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"BABIES WITH SOME ANIMAL DNA IN THEM":

A WOMAN'S CHOICE?

Françoise Baylis

Abstract

In April 2007, as part of its public consultation initiative, the Human Fertilisation and Embryology Authority (HFEA) in the United Kingdom published *Hybrids and chimeras: A consultation on the ethical and social implications of creating human/animal embryos in research*. This HFEA document identifies a number of possible arguments against the creation of human/animal embryos. One of these arguments concerns the worry that human/animal embryos "might be transferred to a woman to create babies with some animal DNA in them." Although the HFEA dismisses this slippery slope argument, I argue that this possible future is not as farfetched as one might think. For example, human admixed embryos might be transferred to women in an effort to prevent the transmission of mitochondrial diseases. The ethical acceptability of this possible future practice is examined from different feminist perspectives with a focus on issues of reproductive freedom and social justice.

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In April 2007, the Human Fertilisation and Embryology Authority (HFEA) in the United Kingdom published *Hybrids and chimeras: A consultation on the ethical and social implications of creating human/animal embryos in research* (HFEA 2007a). In this document the HFEA identified a number of possible arguments against the creation of human/animal embryos, be they part-human hybrids, chimeras, or cytoplasmic hybrids.[1] One of these arguments—promptly dismissed by the HFEA—concerned the worry that human/animal embryos might be used "to create babies with some animal DNA in them" (HFEA 2007a, 15). In dismissing this concern the HFEA insisted that:

> No scientist or clinician has ever expressed a desire to create a hybrid or chimera baby. However, even if anyone did wish to do so, they would be committing a criminal offence if they transferred either a hybrid embryo (created by mixing human and animal gametes) or a cytoplasmic hybrid embryo (created through CNR using animal eggs) to a woman. (HFEA 2007a, 12)

In this paper I show that although there are significant scientific and legal obstacles to the creation of human babies with some nonhuman animal DNA in them, this imagined future is not pure science fiction. For example, it is possible that in the future, human admixed embryos[2] might be transferred to women in an effort to prevent the transmission of mitochondrial diseases. The ethical acceptability of this possible future practice is examined from different feminist perspectives—first with a focus on reproductive freedom and then with a focus on issues of social justice.

Treating mitochondrial diseases

Mitochondria are the power sources of the cell. They combine food molecules (sugars, fats, and other chemical fuels) with oxygen to produce adenosine triphosphate (ATP), which is the primary energy source of the cell. As brain and muscle tissues have high energy needs, these critical organs are more likely to be affected in mitochondrial diseases. Some mitochondrial diseases are caused by nuclear DNA mutations that affect the functioning of the mitochondria. Other mitochondrial diseases are caused by mutations in mitochondrial DNA (mtDNA) (Brown et al. 2006; Vu, Hirano, and DiMauro 2002). Currently, there are over fifty diseases attributed to defects in mtDNA, causing symptoms as diverse as neurodegenerative diseases, stroke-like episodes, blindness, muscular dystrophy, diabetes, and deafness.

To understand the etiology of mitochondrial diseases caused by mutations in mtDNA, it is important to know that there are multiple mitochondria present in each individual cell and that each mitochondria possesses multiple, separate mitochondrial genomes. Sometimes there are important genetic differences in a subset of these genomes, and sometimes these genetic differences (deleterious mutations) affect mitochondrial function resulting in adverse medical symptoms.

MtDNA passes through the female line from women to their children (males and females). Human eggs contain close to one hundred thousand different copies of the mitochondrial genome, and each child inherits a subset of this population. Women with mtDNA mutations pass these mutations on to their children (in turn, their daughters pass these mutations on to their children). Children who inherit a small percentage of mitochondrial genomes with a deleterious mutation may have no adverse medical symptoms. Children who inherit a large percentage of affected mitochondrial genomes will experience severe mtDNA disease.

Prenatal diagnosis is an option for some women at risk of having children with mtDNA-related diseases. However, there are few proven treatment options. This explains the focus on preventing disease transmission. Current approaches include genetic counseling, egg donation, chorionic villus sampling, and amniocentesis, possibly followed by termination of pregnancy, as well as pre-implantation genetic diagnosis, followed by selective transfer of "unaffected" embryos (Brown et al. 2006). More novel approaches include human cytoplasmic transfer and human pronuclear transfer. In the first of these two novel approaches, healthy human ooplasm is transferred to affected human eggs to dilute the mutant mtDNA to non-pathogenic levels. With the second approach, human pronuclei are removed from affected fertilized eggs and stripped in vitro of their cytoplasm (and hopefully all of the mitochondria) and then transferred into unaffected enucleated human eggs.

A problem for both of these novel approaches is the shortage of human eggs for (i) current and future research on mtDNA diseases (e.g., research on mitochondrial dependence on nuclear-encoded mitochondrial genes and the dysfunction that may arise from any incompatibility) and (ii) future clinical practice resulting from such research. One plausible interim solution to this problem would be to proceed with research using nonhuman animal eggs instead of human eggs (research recently legalized in the United Kingdom in response to the shortage of human eggs for cloning-based, human embryonic stem [hES] cell research [Human Fertilisation and Embryology Act 2008]).

If mtDNA research using nonhuman animal eggs were successful and the findings were transposable to humans, then research using (fewer) human eggs

could follow, eventually leading to safe and effective therapeutic interventions. But if the shortage of human eggs for both mtDNA research and future clinical practice were to persist, then there would be reason for clinician-scientists to research ways in which to make human admixed embryos clinically safe and effective (e.g., by significantly reducing [if not eliminating] the risk of zoonotic infection and by using eggs from proximate species to increase the probability that the nuclear and mitochondrial genomes would be compatible [e.g., using higher primates such as orangutans]). If the transfer of human admixed embryos could be done safely and effectively, then clinician-scientists could proceed with this work in jurisdictions that did not legally prohibit the transfer of human admixed embryos to women. In jurisdictions that did legally prohibit such transfers, presumably clinician-scientists (and others) would be highly motivated to lobby governments to remove such prohibitions.

