Discussion (day 2 session 2): Modern genetics and the human embryo *in vitro*

Chairpersons: Jeff McMahan, Jacques Cohen

Speakers: Minoru Ko, Martin Johnson, John Robertson, Timothy Murphy

Discussants: Peter Brinsden, John Robertson, Fatima Hussein, Martin Johnson, Jacques Cohen, Julian Savulescu, Anne Mclaren, Sheila McLean, Timothy Murphy, John Harris, Joe Schulman, Robert Edwards, Minoru Ko, Pedersen, Gregory Stock, Gedis Grunzinskas, Jacky Bovin

Peter Brinsden: What is morally and ethically acceptable in choosing our children may not be so acceptable from the legal point of view. We as practitioners, either physicians or scientists in the field, are increasingly under threat from the lawyers of litigation for our actions. There are two examples that I can think of that could be a problem in the future. A child that was chosen as an embryo to have certain characteristic may well sue his parents in the future and also sue the clinic for having selected that characteristic. That is now happening, and children are suing their parents. I was faced last week with a very angry father and his wife and their 19 year-old son who we had all helped to create 19 years ago. He was overtly gay and happy and comfortably proud of being gay. But the father was angry with us for having 'provided the hormones and the background and the treatment that actually made him gay', and however much I tried to persuade him that they were totally disassociated and there was no trend, he continues to be angry and indeed is threatening litigation against us. In spite of the moral and the ethical acceptance that we should be allowed to choose, there is also the practical and legal angle that we as practitioners may be subjected to.

John Robertson: Perhaps I could address that query. I would say that you were perhaps misinformed about what is legally possible. If the claim in the suit is from the child or from the parents on behalf of the child that the child should not have been born at all, then that legal claim would not be recognized in any nation in the world. Such claims for 'wrongful life' have been rejected everywhere. The only viable claim would exist is possibly one for 'wrongful birth' on behalf of the parents, if the physician had not properly informed them in advance of available tests or other options. The only recognizable claim for a child who is affected would have to be based on a claim that the child would have been born normal but for some negligent action or intervention that caused it to be born handicapped or with damage of some sort. But that is not the kind of case that I think you are raising, e.g. where the child is claiming that he has been affected by the birth itself. That kind of claim simply is not recognized in the UK or elsewhere.

Timothy Murphy: From the way you described it, the homosexual cases claimed would have involved children that were born normal. But [the claim is that] you gave him drugs that may have made him homosexual. I think it will be extremely hard to prove something of that sort. But if one could, then it might belong to a second category, where the harm was avoidable and consistent with the birth of that child.

Fatima Hussein: I have a query on Dr Brinsden's comment and also on Dr Johnson's presentation with regard to the Barker hypothesis. This is concerned with the fetal origins of adult life. We are actually pushing back knowledge of those boundaries to the preimplantation embryo. My question to Dr Johnson concerns this new technique where mitochondrial DNA in oocytes of older women is replaced using cytoplasmic transfers from oocytes of younger women, with a view to getting higher pregnancy rates for the former. Does he think this is on the edge of acceptability and should be pursued as a proper research trial? We do not know the consequences, which still remain a matter of some debate.

Martin Johnson: I raised 'mitochondria' as an example of a potential epigenetic mechanism for transmission of heritable change across cell generations during development and into adulthood. The stimulus for these thoughts was very much the exciting work of Josie McConnell, which I discussed in my paper. However, these are very early days in this field of study. The issue you raise is related but different. While defects in mitochondrial DNA (both qualitative and quantitative) have the potential to adversely affect development and health in later life, the question of whether eggs from older women (or indeed any women) have defects in their mitochondrial DNA, which can be treated by cytoplasmic transfer, is not really resolved yet. Perhaps our Chairman Jacques Cohen is best placed to comment on this matter. My own view about any novel therapy is that, before embarking on treatment of patients, one should have a clear evidential base for proceeding, and a clear hypothesis about what might happen after cytoplasmic transfer. For example, perhaps a controlled study is desirable in which transfer of 'young' ooplasm is compared with that of 'older' ooplasm, and the outcomes compared with mock transfer. This research is best done first in animals. Then you might do it in human eggs as a research project, measuring the

Ethics, Law and Moral Philosophy of Reproductive Biomedicine, Vol. 1, No. 1, March 2005

Published by Reproductive Healthcare Limited

outcome on embryos *in vitro*. Only then might you apply it in a limited controlled and monitored trial in human patients. That would be my course of action with regard to any novel technique, but I am not sure whether that answers your question.

