Bioethics for clinicians: 26. Assisted reproductive technologies

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Abstract

ASSISTED REPRODUCTIVE TECHNOLOGIES (ARTs) can be very helpful for certain patients, but ethical concerns have been raised about the inherent nature of specific techniques and the contexts in which many techniques are used. Physicians play important roles in supporting those who wish to become parents and in educating patients about impediments to fertilization and ways to promote conception. We discuss various ethical issues surrounding ARTs, including family relationships, informed choice, gender issues, embryo status and the commercialization of reproduction, as well as legal and policy issues. We examine the empirical evidence of the effectiveness of ARTs and suggest ways to approach ARTs in practice.

he waiting room walls display Picasso's *Maternité* and photo collages of babies born in this busy fertility clinic. Rachel sits alone, glad that Ray could not leave work today. Both in their late 20s, they assumed it would be easy to have a baby when they felt ready. After several months of trying, Rachel has just had another period. She feels depressed, discouraged and guilty that she is unable to become pregnant. She feels like a failure. She appreciates the many choices open to her but still feels that she really has only one: to have a child or be somehow "incomplete." She and Ray are increasingly irritable when together, so they withdraw into themselves. Their sexual relationship grows more formulaic each month. They are embarrassed when family, friends and coworkers ask "when?" or "why is it taking so long?" Rachel no longer sees her friends just as friends, but as mothers or almost-mothers; she increasingly declines social invitations to avoid child-centred conversation. She is beginning to panic that she will never get pregnant. After seeing a television documentary on infertility and reproductive technologies, Rachel asked her family physician to refer her here, to an infertility specialist.

What are assisted reproductive technologies?

The first assisted reproductive technology (ART) was noncoital insemination, which may be intrauterine or intravaginal, using sperm either from a donor or from the woman's partner. Sperm has been almost exclusively from anonymous donors, as opposed to sperm from known donors, since 1970.

Hormonal ovarian stimulation can be used to treat anovulation or may increase the likelihood of conception in idiopathic infertility by increasing the number of mature oocytes. Ovarian stimulation may also accompany intrauterine insemination.

With in vitro fertilization (IVF), multiple ova are matured through hormonal stimulation and retrieved by transvaginal ultrasound-guided needle aspiration. Fertilization occurs in the laboratory either by adding sperm to the culture medium or by injecting a single sperm into the ovum (intracytoplasmic sperm injection).¹ Resulting embryos may be transferred to the woman's uterus or cryopreserved for future use. In rare cases preimplantation genetic diagnosis may be used for specific genetic disorders.² Embryos may be transferred to the woman who produced the ovum (standard IVF), to another infertile woman (embryo donation) or to a woman who is contracted to carry the pregnancy for someone else (a "surrogate" mother). Embryos may also be donated for research.

Review

Synthèse

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Series editor: Dr. Peter Singer, University of Toronto Joint Centre for Bioethics, 88 College St., Toronto ON M5G 1L4; fax 416 978-1911; peter.singer@utoronto.ca

Return to May 29, 2001 Table of Contents Future reproductive possibilities include the creation of offspring genetically identical to an existing or deceased person (reproductive cloning), and the development of fetuses in mechanical wombs (ectogenesis).

Why are assisted reproductive technologies important?

ARTs can be very helpful for certain patients. However, ethical concerns have been raised both about the inherent nature of certain techniques and the specific contexts in which many techniques are used. ARTs are unique among medical procedures because they aim specifically to create new individuals and family relationships. The ethics of ARTs must be understood within this social context, which is often characterized by tension among competing interests.

Ethics

Family relationships

Although most infertility treatments are sought by a woman and man in a close relationship, as many as 5 adults may play parenting roles in ARTs: the genetic mother and father (ovum and sperm providers), the gestational mother and the intended social parents. Each party has his or her own interests and vulnerabilities. Any offspring who result are the most vulnerable of all, since they could not consent to the arrangements that will profoundly shape their developing identities. The interests of potential offspring must therefore always be central to reproductive choices.

