

ASSISTED PROCREATION: TOO LITTLE CONSIDERATION FOR THE BABIES?

Abstract

Recent studies have revealed much higher risks of cerebral palsy and malformations in babies conceived by in vitro fertilization (IVF) than in babies conceived naturally. Here we question whether parents can legitimately accept this risk on behalf of offspring. We argue that parents can expose their baby to a risk only to preserve it from a worse possibility, and this is not the case of IVF, which is not a therapeutic tool for children because when the IVF decision is taken, the child has not yet been conceived. It is concluded that procreative techniques require considerably more research before being made available to couples.

Keywords: in vitro fertilisation, newborn, embryo

About 1% of children in developed countries are now conceived through in vitro fertilization (IVF). In 2002 at least 8000 IVF babies were born in the UK. In the period 2000 to 2001, 21.8% of all IVF cycles were successful and 25.1% of those in women under 38 years. About 1600 pairs of twins and 100 sets of triplets were born.¹ The bioethical debate has been very hard in two fields. First, on the field of human reproduction control. On this argument feminist bioethicists also expressed their opinion. For instance Australian feminist Robyn Rowland contends that threats to the welfare of women have received too little attention in discussions about embryo experimentation: "Other elements of the social context that raise the potential for abuse of women's bodies are the increasing commercialisation of reproductive technologies and the increasing control by the male-dominated medical profession over the process of procreation."² Second, on the field of the debate on human right to life, since usually during or after each fertilisation cycle some embryos have to be eliminated with the aim of obtaining the desired baby or a healthy baby. Of course the supporters of the idea that embryos are persons do not accept that human embryos may be sacrificed, while those who argue that future parents' autonomy overwhelm embryos' right to live, do. Now, recent studies have revealed risks for babies conceived by in vitro fertilisation, so what is the extent of these risks, and what is the ethics of choosing a risk the consequences of which will be paid not only by those who accepts the risks but also by the baby?

The State of the Art

In February 2002 a group from Uppsala, Sweden, reported a retrospective cohort study linking and comparing neurological disorders among 5,680 infants born after IVF with 11,360 matched controls. In general children born following IVF were more likely to require the services of a habilitation centre than controls, and the odds ratio for cerebral palsy was 3.7. Most of the difference was among singletons. In a study from Australia, 8.6% infants conceived by intracytoplasmic sperm injection (ICSI) and 8.9% infants conceived by IVF had major birth defects, two-fold greater than controls.³ It appears that the risk of having a baby with a major handicap is higher after assisted reproduction, compared to natural conception.⁴

Infants who have low birth weight are at increased risk for short- and long-term disabilities and death. Three large studies were published in 2002 which showed that the use of assisted reproduction technology is an important contributor to the rate of low birth weight in the United States: there is a higher rate of low birth weight among singleton infants conceived with assisted reproduction technology than among naturally conceived singleton infants.⁵ Children born after IVF have an increased risk of developing neurological problems, especially cerebral palsy,⁶ and infants conceived with use of ICSI or IVF have twice as high a risk of a major birth defect as

naturally conceived infants.⁷ These studies were followed by others and many of these show that being born with IVF is more risky than with common conception.

These observations are obvious to neonatologists: multiple births and prematurity, though trivialized by the mass-media (remember the exultation for the birth of quintuplets), pose severe risks for mothers and babies. JP Relier reports that a high number of hospitalisations in his neonatal intensive care unit (Port Royal Hospital, Paris), were due to IVF.⁸ This is not an unknown problem for neonatologists: twins have a higher risk of death and neurodevelopmental impairment than single births,⁹ and premature babies have similar risks¹⁰: "Grand multiparity is one of the risks of assisted reproduction and can lead to preterm birth."¹¹ The news is that even for single-embryo pregnancies conceived by IVF, the risk is higher than for normal pregnancies. A recent analysis of 25 scientific studies published in the British Medical Journal concludes: "Singleton pregnancies from IVF have a significantly worse perinatal outcome than non-assisted singleton pregnancies", however, "this is less so for twin pregnancies."¹² Other risks for genetic pathologies are raised: "Intracytoplasmic sperm injection may increase the risk of imprinting defects",¹³ and some hypotheses are given to explain this.¹⁴ The debate over the safety of assisted reproduction has now spread to rare disorders affecting genetic imprinting. Andrew Feinberg of Johns Hopkins University in Baltimore, Maryland, and Michael DeBaun of Washington University in St Louis, Missouri, were struck by the fact that 4.6% of their registered patients were conceived by assisted reproduction, a high proportion given that less than 1% of the general population is conceived artificially. Most recently five Dutch children conceived by assisted reproduction have been diagnosed with retinoblastoma, a childhood cancer of the retina that occurs in just 1 in 17,000 births.¹⁵

