difficult for a variety of reasons. Much of the research about effectiveness and risks of treatment suffers from lack of controlled clinical trials, small study samples, and lack of agreement on definitions and outcome variables. Exacerbating this problem is the fact that, for most of the past quarter of a century, Congress has banned the use of federal funds for the support of embryo research. Neither risk nor benefit has been clearly established for many of the most common treatments, both low and high tech.

"Low tech" therapies. Technologies that do not involve retrieval of oocytes or fertilization outside the body—"low tech" procedures—constitute more than 95% of the treatments provided for infertility.⁴⁷

For many patients with impaired fertility in which there is no obvious diagnosis, treatment plans begin with attempts to stimulate the ovaries to produce more than one egg ("superovulate") by the use of one or more drugs, often in concert with intrauterine insemination. Intrauterine insemination is a procedure in which concentrated sperm are introduced directly into the cervix with the goal of improving oocyte quality, increasing the number of oocytes available for fertilization, and giving sperm an "assist" by placing them higher up in the reproductive tract. Conception rates after intrauterine insemination have ranged widely in different studies,⁴⁸ and valuable time may be lost for the older woman if this strategy is employed, as is often the case, for many months prior to attempting IVF. There is evidence for a treatment-independent or placebo effect that can confound the interpretation of success rates for these infertility treatments, even in cases of longstanding infertility.⁴⁹ In one large series, no difference in conception rates could be demonstrated between treated and non-treated groups of infertility patients.⁵⁰ Although the federal government is now engaged in surveillance of outcome data from "high tech" procedures,

there is no formal monitoring process or mandated reporting for "low tech" therapies.

"High tech" procedures. Given their lack of success with intrauterine insemination, Bob and Roberta decide to go on to one of the ART procedures—treatments or procedures that involve the handling of human eggs and sperm for the purpose of helping a woman become pregnant. They are not alone. In 1996, more than 64,000 ART procedures were carried out in clinics in the United States.⁵¹ The most common ART procedure is *in vitro* fertilization (IVF), which involves removing a woman's eggs from her ovaries, fertilizing them with sperm outside her body, and transferring the resulting embryos into her uterus through the cervix. All ARTs, including IVF, are most commonly performed using fresh (non-frozen) embryos developed from the woman's eggs (71% of all ART procedures), but it can also be performed using frozen embryos (14%) and donor gametes or embryos (8%).⁵¹ Other ARTs include zygote intrafallopian transfer (ZIFT) (2% of ARTs) and gamete intrafallopian transfer (GIFT) (5%).⁵¹ ZIFT differs from IVF in that the embryos are transferred to the fallopian tubes rather than to the cervix. In the GIFT procedure, unfertilized eggs and sperm are placed with a laparoscope into the woman's fallopian tubes, where fertilization is expected to occur.

In her IVF cycles, Roberta was unable to produce mature oocytes with which to attempt fertilization. Had she undergone oocyte retrieval, what would have been her chance of getting pregnant? In 1996, the overall rate of pregnancies per cycle for all ARTs was 27%⁵¹ (Figure 1),

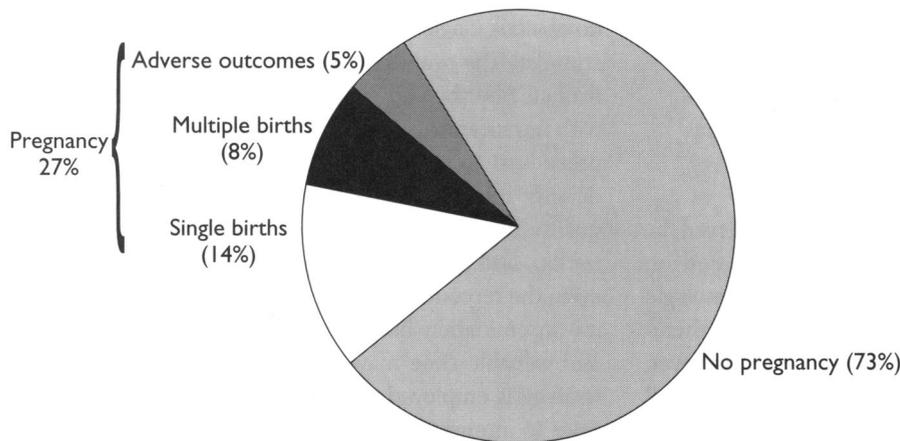
while the rate of *live births* per cycle was 22.6%. That rate differs, however, according to a number of factors, including patient age, diagnosis, length of infertility, the number of previous IVF attempts, and the size and quality of the clinic.⁵¹ Most important of these factors is age, with a 28.7% rate of live births per cycle reported in 1996 for women younger than 35 years of age, compared with 21.3% among women ages 35–39, and only 8.7% among women older than 39 (Figure 2).⁵¹

