The other woman: Evaluating the language of 'three parent' embryos

Body text

In February 2015 the British Parliament approved regulations to allow techniques, to be used under licence, 'to prevent the transmission of serious mitochondrial disease from a mother to her child'.[1] Though these regulations refer to 'mitochondrial donation',[2,3, 4] in the media the 'vast majority'[5] of reports about the issue have made reference to, or included in their title, 'three parent' babies, 'three parent' IVF or 'three parent' embryos. The aim of this paper is to examine the main terms in which this public policy debate has been conducted and, in particular, to evaluate the term 'mitochondrial donation' and the description 'three parent'. The analysis of these terms will then be used to inform ethical reflection on the techniques proposed.

Mitochondria are organelles of the cell, microstructures which convert energy from one form obtained from outside the cell to another that is more readily used within the cell. The mitochondria, like all parts of the cell, are under the regulation of the DNA found in the nucleus. The nuclear DNA contains most of the genes and, in human beings, codes for and regulates some 20,000 or so proteins used in or produced by the cell. In addition the mitochondria also contain DNA with 13 coding genes. If the mitochondrial DNA is defective then this may cause a serious disorder which could be passed down the female line. Mitochondria are present in the egg but not inherited from the sperm.

The aim of the techniques proposed in the regulations is to enable women who carry mitochondrial mutations to have children who are related to them genetically but who are free from mitochondrial disease. One technique, known as Maternal Spindle Transfer or Metaphase II Spindle Transfer (MST), involves modifying eggs prior to fertilisation. A second technique, known as Pro-Nuclear Transfer (PNT), involves modification of embryos. In both cases the aim is to produce an embryo with nuclear DNA from one woman (via her embryo in the case of PNT) and healthy mitochondria from a second woman (again, via her embryo in the case of PNT).

This paper will focus on MST and ask whether fertilisation of an egg modified by MST generates a 'three parent' embryo. By way of contrast the paper will also examine the term 'mitochondrial donation', which is the preferred official nomenclature.

Organelle transplants?

As stated above, the preferred governmental terminology for these techniques is 'mitochondrial donation'.[2, 3, 4] This phrase clearly, and perhaps deliberately, echoes the language of organ or tissue transplantation. Just as organ donation consists in the transplant of a healthy functioning organ into the body of a recipient, so 'mitochondrial donation' suggests the transplant of organelles from a donor into a recipient cell. The picture evoked provides reassurance that receiving the donor organelles does not raise novel ethical questions or have implications for identity or parentage. According to this picture, 'transfusing mitochondria is not unlike transfusing red blood cells in a case of severe anaemia'.[6]

One fundamental problem with this picture, and with the terminology of 'mitochondrial donation', is that it does not accurately reflect the process involved in MST. The mitochondria are not transferred between eggs. It is not the mitochondria that are 'donated' or 'replaced'. The regulations make clear that the egg is 'modified' by the removal and insertion of 'nuclear DNA',[7] not by the removal or insertion of mitochondria. It is the healthy egg from the egg donor that is 'modified', and it is modified by replacement of its nuclear DNA. The phrase 'mitochondrial donation' suggests that the mitochondria are the only parts of the donor egg 'used in the reconstruction of another egg'[8] but in fact it is the great bulk of the donor egg that is used: virtually the whole cell apart from the nuclear DNA and associated structures.

For a similar reason the metaphor of 'replacing the battery in a camera',[9, 10] which was invoked very frequently in the public debate,[11,12,13] is also misleading. In the first place, as a general rule, one should beware mechanical metaphors when applied to living systems, for mechanical devices are made from parts and some parts (such as batteries) are designed to be replaceable. In contrast,

the parts of organisms do not exist prior to the whole (either temporally or logically).[footnote i] The metaphor of batteries also may understate the interaction of the mitochondria with the cell as a whole. 'There is strong evidence that the mitochondrial genome, for example, "talks to" the nuclear genome, and has pervasive effects on cellular and organismal functioning.'[14]