Depending upon one's perspective, this scenario might seem like irresponsible scaremongering or wishful thinking; however, it is neither. Rather, it is a call to exercise our moral imaginations and to carefully reflect on one possible outcome of current research in stem cell science and in reproductive medicine. Already, in certain policy circles, there is speculation about the prospect of creating human/animal beings. For example, it is reported that in comments about human-animal chimera research before the Joint Committee on the Human Tissue and Embryos (Draft) Bill in the United Kingdom, Stephen Minger suggested a future interest on the part of some to "take human embryonic stem cells and put them into a primate blastocyst and take that blastocyst to mid-gestation or maybe to birth or maybe to ten years of age" (Lords Hansard 2007). Regarding the present discussion, currently there is ongoing research involving the creation of human admixed embryos for stem cell science, and there is ongoing research involving pronuclear transfer for reproductive medicine. Some of this research is ongoing at the same institution (e.g., Newcastle University), and it is not wholly outside the realm of possibility that the respective research teams might one day collaborate on a common project, potentially leading to the transfer of human admixed embryos to women in the hope of creating babies free of mtDNA diseases.

All too often we lament the fact that our ethical analysis lags behind our science and that as a result "what we can do" inappropriately drives the answer to any question we might ask about "what we should do." Here we have before us an opportunity to carefully reflect on how we should respond to the prospect of creating human babies with some nonhuman animal DNA in them, not as an entertaining exercise in science fiction, but as a preparation for responsible

engagement in future ethical and policy debates. This opportunity ought not to be squandered. Now is the time to consider seriously whether creating human babies with some nonhuman animal DNA in them is something feminists should celebrate, tolerate, or condemn. In anticipation of this discussion, I briefly review below some of the relevant facts regarding the feasibility of the science, the shortage of human eggs for research, and the harms to women associated with ovarian hyperstimulation and egg retrieval.

Creating human admixed embryos

The creation of human admixed embryos by inserting the nuclei from adult somatic cells into enucleated nonhuman animal eggs and reprogramming the nuclei to their totipotent state is technically feasible (Baylis 2008). However, the viability of such human/nonhuman animal combinations currently is open to question.

In 1998, in the early days of stem cell research, Advanced Cell Technology publicly announced that it had successfully inserted human DNA into enucleated cow eggs (Wade 1998), and later it reported having derived a colony of cells resembling embryonic stem cells (Lanza, Cibelli, and West 1999). Five years later, in 2003, Hui Zhen Sheng and colleagues reported successfully inserting human nuclei from skin cells into enucleated rabbit eggs (Chen et al. 2003). Then, in 2006, Illmensee and colleagues reported successfully inserting human granulosa or fibroblast cells into enucleated cow eggs (Illmensee, Levanduski, and Zavos 2006).

Although these achievements have yet to be independently confirmed, on the basis of this limited interspecies research, the HFEA concluded in September 2007 that research involving the insertion of human nuclear DNA into enucleated nonhuman animal eggs was a licensable activity. Since then, three separate one-year research licenses have been issued—one to King's College London (January 2008), one to Newcastle University (January 2008), and one to the University of Warwick (July 2008).[3] In April 2008, researchers at Newcastle University announced that they had successfully created part-human, cytoplasmic hybrid embryos using human nuclei and enucleated cow eggs (Newcastle University 2008) and by June of that year, there were media reports of success in creating close to 270 human/animal, cytoplasmic hybrid embryos (Cookson 2008).[4]

To be sure, this research summary suggests relatively limited success in creating human admixed embryos. No doubt this is due, in part, to technical and scientific challenges. Also relevant, however, is the fact that few jurisdictions explicitly permit the production of embryos that are part human and part nonhuman animal (Stevens and Newman 2007). A notable exception is the United Kingdom, which

recently legalized research involving the creation of human admixed embryos (Human Fertilisation and Embryology Act 2008). This new law is of consequence because the United Kingdom is an international bellwether for embryo research. Meanwhile, in the United States, privately funded research is unregulated in many states and in early 2009, researchers at Advanced Cell Technology and their colleagues reported on the successful creation of human-human, human-bovine, and human-rabbit combinations in research designed to compare the reprogramming ability of human and nonhuman animal eggs (Chung et al. 2009).

Creating human admixed embryos to study mtDNA diseases

As noted above, in the original HFEA public consultation document on the ethical and social implications of creating human/animal embryos, the HFEA insisted that there was no interest on the part of scientists or clinicians in transferring such embryos to women in the hope of creating a baby (HFEA 2007a, 12, 15). In subsequent documents, however, the HFEA explicitly recognized that a past lack of interest is not a reliable indicator of future possible interests. In the September 2007 HFEA Authority Paper, *Hybrids and chimeras: Findings of the consultation* (HFEA 2007b, 16), and in the October 2007 HFEA public report, *Hybrids and chimeras: A report on the findings of the consultation* (HFEA 2007c), the following text appears: "although there is not currently a demand for the creation of these entities [human transgenic embryos, true hybrids or human chimera embryos] it is always difficult to predict how scientific research may develop in the future" (HFEA 2007b, 16; HFEA 2007c, 19). And indeed, scientists have speculated that:

> [t]he impetus to develop hybrid embryos beyond guideline limits will be inexorable and there will be no obvious stopping point. Some will encourage development of hybrid embryos to late term or even birth because, not being entirely human, they would be available for experimentation. It will be difficult to resist their arguments when long-held compunctions are weighed, as they will be, against promises of cures. (Stevens and Newman 2007)

Further, in the first of the two HFEA documents reporting on the public consultation, the HFEA draws attention to its regulatory responsibilities and suggests that if anyone were interested in creating and transferring transgenic embryos, true hybrids, or human chimera embryos, the HFEA would likely know about this before a license application was submitted (and presumably would deal with this in a responsible manner):

> Throughout the consultation the Executive has built good relationships with members of the scientific community with an interest in this area of research. We are therefore confident that any intention to undertake research involving other types of human-animal embryos will be picked up well before an application is received. (HFEA 2007b, 18)

And in the second of the two HFEA documents reporting on the public consultation, the public is assured that if human/animal cytoplasmic hybrid embryos were transferred to women in the hope of creating babies (presuming this were legal and the research had been licensed), there would be nothing to worry about: "[t]he Royal Society, the British Fertility Society and key researchers in the fields of mammalian embryology, developmental biology and reproductive genetics . . . [have all agreed that the embryos] would be unlikely to be viable beyond early development and would be unlikely to develop if implanted in a woman" (HFEA 2007c, 92). In the unlikely event that these embryos did develop, however, the public is still not to worry because the HFEA's Scientific and Clinical Advances Group has determined that the human mitochondria would likely have a replicational advantage over the nonhuman animal mitochondria (HFEA 2007c, 92).