The goal of most couples attempting IVF is to become pregnant and give birth to one healthy baby. If Roberta had become pregnant through IVF, what would have been her chances of achieving that goal? Of the 27% of IVF procedures performed in 1996 that resulted in a pregnancy, approximately one-half (52.3%) resulted in a single birth (Figure 3).⁵¹ About one-quarter (26.3%) resulted in twins, and 5.8% triplets or greater. The remaining 15.6% resulted in an adverse outcome (ectopic pregnancy, induced abortion, spontaneous abortion, stillbirth).

Risks of therapy. In addition to the risks inherent in the use of invasive procedures, all treatments that require superovulatory drugs to stimulate the production of mature oocytes carry added risk.⁵² The use of these drugs has been linked to a number of significant health risks, including ovarian hyperstimulation syndrome (OHSS), which is characterized by a combination of ovarian enlargement and an acute fluid shift out of the intravascular space. Severe OHSS can be a life-threatening event. Though it is relatively rare,⁵³ it must remain a concern to both clinician and patient.

Another concern is that superovulation may be associated with an increased risk of ovarian cancer. The first epidemiologic study to document the possible link was reported by Whittemore et al.,⁵⁴ who analyzed combined data from 12 case-control studies conducted in the US. The nature of this association has been a matter of controversy since then.⁵⁵ Though few dispute that the association exists, there is substantial disagreement as to whether it is causal. A highly plausible explanation for the observed association is that women with particularly refractory

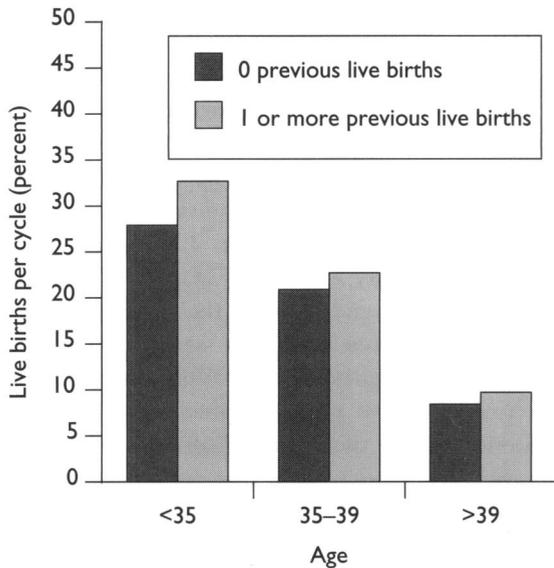
Figure 1. Results of fresh, nondonor ART cycles, United States, 1996



SOURCE: Reference 51

Fresh = embryos not frozen
 Nondonor = woman's own eggs used
 ART = assisted reproductive technology

Figure 2. Live birth rates for fresh, nondonor ART cycles, by woman's age and number of previous live births, United States, 1996



SOURCE: Reference 51

Fresh = embryos not frozen
 Nondonor = woman's own eggs used
 ART = assisted reproductive technology

has focused on a high rate of multiple births among women pregnant as a result of ARTs, the same drugs are widely used to treat ovulatory function in contexts not associated with IVF, such as intrauterine insemination. Their use in these cases is not monitored or reported.