Jacques Cohen: I think, in principle, that the transfer technology is acceptable. We believed it did not constitute transferring genes that were non-existent in the recipient to unrelated lines of germ cells. Despite much news in journals and the media on that point, the concept was mistakenly considered as gene transfer, yet the genes were not new or experimental. Precedents for the recipients may attract some debate from that perspective, but I think the situation is quite clear. Indeed, the issues are its efficacy and the involvement of newer technology, which are important. You mentioned older patients: we never applied this work to them. The patients were young and had repeatedly failed to achieve implantation. We are certainly familiar with mitochondrial disease and there is indeed a high risk of its transmission to offspring. The genetic diagnosis of mitochondrial disease in preimplantation embryos could have some application to this sort of technology.

Julian Savulescu: Martin Johnson gave a fascinating and important talk on the risks of ex-vivo maturation and the culture of the human embryo. One of the philosophers' favourite issues is the idea of ectogenesis, the purely artificial gestation of a human embryo all the way through to the stage of a baby, and the implications this would have for spare embryos and abortions and so on. This situation seems completely fantastic. I recently read a paper, and wrote a small comment on it, on taking immature spermatozoa from young boys prior to chemotherapy and maturing them in the rat. It raises the issue of whether the human embryo could ever be purely gestated in a non-human animal. It seems to me that we can use xeno-transplantation to perfect the modification of animals to produce organs. It is not a completely fantastic idea. Would the human embryo be able to gestate or mature outside the human and in a non-human animal? I wonder if you could comment on the possibility of that and what issues you see it is raising?

Martin Johnson: I think it is a fairly fantastic idea, but not necessarily impossible! Certainly some limited progress has been made to improve the in-vitro culture of different embryogenic and embryonic stages (mostly in mice and rats), and of course the capacity to sustain later fetal stages recovered prematurely is developing steadily. However, it is clear that life *in vitro* for all these stages has the potential to leave residual damage, and it is also clear that we are a long, long way from being able to undertake the whole of development *in vitro*. Even the short periods of development referred to above are unsuccessful in many if not most cases.

Anne McLaren: Professor Murphy suggested most heterosexual couples and some homosexual couples would prefer heterosexual children. I think that might well be rather common, and a relatively unobjectionable reason may be that they look forward to having grandchildren. Now if it becomes more customary for same-sex couples to have children, might that alleviate that particular concern?

Timothy Murphy: In the case mentioned here earlier, one of the objections to homosexual sons as I understood it was a fear that there would be no grandchildren. I do not know how he knew that. I think there are a lot of alternative arrangements that people are making largely on their own in this area. This topic is not especially well studied but I do know that various clinics will or will not participate with same-sex couples in these particular matters. It tends to be a little easier for women couples who come down to a local bookstore or buy a handbook that tells them how to have a grandchild. I suspect that even there, a generational shift is now in progress and more gay people are seeing themselves as having children and grandchildren. I will add that we talked a little bit yesterday about whether it is safe for kids to grow up in same-sex homes. I think it is also important to think about whether it is safe for homosexual children to grow up in heterosexual homes. A lot of times the answer is no. So towards building better families, I think exactly that same-sex coupling will be a good thing. The religious right is desperately afraid of that because it will create trans-generational gay advocacy, which does not exist really at the present time. Right now, a lot of gay advocacy consists of individuals testifying before Congress and this kind of thing. It will be a different tenor altogether when children come and say 'I want you to come and protect my mothers', that sort of thing.

John Harris: I wish to make a comment prompted by Tim Murphy's presentation but also relates to John Robertson's comments. In particular, I ask about the basis for the justification of procreative liberty which I believe you have partly discussed at least in terms of outcomes. Certain outcomes may include those that the procreators will not desire, as in the case of deafness for example. I am fond of characterizing my own situation as not having a spiritual cell in my body. If spirituality is partly a genetic predisposition, then perhaps its opposite might also be at least partially genetically derived. This raises, I think, quite interesting issues. I think it was Ronald Regan when he was Governor of California talking about a group of outside agitators and known cynics, now it may be the religious right, for example, that would want to deselect traits to predispositions, to sceptisim and cynicism, whereas others may prize those traits. I wonder how far procreative liberty will aspire, assuming there are genetic predispositions of this sort.

John Robertson: Well, as I said in my talk, it really depends on the extent to which we accept genetic selection as an essential part of procreative liberty. I think we know a great deal about disease states and children, and allow

Ethics, Law and Moral Philosophy of Reproductive Biomedicine, Vol. 1, No. 1, March 2005

Published by Reproductive Healthcare Limited