In a matter of few months, the HFEA's stance shifted dramatically. Instead of dismissing public concerns about creating human babies with some nonhuman animal DNA in them as unfounded because "[n]o scientist has ever expressed an interest in transferring such embryos in the hope that a baby, if that were medically possible, would develop" (HFEA 2007a, 15), the HFEA attempted to assuage public concerns with (i) assurances of proper oversight, (ii) predictions of embryonic non-viability, and (iii), in the event of unexpected viability, predictions of humanization. This change in perspective (or strategy) can perhaps be explained by the fact that during the scientific consultation, the reasons given for creating human/animal cytoplasmic embryos were not limited to stem cell research. As summarized by the HFEA:

> [E]mbryos created in this way could be used to investigate the mechanism used to reprogram DNA to a pluripotent embryonic state and this knowledge could potentially be used to create methods to produce stem cells from somatic cells (therefore avoiding the use of human eggs and embryos). In addition as cytoplasmic hybrids will contain animal derived, and possibly some human derived mitochondria, they could be a useful tool to study mitochondrial disease and the relationship between the mitochondria and the nucleus. (HFEA 2007c, 5)

More specifically:

> This technique could be used to investigate the inheritance of mitochondrial DNA and investigate ways to reduce heteroplasmy with the aim of enhancing the reproductive success of 'older' oocytes or developing therapies for mitochondrial diseases. (HFEA 2007c, 94)

> These research projects could include investigating the interaction of mitochondrial and nuclear DNA in order to study mitochondrial diseases. (HFEA 2007c, 98)

Human cytoplasmic transplantation to prevent mtDNA diseases

For some women the only effective way to avoid an elevated risk of passing on an mtDNA disease is in vitro fertilization (IVF) using donated or purchased eggs from healthy egg providers (Thorburn, Dahl, and Singh 2001). Future, unproven options include human cytoplasmic transfer and human pronuclear transfer. A benefit with either of these options is that the women with mtDNA mutations would be able to bear genetically related children without an increased risk to their offspring of developing symptoms of mtDNA disease.

In the mid-1990s Jacques Cohen and colleagues began injecting small amounts of healthy ooplasm from donor human eggs into recipient human eggs with defective ooplasm as a "treatment" for infertile patients with recurrent implantation failure, possibly caused by an abnormality in the mitochondrial genome. Success was reported in 1997 with the announcement of the first birth following human cytoplasmic transfer (Cohen et al. 1997). Within a year, the total number of live births had increased to five (Cohen et al. 1998). The mechanisms involved in this "effective" intervention were not completely understood, and while some suggested that the injected ooplasm somehow "kick started" mitochondrial function (Thorburn, Dahl, and Singh 2001, 124) others imagined that the healthy ooplasm restored "some unknown property lacking in the recipient oocyte" (Hawes, Sapienza, and Latham 2002, 850).

By 2001 Cohen and his team had a total of fifteen live births (following twenty-eight cytoplasmic transfer procedures in twenty-five women), half of the estimated thirty babies born worldwide (Barritt et al. 2001). Among these children, there were two cases of mtDNA heteroplasmy, that is, two one-year-old children had two mtDNA genomes, one from the pregnant woman and one from the woman egg provider. This finding—described as the "first case of human germline

genetic modification resulting in normal healthy children" (Barritt et al. 2001, 513)—was followed by calls for public discussion, as well as public oversight (Naviaux and Singh 2001; Parens and Juengst 2001; Templeton 2002). The ethical objections to treating infertile women by creating potentially heteroplasmic individuals were three-fold. First, there were concerns about health and safety, including potential harms to the developing fetus (e.g., Turner's syndrome) and potential harms to apparently healthy children born of this technique who might later (during puberty or midlife) manifest a disease associated with mitochondrial heteroplasmy. Second, there were concerns about issues related to kinship and family law. Third, there were concerns about the risk of inadvertent germ-line genetic modification, given the potential heritability of unknown genetic effects through the female line. Shortly thereafter, this research came to a halt.

The Food and Drug Administration (FDA) in the United States issued a letter notifying infertility specialists that an investigational new drug (IND) exemption was required for research involving human cytoplasmic transplantation (FDA 2001). Rather than submit to the IND process, infertility specialists in the United States stopped the research. Sean Tipton, then spokesperson for the American Society for Reproductive Medicine, explained that fertility clinics lacked both the "'incentive and the financial resources to pay for the FDA review process" (Abboud 2002). About a year later, following a public meeting on human cytoplasmic transfer, the FDA concluded that additional preclinical data were required before it would permit further clinical trials (Center for Genetics and Society 2003).

Since then, researchers in the United Kingdom have determined that it is technically much easier (and likely, more effective) to transfer egg- and sperm-derived pronuclei from fertilized eggs with dysfunctional mitochondria into enucleated eggs with unaffected mitochondria, than it is to inject unaffected cytoplasm into embryos with dysfunctional mitochondria. To pursue this work in humans, researchers at the Newcastle Centre at Life requested an HFEA license for mitochondrial research involving human cytoplasmic transplantation. The original request was denied in the belief that the Human Fertilisation and Embryology Act 1990 prohibited such research. Paragraph 3.4 of Schedule 2 of the Act prohibits "altering the genetic structure of any cell while it forms part of an embryo." This decision was appealed, and in September 2005 a license was issued (HFEA 2005). In February 2008, limited success in transferring human pro-nuclei into enucleated human eggs was reported along with the promise of effective interventions for serious mtDNA diseases within three to five years (Hirschler 2008).

But this promise presumes there will be healthy human eggs in sufficient number for such treatment when, in fact, human eggs are known to be in short supply.

The shortage of human eggs for research

The shortage of human eggs for cloning-based hES cell research is the engine that drove the HFEA to license, and the U.K. government to legalize, research involving the creation of human/animal embryos (Baylis 2009). Indeed, had there been large numbers of human eggs available for cloning-based hES cell research, it is not clear that human/animal embryo research would have been construed as useful.