Last but not least, a recently published book by a famous French psychiatrist provokes a reflection on the long-term risks of IVF.¹⁶ Though many progresses have been done in this field in the last few years and its safety has recently improved, IVF is an in progress technique and it has to be improved before we can say it has reached the gold standard of "natural" conception. A recent paper is reassuring,¹⁷ but a few concerns are still raised by some observations: ICSI technique introduces sperm into the oocyte not by fusion of the cell surfaces, but by an injection that does not take part in normal fertilisation; embryos obtained with defective sperm may inherit the sperm defect and produce humans who are in turn infertile, bypassing the natural selection of certain pathologies; oocytes of aged women are at risk for genetic problems.

Accepting the Risks

This short review shows that the risks of IVF for babies:

- * Are not negligible
- * Are not due only to twin pregnancies
- * Are due to techniques, but also to bypassing a natural self-defence barrier which do not allow "old" oocytes or defective spermatozoa to create a new human being.

This argument raises a question: is it right to use a technique which has such a failure rate? If a drug which could double the risk of brain damage was to be produced, it would be rapidly withdrawn. This is the case of the common Acetylsalicylic acid: as it was demonstrated to produce in certain cases a severe syndrome (Reye's syndrome), its use has been proscribed for children and pregnant women. This is also the case of the "mad cow" syndrome: for few cases of spongiform encephalitis, cow meat use has been prohibited in Europe. Now, the problem would not be raised if we would

deal with adults accepting for themselves a certain risk, or accepting the risk on behalf of their baby for his/her interest. But in this case is the baby's interest the goal for accepting the risk? Someone may answer that the good goal is bringing him/ her to the world, as he/she would not be born without IVF. But in this case, at the moment of deciding, the baby has not already been conceived. We are not benefiting an "actual baby", but an hypothetical "future baby"; with IVF we do not improve his/her health, because he/she does not exist. In other words, IVF is not a therapy to the baby¹: if being killed is the loss of "something" (life, health...) for the person, not being conceived is not a loss for him/her, because we are not taking away life from a person but from a hypothesis. The crucial point is that with IVF we are not improving babies' state (he/she does not exist), but we are exposing them to a risk. Some may say that accepting this risk should be the woman's choice,¹⁸ though we should wonder whether this risk is consciously accepted: some gynaecologists write that "even with counselling the risks of triplets are generally underestimated by parents."¹⁹ But even if we admit that being conceived is better than not being conceived, we cannot admit superficiality and permit the use of a so far risky technique. Moreover, in several cases sterility of either male or female is not even verified on clinical parameters, so assisted reproduction (and its risks) may indeed be unnecessary²⁰: "A real concern is that the increased marketing of these services will lead to their use by couples who, in previous years, would have waited longer before seeking help. We can expect that such marketing will attract at least some couples who would have conceived without assisted reproduction technology had they tried to conceive naturally for a few months longer."²¹

Prudence

At this point one may say: "Yes, IVF is risky, it is not an improvement for the baby's health, as he/she does not exist yet, but bringing children into life is however worthy, so we should consent to conceive children in a risky way." We suggest that this objection may be rejected on the ground that an obligation to shield children from preventable induced impairments must be balanced against the parental right to try to create a child.²² Mothers who assume drugs potentially harmful to their child-to-be are commonly discouraged, in the interest of their future child, from falling pregnant until they use them. The haste with which IVF has been made available is criticised in various papers, which highlight the need for extensive study in animal models before applying them to humans.¹⁵ "Some therapies, which on any assessment are highly empirical or unproven, are being used in human subjects before they have been validated by proper cell culture experiments or detailed animal research."¹⁴

Thus we believe that a serious reflection is necessary: it is an ethical principle that one should be exposed to a risk only in the name of his/her health or happiness. M. Häyry paradoxically wrote that it is immoral to conceive children as life is very frequently painful and sad. We do not agree with his pessimism, because life is not negative in itself; and, if bearing children is a risk, this risk is acceptable and worthy. However, he is right when he argues that "it is morally wrong to cause avoidable suffering to other people"; to risk somebody's health without his/her permission is intolerable.²⁴ Thus, is it ethical to perform IVF "here and now"?