A host of serious consequences are associated with multiple births, particularly higher order births. Neonatal complications include prematurity and resulting long-term complications, low birth weight and resulting complications, congenital abnormalities, and respiratory distress syndrome.⁵⁸⁻⁶⁰ Infant mortality is 15 times higher for higher-order multiples than for singletons.⁶¹ Among the potential medical complications for the mother are hypertension, anemia, postpartum hemorrhage, and depression.^{58,62-64}

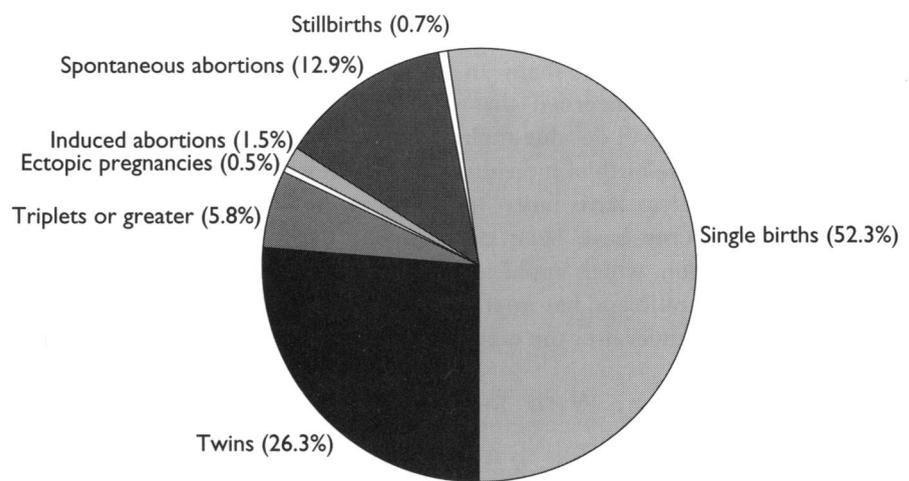
The financial costs related to the delivery and perinatal care of multiples are substantial, straining an already over-stressed health care system. The maternal and neonatal costs for a triplet pregnancy have been estimated at \$64,000.⁶³ The in-hospital costs of multiples resulting from ART at one Boston hospital alone were estimated at \$3 million per year.⁶⁵

In addition to obvious physical risks to both mother and children and the monetary costs of higher order multiple births, there are harder to measure, but very significant costs and stresses on all members of the family—extreme sleep deprivation, anxiety, depression, lack of personal time for parent and child, and long-term financial strains.

infertility, who are likely to use ovulation enhancing drugs, may constitute a high-risk population for developing ovarian cancer. It has been suggested that "precancerous ovarian conditions may have 'caused' [superovulatory] therapy rather than the reverse."⁵⁶

The most obvious and well-publicized side effect of superovulation therapy is the increased risk of multiple births. Wider use of ARTs has greatly increased the number of twins and higher order (triplets or higher) multiple births.⁵⁷ In 1996, 38% of all ART births in the US were multiple births, compared with 2.7% of births in the general population.⁵¹ Although public discussion

Figure 3. Outcomes of pregnancies resulting from fresh, nondonor ART cycles, United States, 1996



SOURCE: Reference 51

Fresh = embryos not frozen
 Nondonor = woman's own eggs used
 ART = assisted reproductive technology

Expanded indications and new uses of ARTs. Although IVF was first developed to address a single medical indication, blocked fallopian tubes, ARTs are now used to treat almost all infertility conditions that do not respond easily to conventional therapies. It has even been suggested that it is cost-effective for patients to utilize an ART technique as a *first line* therapy for endometriosis and anovulation, common medical causes of infertility.⁶⁶

In addition, IVF is now commonly used to treat non-infertile couples for concerns and problems that are not related to infertility. IVF may be undertaken as an elective procedure to allow use of embryo biopsy for purposes of sex selection and genetic diagnosis. In these situations, ovulation induction medications are used to increase the number of available oocytes, which are retrieved and cultured with sperm in the IVF laboratory. A single cell is removed from each of the resultant pre-embryos. The DNA in the removed cell is then amplified using polymerase chain reaction techniques and analyzed to determine genetic sex, or presence of chromosomal abnormalities or markers for diseases such as cystic fibrosis or Tay-Sachs. Pre-embryos that demonstrate the desired genetic makeup are then implanted in the uterus and allowed to grow.⁶⁷

The rapidly expanding market for ARTs raises a number of concerns. The complexity of these procedures makes it difficult for patients to evaluate whether a specific ART treatment that is offered to them is really necessary or is appropriate, especially early in their treatment. Furthermore, the ethics of using these technologies is complex. It is certainly understandable that couples who have experienced the birth and death of child with a serious genetic disease are anxious to prevent a reoccurrence. However, many in the disability community are equally concerned that the ability to select a "designer" child will devalue their own lives and struggles and prevent the birth of individuals who are not "perfect" but nevertheless have much to contribute to society. Similar concerns have been raised about the practice of sex selection, which could result in changes in the male-to-female ratio and has implications for societal valuation of one gender over the other.