Meanwhile, as human embryo research has continued to expand, so too has the demand for human eggs. At the present time, these are two sources of human eggs for embryo research. Human eggs can come from women who are undergoing ovarian hyperstimulation and egg retrieval as part of their infertility treatment and who agree to donate, sell, or trade their eggs. Eggs can also come from women who are not involved in infertility treatment, who agree to undergo ovarian hyperstimulation and egg retrieval to produce eggs for research for altruistic or financial reasons. Eggs from women in the first category are (and are likely to remain) scarce as infertility patients have good reason to keep their (fertilized) eggs for their own reproductive use in a current or subsequent cycle (McLeod and Baylis 2007).[5] Beyond this, it is anticipated that in the near future the incentive to keep one's eggs (and embryos) for one's own reproductive use will increase as a direct result of changing clinical practice. There is, at the present time, an interest in moving toward mild ovarian stimulation and single embryo transfer in an effort to reduce the harms to women associated with ovarian hyperstimulation and multiple pregnancy and birth (Heijnen et al. 2007). With mild ovarian stimulation, a reduced number of eggs mature. In turn, this reduces the number of embryos created and transferred, thereby reducing the risk of multiple pregnancy and birth.

Because women infertility patients are generally reluctant to provide eggs for research (without some form of compensation) and because of the poor quality of eggs and embryos typically available for research following infertility treatment, of late there have been increased efforts to solicit eggs from young (under-thirty), healthy women volunteers—women who are not pursuing a personal reproductive project and who agree to undergo medical procedures without any prospects of medical benefit. These women, however, generally have been disinclined to accept the potential harms of ovarian hyperstimulation and egg retrieval without payment for the risks incurred.

The most common risk associated with ovarian hyperstimulation is ovarian hyperstimulation syndrome (OHSS). Typical side effects of mild or moderate OHSS include nausea, vomiting, diarrhea, and abdominal distension and/or pain. Less common, but more serious harms include rapid weight gain and respiratory difficulty. And the most serious, least common harms include life-threatening complications such as "renal failure, adult respiratory distress syndrome (ARDS), hemorrhage from ovarian rupture, and thromboembolism" (Practice Committee 2008, S189). As reported by Helen Pearson, though severe cases of OHSS are rare, they are known to have resulted in death (Pearson 2006). In addition to the short-term physical risks associated with OHHS, there are the unknown long-term physical risks that include the risk of ovarian cancer (Beeson and Lippman 2006). In addition to the above, there are the risks associated with egg retrieval. Egg retrieval is a surgical procedure that is painful for some women and feared by many (Eugster and Vingerhoets 1999). There is the risk of an adverse response to anesthesia and the risks of infection, bleeding, and unintended puncture of an organ.

Whereas it is clear that women infertility patients may freely consent to the various risks associated with ovarian hyperstimulation and egg retrieval in pursuit of their reproductive project, it is much less clear that young, healthy, women volunteers should be asked to accept these risks when there is no prospect of direct benefit to themselves, and there may be no prospect of direct benefit to others with whom they have some affinity (McLeod and Baylis 2007). Further complicating any harm–benefit calculation is the fact that there is still uncertainty regarding the potential harms of ovarian hyperstimulation and egg retrieval, and how these might vary by subject population and by clinic. Indeed, a recent study of potential physical harms suggests that healthy women volunteers experience fewer harmful consequences than women infertility patients undergoing IVF (Maxwell, Cholst, Rosenwaks 2008). One explanation for the difference is a commitment on the part of clinicians "to work assiduously" to reduce the risks of harm to healthy volunteers because they are undergoing potentially harmful medical procedures without the prospect of compensating medical benefit (Maxwell, Cholst, Rosenwaks 2008, 2165). This explains a liberal cancellation policy when there is an increased risk of OHSS. It is also hypothesized that the risk of OHSS may be lower in healthy egg providers because they do not become pregnant—there is no embryo transfer following egg retrieval.

In an effort to overcome the shortage of human eggs for research and to increase the benefit side of the harm–benefit equation, some have suggested paying

women egg providers in cash or in-kind. One argument in support of cash payments is that healthy volunteers are routinely paid for research participation, and similar sorts of payments should be available to women who provide eggs for research (ISSCR 2006; Hudson cited in Vogel 2006; Ballantyne and De Lacey 2008). Another argument in support of this strategy highlights the hypocrisy of allowing women to be paid to provide eggs for reproductive purposes, but expecting them to undergo the identical ovarian hyperstimulation and egg retrieval procedures without payment when the eggs are for research purposes (Spar 2007).

While some argue that healthy women volunteers should be paid to provide eggs for research, others argue that women should not be solicited as paid egg providers (at most, they should be compensated for direct receipted expenses). In addition to concerns about the risk of harm to identifiable women, there are concerns about the risk of undue inducement and the risk that economically disadvantaged women will be exploited (Baylis and McLeod 2007). Others who object to purchasing eggs for research include the scientists who advocate the use of animal eggs for cloning-based hES cell research. For example, Minger writes:

> I am opposed to young women donating eggs for money. I do not feel it is appropriate to encourage women to undergo a risky and invasive procedure for which they receive no direct medical benefit and where most of the donated eggs are wasted. (Minger 2006)

Against this backdrop of controversy on the ethics of buying and selling human eggs for research, the HFEA recently approved two policies aimed at addressing the short supply of human eggs for research. Compensation for women infertility patients who agree to egg sharing for research purposes is permitted, as is the use of animal eggs for cloning-based hES cell research. It now remains to be seen whether the decision to reward women infertility patients for their eggs sufficiently increases the supply of human eggs for research and whether the decision to allow the research use of animal eggs sufficiently decreases the demand for human eggs.

The strategy that involves indirect financial compensation of women infertility patients may be effective in the short term, but in all likelihood this strategy will prove to be cost-prohibitive in the long term. According to Ann Kiessling, the Director of the Bedford Stem Cell Research Foundation in Somerville, Massachusetts, who has been successful in collecting human eggs for research by compensating women for time, travel, and child care expenses, the average cost per cycle is US$27,200 (with women receiving between US$560 and US$4004 per cycle) (Vogel 2006). In the United Kingdom, in those instances

where the eggs available for research come from women who agree to give away half of their eggs in exchange for half-price IVF, the cost per cycle is considerably less (i.e., £1,500 per cycle, or approximately US$3,000 per cycle), but it is nonetheless expensive in relation to typical research budgets—especially when compared to the minimal cost of retrieving animal eggs from the abattoir.