If we decided to cure an illness with a dubious substance like urine, would it be correct to say a priori that we refuse to use it because it is an unworthy bodily waste? Or that we must use it because the result justifies the means? Before judging its morality, it is obviously necessary to determine whether it really works and is without unacceptable side-effects.^{24, 11}

The same approach should be used for IVF. We may accept them acritically; we may go on and make an analysis of the damages we have provoked some years later; or we may suspend it until we are sure it is absolutely safe. We suggest this last solution: the children's defender of the French Parliament, Claire Brisset, has asked for a moratorium on the ICSI technique in the interest of the

future children conceived by this technique. The French Ethical Committee is moving in this direction.ⁱⁱⁱ The New York State Task Force on Life and the Law has suggested that physicians are "entitled to consider the welfare of any child who might be born" as a result of reproductive and genetic procedures.²⁵ Although the task force staunchly supports procreative liberty, it does, in the name of child welfare, identify circumstances that may warrant refusing prospective parents access to assisted-reproductive services. Consequently, despite a general reluctance to address well-being issues in reproductive policy, there are precedents for defining limits to procreative liberty in the name of child welfare in public policy.²² Should we not feel a sense of responsibility for the increasing frequency of brain damage, with personal and social costs, caused by these techniques?

We cannot ignore the clouds lowering over IVF. This could have a profound influence on the progress of medical sciences, not only in this high-profile field, but in others too.¹⁴

Without IVF many babies would not have been born, and many couples would have remained childless. Nevertheless the fear exists that the choice to procreate may outweigh the choice of children's health.

Endnotes

i However, some argue it is a therapy for the mother or for the couple. This argument is still under debate.

ii "Perhaps we can make more sense of the choice by starting, as the HFEA seems to imply we should, from the situation of the child born through assisted conception and born sick or disabled. Has he been wronged? If he has, does this permit us to frame a rule that would bar the use of the technique in general, or bar its use for some parents who can be characterised as being at a qualitatively greater risk than baseline?"

iii Even the concept that the risk of conceiving impaired children may be accepted because of the possibility of choosing medical abortion is misleading, as most pathologies provoked by IVF are not detectable before birth, and because abortion is obviously not universally accepted.

References

1 Tindall G: Mixed blessings: ethical issues in assisted conception. *J R Soc Med* 2003;96:34-35.

2 Rowland R. Making women visible in the embryo experimentation debate. *Bioethics*. 1987 Apr;1(2):179-88.

3 Koren G: Adverse effects of assisted reproductive technology and pregnancy outcome. *Pediatr Res* 2002;52: 136.

4 Anonymous: Neurological sequelae and major birth defects in children born after in-vitro fertilization or intracytoplasmic sperm injection. *Eur J Pediatr* 2003;162: 64.

5 Schieve LA, Meikle SF, Ferre C, Peterson HB, Jeng G, Wilcox LS: Low and very low birth weight in infants conceived with use of assisted reproductive technology *N Engl J Med* 2002; 346(10):731-7.

6 Stromberg B et al: Neurological sequelae in children born after in-vitro fertilisation: a population-based study. *Lancet* 2002;359:461-5.

7 Hansen M et al: The risk of major birth defects after intracytoplasmic sperm injection and in vitro fertilisation. *N Engl J Med* 2002;346(10):725-30.

8 Relier JP: *Adrien, ou la colère des bébés*. Ed J'ai lu, Paris 2003.

9 Shinwell ES, Blickstein I, Lusky A, Reichman B: Excess risk of mortality in very low birthweight triplets: a national, population based study. *Arch Dis Child Fetal Neonatal* Ed 2003;88:F36-F40.