IVF allows a woman to gestate a fetus genetically unrelated to her, either as the recipient of an ovum or embryo donation or as a contracted surrogate mother. Both genetic and gestational mothers are biological mothers, but neither is consistently identified as the legal mother. A recent US case involving all 5 possible reproductive collaborators left the resulting child without any legal parent until she was 3 years old. Other family variations — such as women who bear their own genetic grandchildren, postmenopausal pregnancies and reproduction by members of same-sex couples — challenge social, legal and historical norms. These new possibilities often leave family members without social or legal support.

Donor anonymity protects the privacy of donors and recipients, but it undermines the interests of offspring regarding their genetic medical history and ancestral heritage. We should consider carefully the role of secrecy in close family relationships and guard against the temptation to cut moral corners to ensure a supply of donors. Childcentred reproduction favours openness of donor records, but families often struggle with whether, when and how to share donor information with the offspring.

Preimplantation genetic diagnosis allows parents to diagnose conditions before pregnancy has been initiated, thus

avoiding situations in which mid-trimester pregnancy termination might be sought.² Despite consensus that genetic diagnosis should focus on severe diseases rather than traits such as sex or appearance,⁷ the definitions of "disease" remain unclear. Another question is whether the advantages of avoiding abortion warrant the extension of IVF with preimplantation genetic diagnosis to fertile couples.

Informed choice

Informed consent⁸ requires full disclosure and fair representation of all potential medical, social and emotional outcomes and risks. Unfortunately, we often lack sufficient information to provide the full disclosure needed for truly informed choice. Supportive counselling can assist patients to make these profoundly meaningful life choices¹⁰⁻¹² and to prepare realistically for suboptimal outcomes such as medical complications, multiple births, pregnancy loss and having no pregnancy at all.

Many clinicians try to create an optimistic atmosphere through the choice of the program name, the decorative use of baby pictures and the wording of their informational materials. Although these positive images may support patients through a trying procedure, they may also become manipulative. An emphasis on success rates masks failure rates; both sides of this truth are essential to the patient's decision to proceed. News media may also skew perceptions of new treatments with references to "miracle babies" and medical breakthroughs while downplaying associated risks and uncertainties.

Research

Research on the efficacy, long-term safety and psychosocial implications of most ARTs remains incomplete, but recent studies are beginning to address these concerns. Although many of the techniques questioned by the Royal Commission on New Reproductive Technologies7 have since been proven effective, 13,14 new techniques are rapidly introduced into clinical use without patients (and many clinicians) appreciating that they are still experimental. Explicit clarification must be made among procedures that are experimental, innovative, common but not yet validated, and truly validated, with special attention to possible risks. Key factors that motivate research — including desires to overcome infertility, to be helpful, to achieve professional advancement and to acquire financial gain — have resulted in rapid technical advancements that outpace social and ethical reflection.

Research on embryos must be understood as a women's health matter, since embryos cannot be acquired without first retrieving ova from women. When ova or embryos are sought for use in research, the fundamental ethical consideration must therefore be the well-being of the donor.¹⁵ The research question must be compelling and scientifically important, not merely a matter of interest. Clinicians

must avoid potential conflicts of interest between the patient's or donor's best medical care and the interests of research or financial gain.^{16,17} The demand for ova and embryos for research is expected to increase as a result of recent advances in stem cell research for possible tissue transplantation.^{18–20}

Fertility protection has received very little research funding to date. Medical research, education and practice should emphasize the protection and restoration of reproductive health, where possible, above methods that merely circumvent infertility.⁷

Gender issues

The desire to have a child is significantly influenced by societal assumptions about women's mothering role and, to a lesser extent, about men's virility as a mark of masculinity. Of Gender issues are thus central to the ethics of assisted reproduction. Until recent generations, women were denied most education and employment opportunities, thus leaving very few opportunities for financial and social success outside of motherhood. This "pronatalist" social imperative for women to have children dates to ancient times and retains its power despite critical scrutiny in 20th century feminism. Harder for some women to end their pursuit of maternity. Of The social imperative to reproduce may have important implications for informed consent.