COST OF TREATMENT: WHO SHOULD PAY?

Once they understand the procedures being recommended, Bob and Roberta must face a practical obstacle in their decision whether to proceed: can they afford it? The cost of ARTs is quite high, ranging from \$7000 to \$11,000 per treatment cycle. In 1988, the federal Office of Technology Assessment determined that the cost of one IVF procedure to a couple with health insurance would equal 23% of the annual house-

hold income of a couple in the middle-income bracket (median annual income: \$27,500) and 67% of the annual income of a low-income couple (median annual income: \$10,000).¹¹

Health services researchers can now provide estimates of the actual cost of insurance coverage for infertility services, and those estimates can promote rational political discussion.⁶⁸ Insurance coverage is necessary if infertility treatment is to be available to the majority of those who seek it, yet there is substantial controversy about whether infertility is a condition that should be covered by insurance. At present, 12 states have laws dealing with infertility insurance⁶⁹ (Figure 4). They vary widely in the nature and scope of the required coverage. The definition of infertility varies across states, ranging from one year of unexplained failure to conceive in Massachusetts to five years of infertility *and* the presence of one or more specifically diagnosed conditions in Hawaii. Several states require that certain insurers *offer* coverage for infertility diagnosis and treatment. However, these insurers are not required to *provide* the coverage, nor does the legislation force employers to include it in their employee insurance plans. One such state, Texas, offers coverage only for IVF, while another state, California, specifically excludes IVF. At the other end of the spectrum, Massachusetts requires all health maintenance organizations and insurance companies that cover pregnancy-related benefits to provide coverage for infertility diagnosis and treatment. In Massachusetts in 1986–1993, the cost of providing comprehensive services was 0.4% of the mean total monthly family health insurance premium, or \$1.71 per contact month.⁷⁰ It should be noted, however, that this relatively modest premium increase paid by all subscribers includes only the cost of the ART procedures. Due to its wide-ranging insurance coverage, Massachusetts has seen an increased use of ARTs and a resulting increase in multiple births.⁷¹ The formula used to calculate the estimated premium increase does not include the significant maternal and perinatal medical costs incurred as a result of those multiple births.

Health services researchers are creating a body of population-based research data that can be used to establish policies on access to medical procedures, quality of care, and regulation of service delivery.⁷² Several studies have produced calculations of the cost of certain fertility therapies.^{73,74} Efforts are now underway to establish more sophisticated formulas that include on one side of the cost-benefit equation the costs not only of services but of providing care to the premature infants born as a result of infertility therapies. On the other side of the equation, cost-effectiveness needs to include the equally important calculation of the costs of *not* providing infertility treatment, including the cost of

Figure 4. US states with legislation on health insurance coverage for infertility-related medical services

State	Date enacted	Mandate to cover	Mandate to offer	Includes IVF coverage	Excludes IVF coverage	IVF coverage only
Arkansas	1987					■ ^a
California	1989		■		■ ^b	
Connecticut	1989		■	■		
Hawaii	1987	■				■ ^c
Illinois	1991	■		■ ^d		
Maryland	1985	■				■ ^e
Massachusetts	1987	■		■		
Montana	1987	■ ^f				
New York	1990				■ ^g	
Ohio	1991	■ ^h				
Rhode Island	1989	■		■		
Texas	1987		■			■

SOURCE: Reference 69

^aIncludes a lifetime maximum benefit of not less than \$15,000.^bExcludes IVF, but covers gamete intrafallopian transfer (GIFT).^cProvides a one-time only benefit covering all outpatient expenses arising from IVF.^dLimits first-time attempts to four oocyte retrievals. If a child is born, two complete oocyte retrievals for a second birth are covered.^eBusinesses with 25 or fewer employees are exempt from having to provide the coverage specified by the law. Businesses with 50 or fewer employees do not have to provide coverage.^fApplies to HMOs only; other insurers are exempt from having to provide the coverage.^gProvides coverage for the "diagnosis and treatment of correctable medical conditions." Does not cover IVF as a corrective treatment.^hApplies to HMOs only.