If the market price of human eggs for research remains high, that is, at a comparable price to the price of human eggs for therapy, which in the United States is between $4,000 and $5,000 per cycle (Covington and Gibbons 2007; Ethics Committee 2004), the use of animal eggs for research will be an attractive option from a financial perspective. Alternatively, if the price of human eggs for research can be made to decrease, it can't go too much below the price of human eggs for therapy without affecting the supply of eggs for research, especially when there is no reason to expect a decrease in the demand for human eggs for therapy.[6] In the event of a continued shortage of human eggs for research, increased interest in research involving nonhuman animal eggs (of which there is a potentially unlimited supply) is to be expected.

The supply of human eggs for therapy

In some countries, such as the United States, there is a thriving market for human eggs for assisted human reproduction. Potential customers include:

> Women who have survived cancer treatment, women who are without ovarian function (because of surgery, premature menopause, gonadal agenesis, or for a variety of other reasons), women who carry serious heritable diseases, women who are of advanced reproductive age, and women who have failed repeated IVF attempts. (Maxwell, Cholst, and Rosenwaks 2008, 2165)

Regarding the availability of healthy human eggs for treatment aimed at preventing the transmission of mtDNA diseases, as far back as 1999 John Robertson predicted that "[t]he success of cytoplasm donation . . . could increase greatly the demand for women to donate eggs" (Robertson 1999, 220). He imagined, however, that the market would effectively resolve any "supply" problem that might arise as a result of increased "demand," simply noting that "[i]ncreased demand for donor eggs will raise the price that must be paid to attract more women to undergo the bodily burdens and risks that egg donation entails" (Robertson 1999, 221). Although access to human eggs for therapeutic purposes may not be a problem for affluent women and couples (or women and couples who are willing to incur a substantial debt), the price of human eggs will be cost-prohibitive for some

women and couples. This suggests that unless clinician-scientists succeed in developing alternative sources of human eggs by (1) creating in vitro-derived human eggs from stem cells, (2) collecting germ cells from the ovaries of aborted fetuses and growing and maturing these in vitro, or (3) recovering the developmental potential of human eggs that are currently clinically unusable (e.g., eggs that fail to fertilize), there will be increased interest in using animal eggs instead of human eggs to prevent the transmission of mtDNA diseases.

If research to make human admixed embryos clinically safe and effective were ever successful, then the use of such embryos for reproductive purposes might be a reasonable clinical option for women and couples at risk of having children with mtDNA disease. But would this be an ethically sound option? That is, would it be ethically acceptable for women to consent to the transfer of human admixed embryos (thereby possibly creating "babies with some animal DNA in them") in pursuit of their individual reproductive interest in having genetically related offspring free of mtDNA disease?

"Babies with some animal DNA in them"

We know from earlier debates on access to assisted human reproduction that there are different feminist perspectives on both the ethics of using reproductive technologies to assist fertile and infertile women and couples to procreate, and the ethics of using genetic technologies to allow fertile women and couples to determine the genetic makeup of their offspring (whether to avoid disease transmission, to satisfy aesthetic or genetic preferences, to enhance individual traits, or to improve the human species).

Some feminist thinkers insist on the importance of protecting procreative liberty (e.g., Jackson 2001; Steinbock 2002). In their view, procreative self-determination (reproductive autonomy) is of paramount importance—women can autonomously choose to accept or reject reproductive technologies, and their reproductive preferences should be respected. Among the more ardent proponents of reproductive autonomy, as reported by Rebecca Tuhus-Dubrow, are those who insist that, absent identifiable harm to others, governments have no business "seeking to circumscribe the full range of available 'reproductive choices'" (Tuhus-Dubrow 2007). In this view, it is not for governments to decide if it is acceptable to transfer human admixed embryos to women. This is a personal matter to be decided by women and couples who are capable of making informed choices about which reproductive technologies they wish to avail themselves of (either in the context of research or therapy).

Other feminists object to the unfettered use of reproductive technologies and insist that there is no right to have or to design babies. Although there is general support for "women's freedom to control their own lives and bodies, [there is no support for the desire of some women] to control the lives and bodies of their children" (Tuhus-Dubrow 2007). Here, worries about the commodification of children (as solely a means to another's end of becoming a parent) begin to surface. Beyond this, there is the worry that the desire for children (and especially, genetically related children) is not so much about women's autonomy as it is about the influence of patriarchy and pro-natalism. One proponent of this view, Margaret Brazier, questions "the reality of the so-called 'right to reproduce' because this so-called right is patriarchy in disguise and therefore counter-productive to women's autonomy" (Brazier 1998, 72, 75). Reasoning along similar lines, Laura Purdy notes that a "pervasive pro-natalism . . . persuades women that they will not be fulfilled without having children of their own" (Purdy 1996, 502). In this way, alternative, less costly, less technological means of creating a family (e.g., adoption) are explicitly disvalued, and those who pursue such options are at risk of being stigmatized for having failed to exhaust all available technological options for having a "healthy," genetically related child (no matter how costly or how risky).

Separate from any concern about the way in which individual decision-making is constrained by social and political forces, there is concern among some feminist scholars with the way in which individual choices can have cumulative negative social and political consequences (Sherwin 2003; Seavilleklein and Sherwin 2007). Beyond issues of autonomy, there are justice-related issues of power, oppression, coercion, and exploitation. As Donna Dickenson observes, "while [reproductive technologies appear] to afford women greater reproductive freedom and more control over their bodies [they] have the potential to exploit and oppress women" (Dickenson 2006, 1). So it is that some feminists welcome the regulation of reproductive technologies when these regulations aim to promote and protect the interests of women as a group, as well as the interests of children born of assisted human reproduction. Consider, for example, regulations aimed at curtailing the inappropriate valuing of genetic ties within families, the increasing tendency to see children as commodities, and the use of certain reproductive technologies that might reasonably be constructed as expressing a certain disvaluing of persons with disabilities (Sherwin 2003).

For my own part, I share the concerns of others about the social and political realities that constrain women's reproductive choices. I also believe that there is good reason not to overvalue genetic ties to one's children, not to treat children

as commodities, and not to disvalue persons with disabilities. In addition, regarding the ethics of crossing species boundaries and introducing heritable nonhuman modifications, I have questions about our willingness (and ability) to fully embrace the moral consequences of such genetic tinkering. I have written about this elsewhere in terms of inexorable moral confusion (Robert and Baylis 2003; Baylis and Robert 2007). But what I want to insist upon here is my belief that we ought not to pursue research involving the transfer of human admixed embryos to women, not because women couldn't autonomously choose this (clearly some women could autonomously make this choice), and not because such research is inherently objectionable (I remain agnostic on this point), but because there are more pressing needs to which we must attend, and with haste.