For many infertile people, reproductive expectations prompt devastating feelings of inadequacy and abnormality. These perceptions are often gender-specific ("pregnancy makes a woman complete" or "real men get women pregnant"), but they may also be expressed as general perceptions of failure. Some aspects of treatment may also cause gender-specific distress: many men feel humiliated at producing a sperm sample through masturbation, ¹² and some women feel that repeated internal exams are similar to sexual violence. ¹⁰

Embryo status

The ethical and legal status of human embryos has long been a core ethical concern in ARTs.²⁴ The range of legal definitions include embryos as persons, embryos as property or objects, and embryos as a unique category.⁵ The Supreme Court of Canada has consistently held that fetuses are "unique" but not persons under the law, and it would likely treat embryos similarly. Health Canada's working group on embryo research also adopted the third option, identifying human embryos as having special status as a human entity but less than children or adults, and it recommended that embryos not be created specifically for research purposes.¹⁵ Religious views must be considered both in policy contexts and in helping specific patients select their most appropriate treatment options. All major religions attach special meaning to embryos, al-

though significant disagreement exists about the details of embryo status. The Vatican considers embryos to be persons from conception and rejects IVF because it separates sex and reproduction.²⁵ Conservative and Orthodox Judaism both attach greater but varying significance to embryos after the 40th day of conception, while both the Sunni and Shia branches of Islam believe that ensoulment (the condition for being a person) occurs around the fourth month of gestation.²⁶ Protestant Christian views vary widely, considering personhood to arise anywhere from conception to birth.

Access

The distress caused by infertility clearly deserves a helpful and sympathetic response. The difficulty lies in ensuring access to medically necessary and appropriate treatment while avoiding inappropriate overuse at both micro (individual patient) and macro (health policy) levels. Restriction on public funding for ARTs promotes suboptimal treatment for less wealthy women,²⁷ and free enterprise often promotes the use of incompletely tested technology. Providing the safest and best available treatment for a patient's needs is essential to ethical health care service.

At a macro level, accountability and justice in the distribution of resources²⁸ create new tensions and frustrations in a publicly funded health care system. Decisions regarding whether to cover specific health care interventions must be justified by continual evidence-based assessment of the intervention's safety and effectiveness, the full costs of the intervention to the health care system (e.g., total costs per successful outcome and the costs of complications)29,30 and the availability and comparative results of other options. Values-based assessments include balancing competing health care priorities and the right of fair access to the best available interventions across all types of health care needs. The social effects of increased usage, such as reinforcement of pronatalist attitudes in the case of assisted reproduction, must also be considered. Canada has one of the few remaining publicly funded health care systems that does not cover IVF. One author of this paper is committed to full IVF funding for all patients, whereas the other struggles to reconcile fair access to treatment with competing policy considerations.

Social factors have also been used as criteria for access to ARTs. Concern for the well-being of future children stemming from clear evidence (e.g., a prospective parent's history of violence or substance abuse) must be distinguished from social biases that might be unfounded (e.g., same-sex couples or single parents). The community's interest to avoid supporting more children on welfare must be balanced against interests in parenting regardless of socioeconomic status. Pregnancy in women of advanced age challenges stereotypes of "normal" motherhood and raises the concern that the parents' good health and life expectancies may end before the child reaches maturity.

Commercializing reproduction

Markets in human gametes, embryos and pregnancy raise widespread ethical alarm.³¹ Despite chronic and life-threatening shortages of blood and transplant organs, the sale of these tissues is widely rejected and is in most instances illegal.⁵ Normally, the only appropriate payment for tissue donations is reimbursement for direct expenses such as travel. It is unclear why reproductive tissues are treated differently.

Women who provide reproductive tissues or services tend to be from lower socioeconomic groups, whereas recipients tend to be more socially and economically advantaged. Reducing treatment costs by "sharing" ova or embryos³² is a form of sale: the donor's treatment is paid for by the recipient in exchange for acquisition of gametes or embryos. "Sharing" programs may also undermine informed consent, as the strong desire to have children (and thus to attempt IVF) may overshadow the implications of donation for both the donor and recipient.

Gamete providers who are influenced by financial or other considerations rather than informed commitment to donor parenting may later regret the possible creation of unknown offspring. Such regrets may be especially severe if the donor later experiences infertility or, in sharing programs, a failure of IVF to result in the birth of a child.