treatment of depression, decreased work productivity, and the costs of adoption and other alternatives.⁷⁵ Risk-benefit and cost-benefit ratios for specific treatment alternatives are also being compared, in order to enhance rational decision-making.⁷⁶

In discussing the nature of public health, Sir Geoffrey Vickers wrote, "Every new technique, by opening a possibility, awakens a need—at least in our Western culture, where in matters of health we have a highly developed sense that whatever is possible for any should be available to all."⁷⁷ Vickers continued, "The development of the automobile did more than provide us with a new means to satisfy our needs. It set new needs, new expectations, new norms of mobility, even new limits of unacceptable immobility." These words were written in 1958, yet they are clearly relevant today to ARTs. The introduction and increasingly widespread use of ARTs is setting new expectations for infertile couples, many of whom will no longer accept their fate without trying every possible remedy.

In our ethical dialogue in the past decade, we have seen an expansion of concerns from the sustainability of life to the quality of life. One question at issue is whether public funds should be made available to improve the

quality of life of infertile people by providing them with the possibility of creating a biologic family. We live in a world characterized by major social inequities. Children languish in our foster care system; large numbers of families are homeless; 44 million Americans lack health insurance coverage.⁷⁸ There are those who would argue that in a world of many competing needs, not all needs can become rights, and we are obligated to living persons before we spend money on potential persons. From this point of view, infertility belongs low on the list of priorities. Couples facing infertility may have a very different perspective. In a world in which we spend public monies for quality of life items such as bicycle paths and recreation facilities and allow tax credits for vacation homes, they do not understand why they are required to pay into the insurance pool that provides pregnancy coverage for others while receiving little or no support for their own family-building needs. Similarly, those who choose to pursue adoption as a means of building their families are often stymied in their efforts by the high costs, most or all of which comes out of their own pocketbooks. These are tough issues. We need public debate among health services researchers, consumers, ethicists, and health care practitioners to achieve a consensus about whether infer-

tile couples have a *right* to have a family, and whether society has a duty to help them.

ETHICAL ISSUES

Given the failure of IVF using Roberta's own eggs, Roberta and Bob decide to proceed with egg donation. A donor is identified through a location service. Half of the \$10,000 fee goes to the donor for her time and trouble, and the other half is paid to the agency. The recipients are told only that their egg donor is a local college student who resembles Roberta in skin, hair, and eye coloring and in body build. A surgical procedure to recover oocytes from the donor is successful, and several mature oocytes are incubated with Bob's sperm in the IVF laboratory. Because fertilization does not occur on the first day of incubation, intracytoplasmic sperm injection (ICSI, or mechanical insertion of a single sperm into each egg) is performed. Four ova subsequently fertilize and are placed in Roberta's uterus. She has a positive pregnancy test 11 days later, and ultrasound at three weeks post-missed menses shows four gestational sacs, each with a fetal heartbeat.

Gamete donation. Gamete donation, whether of sperm or egg, is a process that challenges the concept of family and the definition of parenthood. The complexities of the resulting relationships can be staggering given the range of

third-party techniques available: donor sperm, donor egg, donor embryo, genetic/gestational surrogacy (surrogate uses her own eggs), gestational surrogacy (surrogate uses eggs of intended mother), gestational surrogacy with donor eggs or embryos (surrogate uses eggs or embryos that have no direct genetic relationship to intended parents or to the surrogate). There are very few statutes addressing parental rights and responsibilities in third-party reproduction, and case law has been inconsistent.⁴⁶