To be precise, in my view, research to make possible the future transfer to women of human embryos with some nonhuman animal DNA in them as a means to prevent the transmission of mtDNA diseases would be the fruit of a misguided use of limited research resources (money and talent) in pursuit of a project to meet the needs of a very small minority for whom there are other options (viz., genetic counseling, egg donation, chorionic villus sampling and amniocentesis, pre-implantation genetic diagnosis), at a time when there are much greater reproductive health needs experienced by many women (in both developed and developing countries) that are as yet unmet. From this perspective, I am moved to ask: for how long can we (will we) turn a blind eye to the reproductive health needs of women who have limited or no access to contraception, who have limited or no access to safe abortion, who are at disproportionate risk of contracting HIV through consensual or nonconsensual sexual activity, and who lack access to adequate prenatal care? And for women in developing countries, there are additional burdens. For example, what about the women who die unnecessarily in childbirth? What about the women who are at increased risk of exploitation as egg sellers? What about the women who risk cultural isolation and more if they are unable to produce children (irrespective of whether they or their partners are infertile)? And, what about the women who are subject to culturally-based genital cutting? Clearly these are not so much issues of autonomy and informed choice, but issues of social justice concerning matters of power, oppression, coercion, and exploitation that call for our immediate attention.

Conclusion

If human cytoplasmic transplantation involving either human cytoplasmic transfer or human pronuclear transfer is ever proven safe and effective in pre-

venting the transmission of mtDNA diseases, there will be increased demand for human eggs for assisted human reproduction. If there is a shortage of (affordable) human eggs for this treatment option, then clinician-scientists might be interested in using nonhuman animal eggs for nonhuman cytoplasmic transplantation as a means to avoid the transmission of mtDNA diseases. If so, there would be significant scientific and legal hurdles to this research and to the eventual therapeutic transfer of human admixed embryos.

From a scientific perspective, there must be reasonable assurances that the human admixed embryos likely would be clinically safe (i.e., there would be limited risk of zoonotic infection) and the nuclear and mitochondrial genomes likely would be compatible. And, from a legal perspective, in those jurisdictions where there is a prohibition on the transfer of human admixed embryos to women, the relevant laws must be amended (or interpreted) to remove these prohibitions. These are not insignificant scientific and legal hurdles, but they are also not insurmountable.

Consider, for example, the legal situation in the United Kingdom that permits the licensing of a wide range of research involving human admixed embryos and prohibits the transfer of such embryos to women. The legislation stipulates that only a permitted embryo can be transferred to a woman. A permitted embryo is an embryo "created by the fertilization of a permitted egg and a permitted sperm," and a permitted egg or sperm is an egg or sperm "whose nuclear or mitochondrial DNA has not been altered." The legislation further specifies that a permitted embryo is an embryo in which "no nuclear or mitochondrial DNA of any cell of the embryo has been altered" (Human Fertilisation and Embryology Act 2008, section 3ZA). However, the Act also allows under regulations that "an embryo can be a permitted embryo, even though the egg or embryo has had applied to it in prescribed circumstances a prescribed process designed to prevent the transmission of serious mitochondrial disease" (Human Fertilisation and Embryology Act 2008, section 3ZA). It follows that under the regulations, it might be permissible in exceptional circumstances to transfer to a woman an embryo whose mitochondrial DNA had been altered in an effort to prevent the transmission of serious mitochondrial disease.

In closing, let us assume for the sake of argument that the transfer of human admixed embryos to prevent the transmission of mtDNA diseases is scientifically and legally possible in the United Kingdom (and perhaps elsewhere). Would it then be ethically acceptable to pursue research aimed at ensuring that the transfer of such embryos was clinically safe so that women could eventually consent to have "babies with some animal DNA in them"?

No doubt some feminists (and others) will answer this question in the affirmative and insist that women have a right to avail themselves of all reproductive options. Other feminists will insist that this reproductive option is inherently objectionable and ought not to be available. Still others, like myself, will wonder how we allowed ourselves to get to this point and will bemoan the fact that we were not proactive in helping to develop an ethically sound research agenda that would appropriately prioritize the reproductive health needs of all women.

Notes

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1. Part-human hybrid embryos are created by mixing human sperm and nonhuman animal eggs or nonhuman animal sperm and human eggs. Human-animal chimera embryos are created by adding nonhuman animal cells to human embryos during early development (the reverse—adding human cells to nonhuman animal embryos—would result in the creation of animal-human chimeras). Human/animal cytoplasmic hybrid embryos are created by inserting the nuclei from adult human cells into enucleated nonhuman animal eggs. In other publications, I describe these cytoplasmic hybrid embryos as "humanesque" to make transparent the fact that these hybrid combinations are predominantly human, but not fully human. Further, it is important to note that as humans are animals, it is most accurate to write about human animals and nonhuman animals. For ease of reading, however, I sometimes write in the vernacular and use "human" instead of "human animal" and "animal" instead of "nonhuman animal."

2. A human admixed embryo is defined in section 4A(6) of the Human Fertilisation and Embryology Act 2008 as: (a) an embryo created by replacing the nucleus of an animal egg or of an animal cell, or two animal pronuclei, with:—(i) two human pronuclei, (ii) one nucleus of a human gamete or of any other human cell, or (iii) one human gamete or other human cell; (b) any other embryo created by using:—(i) human gametes and animal gametes, or (ii) one human pronucleus and one animal pronucleus; (c) a human embryo that has been altered by the introduction of any sequence of nuclear or mitochondrial DNA of an animal into

one or more cells of the embryo; (d) a human embryo that has been altered by the introduction of one or more animal cells; or (e) any embryo not falling within paragraphs (a) to (d) which that contains both nuclear or mitochondrial DNA of a human and nuclear or mitochondrial DNA of an animal ("animal DNA"), but in which the animal DNA is not predominant. http://www.opsi.gov.uk/acts/acts2008/ukpga_20080022_en_2#pt1–pb1–l1g1

3. Lay summaries of these three projects are available at: www.hfea.gov.uk/en/1652.html; www.hfea.gov.uk/en/1653.html; and www.hfea.gov.uk/en/1699.html.