Law

Although most Western countries have adopted legislation to govern ARTs, Canada to date largely has not. The handling of sperm is regulated under the Food and Drug Act of 1996, the Excise Tax Act (for imported sperm) and the Family Acts of Quebec, Newfoundland and the Yukon Territory. The Supreme Court of Canada ruled in *ter Neuzen v. Korn*³³ that no implied warranty exists for sperm quality under the British Columbia Sale of Goods Act. The Human Tissue Gift Act in several provinces would seem to extend to sold or donated reproductive tissues, but it has not been enforced in fertility centres. Quebec is the only province to regulate ovum donation, stipulating the gestational mother as the legal mother of the offspring. The suprementation of the offspring.

Restricted access to ARTs may raise Charter challenges regarding a right to reproduce. 5,35,36 Ontario is the only province to fund IVF treatments, but only in cases of bilateral blockage of the fallopian tubes in accordance with recommendations of the Royal Commission on New Reproductive Technologies. The provinces do cover several other forms of assisted reproduction and fertility restoration, such as intrauterine insemination, non-IVF ovarian stimulation and surgical repair of varicoceles or fallopian tubes. In 1999 a Nova Scotia couple argued that infertility is a disability under section 15 of the Charter, making it discriminatory to exclude intracytoplasmic sperm injection from medicare coverage. The discrimination question remains unsettled, as the trial court noted that other infertility treatments are available to infertile people. Both trial and appellate courts, however,

affirmed the provincial right to limit medicare coverage of specific procedures on the grounds of expense, effectiveness and medical necessity. The plaintiffs have appealed to the Supreme Court of Canada.

Policy

Government

The Royal Commission on New Reproductive Technologies (1989-1993) issued 293 recommendations and emphasized a need for an ongoing, federal-level regulatory body.7 Necessary legislation has been stalled since then by multiple cabinet shuffles and 3 federal elections. In July 1995, then-Minister of Health Diane Marleau asked for a voluntary moratorium on specific ART practices including transgenic research, ectogenesis, cloning, the creation of embryos specifically for research and commercialization of human reproductive tissues. In 1996, federal Bill C-47 would have created criminal penalties for the practices listed in the moratorium, but the bill expired without a vote before a federal election. An Advisory Committee on Reproductive and Genetic Technologies was also established in 1996 to advise the minister in drafting new legislation, and several additional working groups have advised Health Canada on topics such as embryo research¹⁵ and genetic testing. In April 2000, Minister of Health Allan Rock announced that comprehensive legislation to regulate ARTs would be introduced that year, but once again it was stalled by an autumn election. In April 2001, he announced that it would be introduced in May to the House of Commons Standing Committee on Health.

Professional associations

The Canadian Fertility and Andrology Society (CFAS) and the Society of Obstetricians and Gynaecologists of Canada (SOGC) developed guidelines for practitioners of assisted reproduction in 1990³⁸ and 1998.³⁹ In conjunction with the Canadian Council on Health Services Accreditation, the CFAS and the SOGC are also developing accreditation guidelines for ART laboratories. The Canadian Medical Association, the CFAS and the SOGC were concerned with the criminalization of procedures as outlined in Bill C-47 and continue to discuss their recommendations for regulation with the federal government.

Empirical studies

Canada has no registry for the comprehensive collection of data on IVF outcomes according to diagnosis and age. The United Kingdom's Human Fertilisation and Embryo Authority (HFEA) 1999 annual report⁴⁰ listed the following live birth rates across 24 889 IVF cycles initiated during 1997/98: 14.9% among women with tubal disease, 16.3% among women with endometriosis and 17.2% among cou-

ples with unexplained infertility. The live birth rate for 9295 cycles of intracytoplasmic sperm injection was 20.7%. The University of Ottawa infertility program's statistics for 422 IVF cycles initiated in 1999 reported a live birth rate per initiated cycle of 29.0% among women under 35 years of age, 18.4% among women aged 35–37, 9.2% among those aged 38–40 and 0% among women over 40 years of age. 41