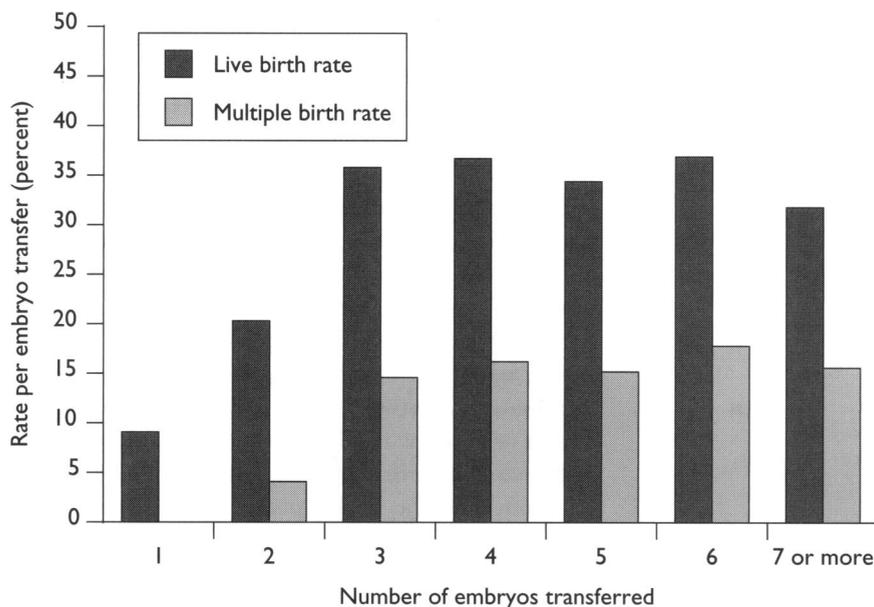
In addition to questions related to the parentage of children born of egg donation, many other ethical and policy issues are created by these means of building a family.⁷⁹ Should egg donors be paid for their time, trouble, and risk? If so, how much? If the price is low, are we asking women to assume health risks, major inconveniences, and potential long-term emotional consequences without compensation? If the price is high, do we turn women into commodities, with their body parts to be bought and sold on the open market? Are we entering the realm of eugenics, in which donors are selected because of their physical attractiveness or intelligence? Society as a whole—not just ART clinics, infertile couples, and gamete donors—has a vital interest in the debate about these questions.

Perhaps most notably lacking from the ART policy arena is discussion of and research on the long-term consequences of ARTs—particularly those involving gamete donation—for the resulting children. More than 20 years have passed since Louise Brown was born as the result of the first successful IVF procedure. Sperm donation was



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Figure 5. Live birth and multiple birth rates for fresh, nondonor ART cycles among women younger than age 35 years, by number of embryos transferred, United States, 1996



SOURCE: Reference 51

Fresh = embryos not frozen

Nondonor = woman's own eggs used

ART = assisted reproductive technology

introduced a century earlier, while egg donation, first used successfully in 1984, is a more recent alternative method of family building. The introduction of third parties into the reproductive process carries the potential for both physical and psychological sequelae. The long-term consequences for the adults involved, for the child, or for society have not been adequately studied. Many of the babies that have been born of these technologies are now grown up. We have a lot to learn from them.

New or experimental therapies. Roberta and Bob have no reservations about the use of ICSI. Their doctor, after all, was trained to make these decisions and they trust that she will advise them well. The reality, however, is that ICSI is a human experiment in progress, one that may well be of sufficient benefit to outweigh any potential risks; however, data are still not available to make that evaluation with certainty or to counsel patients adequately.⁵¹ In the absence of federal funding for embryo research, most of the research in this field is conducted in private clinical settings. Thus, progress in the area of reproductive endocrinology has been driven largely by competition among infertility centers to achieve higher success rates. Although these efforts have led to rapid technological

advances, research activities have not been subject to the kind of scientific rigor or oversight common to federally funded investigations.

Excess embryos. All four of the fertilized eggs were transferred to Roberta's uterus. What if 10 eggs had fertilized, with only three or four to be transferred? What would have happened to the remaining pre-embryos? This is a decision made every day by ART patients in clinics all over the world. There are several options, each fraught with ethical and policy dilemmas.

Cryopreservation, or the freezing and storage of embryos, is widely performed; hundreds of thousands of embryos are currently in storage across the US, without standardized policies regarding how

long they will be kept until being discarded and without clear-cut knowledge of any potential risks to resulting children. The discarding of "excess" embryos, particularly those in which genetic testing reveals a defect, is problematic for those who see embryos as human life and for those who are concerned about the practice of eugenics. In Louisiana, it is illegal to discard an IVF-fertilized human embryo. Donation to other women, though altruistic, carries with it a number of potential emotional and legal risks. Another option is to donate the "excess" embryos to research. Embryo research is the subject of much ethical debate and resulting legal action. Since 1974, the use of federal funds for embryo research has been banned. Five states have relevant legislation: the practice is banned in Louisiana, New Mexico, Pennsylvania, and Illinois (though the ban has not been upheld in Illinois). Embryo research is allowed, with restrictions, in New Hampshire.⁴⁶