10 Hansen BM, Greisen G: Preterm delivery and calculation of survival rate below 28 weeks of gestation. *Acta Paediatr* 2003;92:1335-8.

11 Greisen G: Multifoetal pregnancy and prematurity: the costs of assisted reproduction. *Acta Paediatr* 2002;91:1449-50.

12 Frans M Helmerhorst et al: Perinatal outcome of singletons and twins after assisted conception: a systematic review of controlled studies. *BMJ* 2004;328:261.

13 Cox GF et al: Intracytoplasmic sperm injection may increase the risk of imprinting defects. *Am J Hum Gen* 2002;71:162-4.

14 Winston RM, Hardy K: Are we ignoring potential dangers of in vitro fertilization and related treatments? *Nat Med*. 2002 Oct;8 Suppl:S14-8.

15 Powell K: Seeds of doubt. *Nature* 2003;422:656-9.

16 Bayle B : *L'embryon sur le divan*. Psychopathologie de la conception humaine. Masson, Paris 2003.

17 Ponjaert-Kristoffersen I, Bonduelle M, Barnes J, Nekkebroeck J, Loft A, Wennerholm UB, Tarlatzis BC, Peters C, Hagberg BS, Berner A, Sutcliffe AG. International collaborative study of intracytoplasmic sperm injection-conceived, in vitro fertilization-conceived, and naturally conceived 5-year-old child outcomes: cognitive and motor assessments. *Pediatrics*. 2005 Mar;115(3):e283-9.

18 Chervenak FA, McCullough LB, Rosenwaks Z : Ethical considerations in newer reproductive technologies. *Sem Perinatol* 2003;27(6):427-34.

19 Fisk NM, Trew G: Commentary: Two's company, three's a crowd for embryo transfer. *Lancet* 1999;354:1572-3.

20 Fanny-Cohen B: *Un bébé mais pas à tout prix*. Ed J'ai lu, Paris, 2004.

21 Mitchell AA: Infertility treatment- More risks and challenges. *N Engl J Med* 2002;346:769-10.

22 Parens E, Knowles LP: Reprogenetics and public policy. Reflections and recommendations. *Hastings Cent Rep*. 2003 33(4):S1-24.

23 M Häyry : A rational cure for prereproductive stress syndrome *J Med Ethics* 2004;30:377-378.

24 Thompson JG, Kind KL, Roberts CT, Robertson SA, Robinson JS. Epigenetic risks related to assisted reproductive technologies: short- and long-term consequences for the health of children

conceived through assisted reproduction technology: more reason for caution? Hum Reprod 2002;17(11):2783-6.

25 Dimitriou G, Pharoah PO, Nicolaides KH, Greenough A: Cerebral palsy in triplet pregnancies with and without iatrogenic reduction. Eur J Pediatr. 2004;163(8):449-51.

26 Ashcroft R: A fragile hold on life: the ethics of intensive care of children born through assisted conception. In Proceedings of the Meeting of the Forum on Maternity and the Newborn of the Royal Society of Medicine, November 14, 2002.

27 New York State Task Force on Life and the Law, Assisted Reproductive Technologies, X.

CARLO BELLINI, M.D. AND GIUSEPPE BUONOCORE, M.D.

Carlo Bellieni, M.D., is a member of the European Society of Pediatric Research and of the Bioethics Centre of the University of Siena, and Professor of Neonatal Therapy in the Pediatrics School of the University of Siena, ITALY.

Giuseppe Buonocore, M.D., is Professor at the Department of Pediatrics, Obstetrics, and Reproductive Medicine, and the Institute of Preventive Pediatrics and Neonatology, University of Siena, ITALY.

Carlo Bellieni, M.D., is a member of the European Society of Pediatric Research and of the Bioethics Centre of the University of Siena, and Professor of Neonatal Therapy in the Pediatrics School of the University of Siena, ITALY.

Giuseppe Buonocore, M.D., is Professor at the Department of Pediatrics, Obstetrics, and Reproductive Medicine, and the Institute of Preventive Pediatrics and Neonatology, University of Siena, ITALY.

Copyright Bioethics Press Summer 2006

Provided by ProQuest Information and Learning Company. All rights Reserved