Because multiple births increase the risk of perinatal death, low birth weight and neonatal complications, the physician has an obligation to minimize these risks. 30,42,43 Ovulation induction with menotropins, especially if IVF is not used, greatly increases the risk of multiple pregnancy. Patients must be monitored carefully to ensure that multiple pregnancy does not occur; ovulation-inducing drugs, therefore, should not be prescribed by clinicians without sufficient training in their use.43 The 1999 HFEA report indicated that 47% of babies born from IVF come from multiple pregnancy, a statistic largely unchanged from 1994.40 To reduce multiple pregnancy, it has been strongly recommended that no more than 3 embryos be returned to the uterus at one time; no more than 2 would, except in unusual circumstances, be best for younger women with ovaries that respond well to menotropins.44

Ovarian hyperstimulation syndrome may pose serious and even life-threatening complications for women undergoing ovarian stimulation. 45,46 Lacking conclusive evidence, an increased risk of ovarian cancer has been reported and more recently disputed. Small risks of punctured bladder, damaged blood vessels and pelvic inflammatory disease accompany ovum retrieval.

No increase in observable major abnormalities has been identified in children conceived in vitro, but certain genetic causes of infertility may be passed to offspring conceived by means of intracytoplasmic sperm injection.⁴⁹

How should I approach assisted reproductive technologies in practice?

Infertility and ARTs pose challenges not just for fertility specialists, but also for general practitioners, gynecologists and others providing care for people with fertility concerns.

Women initiate most fertility inquiries, both because they see their physicians more frequently and because social norms assign them greater reproductive responsibility. Their male partners should never be ignored, however, either medically or emotionally.

As in all areas of medicine, invasive or potentially dangerous treatments must be reserved until options with less risk have been exhausted. Contributors to infertility, including alcohol, medications, diet, stress, occupational exposures and other lifestyle factors should be addressed in both partners. Education about reproductive and sexual physiology may increase the chances of conception for some patients. Underlying health problems that contribute to infertility should be investigated and treated appropriately.

For most patients, waiting a year or longer before initiating treatment is appropriate, but advanced age and specific indicators of infertility may suggest accelerated investigation and treatment. Most patients will need reassurance and attention to general health promotion in the interim.

To ensure truly informed consent, all fertility centres should present easily understood tables of live birth rates across all initiated cycles (not merely those that proceeded to ovum retrieval or embryo transfer)⁷ specified by cause of infertility and age. Maternal and perinatal complications should be included. Primary care physicians and specialists alike must assist patients to acquire and appreciate these data.

Supportive counselling must be readily available from primary care physicians¹² as well as from professionals with expertise in the psychosocial dynamics of family, marriage and infertility. Both partners should be encouraged to address personal concerns (e.g., self-esteem), external pressures from family or others, gender expectations, religious or ethnic beliefs, and options such as adoption or not having children. It is especially important for patients to prepare for potential negative outcomes such as medical side effects, miscarriage, perinatal complications, multiple births, social and legal complications involving reproductive collaborators, or the failure of treatments to produce the healthy child they desire to raise. Sadly, ARTs more often than not fail to result in a live birth.

Referring physicians must ensure detailed, ongoing communication with the specialists and remain important allies as the patients decide whether to attempt, continue or discontinue ARTs. Although negative outcomes are understandably devastating, even the birth of a child may not fully relieve the distress of being unable to reproduce "normally," and continuing support may be needed for the family.⁵⁰

The case

Rachel's case illustrates both the psychosocial pain of the imperative to reproduce and the influence of media, family and even the clinic's decor on the patient's thinking. Ray's distress is of note and should not be ignored. Physicians play important roles in supporting those who wish to become parents and in educating patients about impediments to fertilization and ways to promote conception. Both Rachel and Ray should be examined thoroughly to rule out known causes of infertility and to address any underlying health concerns or lifestyle choices that inhibit fertility. Whether or not a specific cause of infertility is found, the couple should be encouraged to promote general good health and to enjoy their sexual relationship. However, treatment should not be denied on the grounds that the cause of the infertility is unknown. Supportive counselling should be offered to assist Rachel and Ray to cope with their current stresses and maintain a positive self-image, whatever their decision about pursuing treatment. If a referral to a specialist is made, assistance should be given to help them reach truly informed and voluntary choices about how to proceed and to prepare for the stresses and possible outcomes of ART protocols.

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