No matter how an individual or couple decides to treat "excess" embryos, it is clear that this is a subject that must be addressed clearly and forthrightly as part of the informed consent process. There must be an agreement between a couple regarding what to do in the case of divorce, separation, or death of one or both

Figure 6. Legislation and guidelines on use of assisted reproductive technologies among principal nations in which *in vitro* fertilization is practiced

Country	Legislation	Guidelines	Neither
Argentina		■	
Australia			
West	■		
South	■		
Victoria	■		
Other		■	
Austria	■		
Belgium			■
Brazil	■		
Canada			■
Czech Republic	■		
Denmark	■		
Egypt	■	■	
Finland		■	
France	■		
Germany	■		
Greece			■
Hong Kong			■
Hungary	■		
India			■
Ireland		■	
Israel	■		
Italy		■	
Japan		■	
Jordan			■
Korea		■	
Mexico	■		
Netherlands	■		
Norway	■		
Poland		■	
Portugal			■
Saudi Arabia	■		
Singapore	■		
South Africa	■		
Spain	■		
Sweden	■		
Switzerland		■	
Taiwan	■		
Turkey	■		
United Kingdom	■		
United States		■	

SOURCE: Reference 84

Selective reduction. Somewhat naively, Roberta and Bob have not given much thought to the results of this cycle of infertility treatment, that is, to the fate of the four transferred embryos. To people who thought that they might never achieve a pregnancy, the thought of four fetuses instead of one at first seems to hardly be a problem, despite counseling about the risks to the fetuses from multiple pregnancies. However, the reality of their situation sinks in when their physician brings up the topic of “selective reduction,” the process by which one or more fetuses are “terminated” with the goal of allowing the pregnancy to continue with a more sustainable number. While there is evidence that the procedure is effective in its goal of producing a successful pregnancy with a reduced number of fetuses,^{80,81} it engenders a multitude of ethical questions.⁸² And the idea of terminating a fetus may be anathema to the potential parent or parents who have endured physical, emotional, and financial hardship to bring it into being.

From a public health perspective, prevention is certainly preferable to treatment of multiple births, either *in utero* or after birth. In the United States, infertility specialists have developed guidelines that call for facilities to transfer no more than the number of embryos that will result in a national triplet rate of 2% or lower,⁸³ but no regulatory process has been established and there are no provisions for incentives or deterrents. Other nations have adopted regulatory policies to prevent prematurity due to multiple births. In England, for example, no more than three embryos may be transferred and no extenuating circumstances are permitted.⁸⁴ This policy seems to be a reasonable approach to reducing the number of multiple births, and it may also result in success rates no lower than those experienced after transfer of four or more embryos. In 1996, the live birth rate among US ART patients increased considerably as the number of embryos transferred increased from one embryo (9% of cycles) to two (20%) to three (36%), but did not increase with the transfer of additional embryos.⁵¹ However, the multiple birth rate was slightly higher with a higher number of transferred embryos (Figure 5).⁵¹

LEGISLATION AND REGULATION

Despite the plethora of controversial issues raised by ARTs, their use has largely been unregulated in the US. A first step in protecting the public was legislation sponsored by Oregon’s Senator Ron Wyden in 1992—the Fertility Clinic Success Rate and Certification Act of 1992.⁸⁵ This legislation was intended to provide the public with information concerning the effectiveness of infertility services and to assure the quality of such services by providing for the certification of embryo laboratories. The statute requires each ART program to report

parties, and that agreement must be in writing. At present, there are no mandates in the US for this level of informed consent.

yearly to the CDC its pregnancy success rates. This has resulted in the annual publication since 1995 of clinic results and national summary data reported by the CDC, with the American Society for Reproductive Medicine, the Society for Assisted Reproductive Technology (SART), and Resolve.