4. The initial university press release (April 1, 2008) indicated that the research data would be verified following the peer review system. At the time of writing, there is no academic publication.

5. Eggs for use in a subsequent cycle will be eggs that are frozen, thawed, and later fertilized, or eggs that are fertilized and then frozen for later thawing.

6. A possible mitigating factor is differences in selection criteria for eggs destined for reproduction versus research.

References

Abboud, Leila. 2002. FDA seeks rigorous review of new fertility treatments. *Wall Street Journal Online*, October 7. http://online.wsj.com/article_email/SB1033940987332846993.html (accessed March 25, 2009).

Ballantyne, Angela, and Sheryl De Lacey. 2008. Wanted—eggs donors for research: A research ethics approach to donor recruitment and compensation. *International Journal of Feminist Approaches to Bioethics* 1 (2): 145–64.

Barritt, Jason A., Carol A. Brenner, Henry E. Malter, and Jacques Cohen. 2001. Mitochondria in human offspring derived from ooplasmic transplantation. *Human Reproduction* 16 (3): 513–16.

Baylis, Françoise. 2008. Animal eggs for stem cell research: A path not worth taking. *American Journal of Bioethics* 8 (12): 18–32.

———. 2009. The HFEA public consultation on hybrids and chimeras: Informed, effective and meaningful? *Kennedy Institute of Ethics Journal* 19 (1): 41–62.

Baylis, Françoise, and Carolyn McLeod. 2007. The stem cell debate continues: The buying and selling of eggs for research. *Journal of Medical Ethics* 33 (12): 726–31.

Baylis, Françoise, and Jason Scott Robert. 2007. Part-human chimeras: Worrying the facts, probing the ethics. *The American Journal of Bioethics* 7 (5): 41–45.

Beeson, Dianne, and Abby Lippman. 2006. Egg harvesting for stem cell research: Medical risks and ethical problems. *Reproductive Biomedicine Online* 13 (4): 573–79.

Brazier, Margaret. 1998. Reproductive rights: Feminism or patriarchy? In *The future of human reproductio*n: Ethics, choice and regulation. Eds. John Harris and Søren Holm, 66–76. Oxford: Clarendon Press.

Brown, D. T., M. Herbert, V. K. Lamb, P. F. Chimney, R. W. Taylor, R. N. Lightowlers, L. Craven, L. Cree, J. L Gardner, and D. M. Turnbull. 2006. Transmission of mitochondrial DNA disorders: Possibilities for the future. *Lancet* 368:87–89.

Center for Genetics and Society. 2003. Ooplasmic transfer. May 30. http://geneticsandsociety.org/article.php?id=381 (accessed March 25, 2009).

Chen, Ying, Zhi Xu He Ailian Liu, Kai Wang, Wen Wei Mao, Jian Xin Chu, Yong Lu, Zheng Fu Fang et al. 2003. Embryonic stem cells generated by nuclear transfer of human somatic nuclei into rabbit oocytes. *Cell Research* 13 (4): 251–63.

Chung, Young, Colin E. Bishop, Nathan R. Treff, Stephen J. Walker, Vladislav M. Sandler, Sandy Becker, Irina Klimanskaya et al. 2009. Reprogramming of human somatic cells using human and animal oocytes. *Cloning and Stem Cells* 11 (2): DOI: 10.1089/clo.2009.0004.

Cohen, Jacques, Richard Scott, Mina Alikani, Tim Schimmel, Santiago Munné, Jacob Levron, Lizi Wu, Carol Brenner, Carol Warner, and Steen Willadsen. 1998. Ooplasmic transfer in mature human oocytes. *Molecular Human Reproduction* 4 (3): 269–80.

Cohen, Jacques, Richard Scott, Tim Schimmel, Jacob Levron, and Steen Willadsen. 1997. Birth of infant after transfer of anucleate donor oocyte cytoplasm into recipient eggs. *Lancet* 350 (9072): 186–87.

Cookson, Clive. 2008. Scientists find hybrid embryos easy to make. *Financial Times*, June 20. http://www.ft.com/cms/s/0/96d72196–3e62–11dd-b16d-0000779fd2ac.html?nclick_check=1 (accessed March 25, 2009).

Covington, Sharon N., and William E. Gibbons. 2007. What is happening to the price of eggs? *Fertility and Sterility* 87 (5): 1001–4.

Dickenson, Donna. 2006. Feminist perspectives on human genetics and reproductive technologies. *Encyclopedia of Life Sciences*. John Wiley & Sons,Ltd: Chichester. http://mrw.interscience.wiley.com/emrw/9780470015902/els/article/a0005592/current/pdf/ .

Ethics Committee of the American Society for Reproductive Medicine. 2004. Financial incentives in recruitment of occyte donors. *Fertility and Sterility* 82. Suppl. no. 1: S240–44.

Eugster, A., and A. J. Vingerhoets. 1999. Psychological aspects of in vitro fertilization: A review. *Social Science & Medicine* 48 (5): 575–89.

Food and Drug Administration. United States. 2001. Letter to sponsors/researchers: Human cells used in therapy involving the transfer of genetic material by means other than the union of gamete nuclei. July 6. http://www.fda.gov/cber/ltr/cytotrans070601.htm (accessed March 25, 2009).

Hawes, Susan M., Carmen Sapienza, and Keith E. Latham. 2002. Ooplasmic donation in humans: The potential for epigenetic modifications. *Human Reproduction* 17 (4): 850–52.

Heijnen, Esther M., Marinus J. Eijkemans, Cora De Klerk, Suzanne Polinder, Nicole G. M. Beckers, Ellen R. Klinkert, Frank J. Broekmans et al. 2007. A mild treatment strategy for in-vitro fertilisation: A randomised non-inferiority trial. *Lancet* 369 (9563): 743–49.

Hirschler, Ben. 2008. Scientists create three-parent embryos. *Reuters*. February 5. http://www.reuters.com/article/healthNews/idUSL0516465820080205?pageNumber=1&virtualBrandChannel=0 (accessed March 25, 2009).

Human Fertilisation and Embryology Act 2008. Chapter 22. http://www.opsi.gov.uk/acts/acts2008/ukpga_20080022_en_1 (accessed March 25, 2009).