Embryo laboratories are currently subject to several limited levels of oversight. Regulations of the federal Clinical Laboratory Improvement Amendments of 1988 (CLIA)⁸⁶ apply to a limited number of procedures carried out in embryo labs. In addition, laboratories must be recognized by an accrediting organization such as the College of American Pathology in order to maintain membership in SART. As mandated in the 1992 legislation, the CDC has developed a model program for the certification of embryo laboratories to be carried out voluntarily by interested states. The resulting model developed and published by the CDC in July 1999 provides detailed standards for assuring consistent performance of laboratory procedures, quality assurance and quality control, maintenance of all laboratory records, and personnel qualifications.⁸⁷

Despite these important accomplishments, many concerns remain. With few exceptions, no state or federal regulations address the complex issues of informed consent; payment to gamete donors or surrogates; limits on the number of embryos transferred; possible eligibility restrictions on patients based on factors such as marital status, age, and sexual orientation; and other ethical issues such as use of donor eggs from human fetuses, use of sperm retrieved from cadavers, and animal-human hybrids.

The American Society for Reproductive Medicine has issued guidelines for the practice of ARTs covering a wide range of issues, including informed consent, donor screening, cryopreservation, protection of a future child, and techniques such as sex selection that have generated considerable controversy.⁶⁹ These guidelines, however, do not have the force of regulation, and membership in the organization or its specialty bodies is not contingent on compliance.

Many other nations have sought to develop some form of control. A recent study reviewed the regulatory practices of 38 countries.⁸⁴ Of them, 20 have legislation governing ARTs, 11 (including the US) have guidelines in place, and seven have no regulation (see Figure 6). Regulatory bodies vary considerably, with jurisdiction delegated to specific ART licensing authorities, to religious bodies, or to agencies that regulate clinical laboratories. The scope of regulatory activities also varies widely. For example, 12 countries have regulations requiring that IVF be offered only to married couples. Nine nations and subjurisdictions have put limits, ranging from two to four, on the number of embryos to be

transferred. Four countries have established time limits for embryo cryopreservation. Austria, Germany, Ireland, and Japan permit sperm donation but not oocyte donation. Some nations with legislation or guidelines address only the types of procedures that are to be performed or the individuals on whom they may be performed, while others provide for specific protective measures such as informed consent, counseling, and evaluation of the suitability of infertile couples for parenthood.

Unlike other nations where there is considerable agreement among medical professionals, ethicists, and the lay public, there is little consensus in the US about what type of regulation would best suit the needs of this country. However, there seems to be a growing understanding among consumers, advocacy groups, professional societies, and government agencies that some form of regulation may be necessary given the complexity of the medical, ethical, and societal issues involved in the practice of ARTs.

CONCLUSION

No one who has endured the trauma of infertility or followed it closely with others can deny its impact on the lives of individuals, couples, and families. But clearly the effects of infertility are even more wide-ranging, with implications for the targeting of preventive efforts, the rational and equitable use of health resources, and ethical, legal, and religious questions that touch on the very meaning of parenting, family, and life itself. A public health perspective is needed in enacting policies that address these issues and protect the rights of all parties, including—and especially—the children that are born as a result of treatment. In addition, consideration must be given to the public health implications of adoption, where the realms of infertility and unplanned pregnancies intersect.

The history of the latter half of the 20th century has been dominated by advances in technology in many spheres, none more remarkable than in the field of medicine. From organ transplants to gene therapy, we are the beneficiaries of medical miracles that would have been unthinkable only a generation or two ago. The advancing technology of reproductive medicine rivals any other aspect of medicine not only for the technologic wizardry that it incorporates but because it deals with the very creation of human beings. With that ability comes the extra responsibility to provide a careful examination of the ethical and moral considerations surrounding the use and potential misuse of each new methodology. Our society needs a public dialogue on the issues raised by the rapid adoption and dissemination of new reproductive technologies. Public health professionals need to be active in the effort to set the direction for public policy

and ensure that our knowledge does not accumulate faster than our wisdom to manage it.

Dr. Fidler is a Centers for Disease Control and Prevention (CDC) Academic Liaison, Public Health Practice Program Office, Centers for Disease Control and Prevention, Atlanta, assigned to the Boston University School of Public Health, where she is Assistant Dean for Environmental Health Practice and Associate Professor of Environmental Health. Dr. Fidler is also an Editorial Consultant for

Public Health Reports. Dr. Bernstein is an Assistant Professor of Maternal and Child Health, Director of the MCH Certificate Program at Boston University School of Public Health, and a member of the Committee on Ethics of the American College of Obstetricians and Gynecologists.

Address correspondence to Dr. Fidler, BUSPH, 715 Albany St., Boston MA 02118; tel. 617-638-4647, fax 617-638-5299; e-mail <afidler@bu.edu>.

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