Human Fertilisation and Embryology Authority. 2005. HFEA grants licence to Newcastle Centre at LIFE for mitochondrial research. September 8. http://www.hfea.gov.uk/en/1108.html (accessed March 25, 2009).

———. 2007a. *Hybrids and chimeras: A consultation on the ethical and social implications of creating human/animal embryos in research*. April. http://www.hfea.gov.uk/docs/HFEA_Final.pdf (accessed March 25, 2009).

———. 2007b. *Hybrids and chimeras: Findings of the consultation*. September 5. Paper number: HFEA (05/09/07) 396. http://www.hfea.gov.uk/docs/2007–09–05_Authority_Paper_Hybrids_and_Chimeras__Findings_of_the_Consultation_396.pdf (accessed March 25, 2009).

———. 2007c. *Hybrids and chimeras: A report on the findings of the consultation*. October. http://www.hfea.gov.uk/docs/Hybrids_Report.pdf (accessed March 25, 2009).

Illmensee, Karl, Mike Levanduski, and Panayiotis Zavos. 2006. Evaluation of the embryonic preimplantation potential of human adult somatic cells via an embryo interspecies bioassay using bovine oocytes. *Fertility and Sterility* 85 (Suppl. 1): 1248–60.

International Society for Stem Cell Research. 2006. *Guidelines for the conduct of human embryonic stem cell research*. December 21. http://www.isscr.org/guidelines/ISSCRhESCguidelines2006.pdf (accessed March 25, 2009). [ISSCR].

Jackson, Emily. 2001. *Regulating reproduction: Law, technology and autonomy*. Oxford: Hart Publishing.

Lanza, Robert P., José B. Cibelli, and Michael D. West. 1999. Human therapeutic cloning. *Nature Medicine* 5 (9): 975–77.

Lords Hansard. 2007. United Kingdom: House of Lords Publications. December 3: Column 1522. http://www.parliament.the-stationery-office.co.uk/pa/ld200708/ldhansrd/text/71203–0006.htm (accessed March 25, 2009).

Maxwell, Kara N., Ina N. Cholst, and Zev Rosenwaks. 2008. The incidence of both serious and minor complications in young women undergoing oocyte donation. *Fertility and Sterility* 90(6): 2165–71.

McLeod, Carolyn, and Françoise Baylis. 2007. Donating fresh versus frozen embryos to stem cell research: In whose interests? *Bioethics* 21 (9): 465–77.

Minger, Stephen. 2006. Junk medicine: Therapeutic cloning. Science must milk the cow. *The Times*, November 11. http://www.timesonline.co.uk/tol/life_and_style/health/features/article631789.ece (accessed March 25, 2009).

Naviaux, Robert K., and Keshav K. Singh. 2001. Need for public debate about fertility treatments. *Nature* 413 (6854): 347.

Newcastle University. Press Release. 2008. Hybrid embryos statement. April 1. http://www.ncl.ac.uk/press.office/press.release/content.phtml?ref=1207065299 (accessed March 25, 2009).

Parens, Erik, and Eric Juengst. 2001. Inadvertently crossing the germ line. *Science* 292 (5516): 397.

Pearson, Helen. 2006. Health effects of egg donation may take decades to emerge. *Nature* 442 (7103): 607–8.

Practice Committee of the American Society for Reproductive Medicine. 2008. Ovarian hyperstimulation syndrome. *Fertility and Sterility* 90: S188–93. http://www.asrm.org/Media/Practice/Ovarian_hyperstimulation_syndrome.pdf (accessed March 25, 2009).

Purdy, Laura. 1996. What can progress in reproductive technology mean for women? *The Journal of Medicine and Philosophy* 21 (5): 499–514.

Robert, Jason S. 2006. The science and ethics of making part-human animals in stem cell biology. *The FASEB Journal* 20 (7): 838–45.

Robert, Jason S., and Françoise Baylis. 2003. Crossing species boundaries. *American Journal of Bioethics* 3 (3): 1–13.

Robertson, John. 1999. Reconstituting eggs: The ethics of cytoplasm donation. *Fertility and Sterility* 71 (2): 219–21.

Seavilleklein, Victoria, and Susan Sherwin. 2007. The myth of the gendered chromosome: Sex selection and the social interest. *Cambridge Quarterly of Healthcare Ethics* 16 (1): 7–19.

Sherwin, Susan. 2003. The importance of ontology for feminist policy-making in the realm of reproductive technology. *Canadian Journal of Philosophy*, Suppl. vol. 26:273–95.

Spar, Debora. 2007. The egg trade—making sense of the market for human oocytes. *New England Journal of Medicine* 356 (13): 1289–91.

Steinbock, Bonnie. 2002. Sex selection: Not obviously wrong. *Hastings Center Report* 32 (1): 23–28.

Stevens, M. L. Tina, and Stuart A. Newman. 2007. Crossing lines: Breaching human-animal and left-right boundaries. *The Humanist*. September–October. http://www.thehumanist.org/humanist/StevensNewman.html (accessed March 25, 2009).

Templeton, Allan. 2002. Ooplasmic transfer—proceed with care. *New England Journal of Medicine* 346:773–75.

Thorburn, David R., Hans-Henrik M. Dahl, and Keshav K. Singh. 2001. The pros and cons of mitochondrial manipulation in the human germ line. *Mitochondrian* 1 (2): 123–27.

Tuhus-Dubrow, Rebecca. 2007. Designer babies and the Pro-Choice movement. *Dissent Magazine*, Summer. http://www.dissentmagazine.org/article/?article=861 (accessed March 25, 2009).

Vogel, Gretchen. 2006. Ethical Oocytes: Available for a price. *Science* 313 (5784): 155.

Vu, Tuan H., Michio Hirano, and Salvatore DiMauro. 2002. Mitochondrial diseases. *Neurologic Clinics of North America* 20 (3): 809–39.

Wade, N. 1998. Researchers claim embryonic cell mix of human and cow. *New York Times*, November 12. http://www.nytimes.com/1998/11/12/us/researchers-claim-embryonic-cell-mix-of-human-and-cow.html?sec=health&spon=&&scp=1&sq=Researchers%20Claim%20Embryonic%20Cell%20Mix%20Of%20Human%20and%20Cow&st=cse (accessed March 25, 2009).