Even if, for the sake of argument, one were to accept the metaphorical description of mitochondria as the 'batteries' of the cell, even so the process of MST would still not be like replacing batteries, for the mitochondria are not replaced. It is the nuclear DNA that is replaced. If the mitochondria are to be imagined as like the batteries within a camera, then MST would not be like replacing the battery. It would be more like replacing the memory card of the camera, or perhaps like replacing the SIM card of a phone. If someone steals my phone – batteries included – and replaces the SIM card then the identity of the phone (and much or all of the personal data) will change. However, there will still be an obvious sense in which I might point to the handset and say 'hey, that's my phone!' I would certainly not be impressed by someone who claimed that it was his phone and he had merely 'replaced the batteries'. All analogies limp and the significance of parts of a living cell is not adequately modelled by simple mechanical or electronic devices such as cameras or phones. Nevertheless, the point of the counter-analogy is to remind us that MST is the modification of an egg by replacement of its nuclear DNA, not the removal of or insertion of mitochondria into or out of an egg. Indeed, the whole purpose of MST is to alter the original identity of the egg by the replacement of nuclear DNA with nuclear DNA from another woman. The distinct genetic identity associated with the mitochondrial genes is thus significant not only in itself but also as an enduring sign of the original identity of the egg before this nuclear DNA replacement.

The ethical implications of this misleading language are explored below after assessing the aptness or otherwise of the description 'three parent' embryos. This assessment first requires some more general reflection on biological parenthood and the different male and female contributions to reproduction.

Unequal partners

According to Aristotle, by a male animal 'we mean that which generates in another', and by a female 'that which generates in itself'.[15] This distinction he applied to all animals where there is a separation of male and female. It is simply what is meant by female or male, biologically speaking. In another place Aristotle claimed that 'what the male contributes to generation is the form and the efficient cause, while the female contributes the material'.[16] Here Aristotle was in the grip of theory and neglected evidence, of which he was aware, that the 'form', in the sense of the sum of inherited characteristics, is evidently passed down from the female no less than from the male. Concomitantly, Aristotle was also mistaken in thinking that males contribute nothing to the 'matter' of the embryo.

Despite these and other mistakes, Aristotle made a significant contribution to reflection on the biology of reproduction. He asked what we mean by 'male' and 'female' when these terms are applied to a variety of different species of animal. He is surely correct that in general we identify as female the one who conceives in herself, who lays the egg or who gives birth (notwithstanding apparent exceptions such as seahorses). The male inseminates or fertilises, and the offspring inherit from him, but he makes relatively little material contribution. The contribution of male and female to generation is thus unequal, and while both contribute to the inherited characteristics, the female also contributes the bulk of the material from which the body is originally fashioned and from which it is first nourished.

That the female produces an egg is true not only of birds and fish but also of mammals. It was William Harvey, in 1651, who generalised Aristotle's schema and argued that all living things, including human beings, come from an egg, '*ex ovo omnia*'. It took nearly two centuries for this thesis to be demonstrated empirically, but it is one of the foundations of modern biology.[17]

In mammals, the female contributes significantly more than the male to the biology of reproduction. She contributes in four ways. First she contributes roughly in equal measure to the male in relation to inherited characteristics. Secondly she contributes the bulk of the body of the embryo, derived from the fertilisation of her egg. Thirdly she gestates and gives birth. Fourthly she suckles the offspring, passing on not only nourishment but also other biological factors: antibodies, for example. This last contribution, from which 'mammals' are named, is characteristic of a mother, but is not essential to biological motherhood. A mammal may suckle young who are not her own or may not be able to suckle young to whom she has given birth.

Fracturing biological parenthood

In nature the first three elements of the maternal biological contribution (genetic inheritance, the body of the embryo from the egg, and gestation) are not found separately. However, the advent of in vitro fertilisation has made possible the separation of the egg mother from the birth mother. The use of an 'egg donor', or a donated embryo, results in three biological parents – the biological father, the birth mother, and the egg mother. It cannot seriously be disputed that the woman who bears the child for nine months and gives birth is a biological mother. However, there can now be another biological mother: the one who provides the egg. In English law there can only be two parents, the birth mother and a second parent (generally the partner of the birth mother).[18] Again, in English law, a sperm donor is not recognised as the parent, but manifestly he *is* a biological parent and this grounds the right of his child, later in life, to knowledge of his identity.[19] In a similar way, the egg mother is also a biological parent and this also is tacitly recognised in the legal right of her child to knowledge of her identity.[19] This separation of egg mother and birth mother strains and weakens the sense of biological parenthood of each of the two mothers, for one is mother of a child to whom she does not give birth and the other is a mother who gives birth to a child that does not inherit her genes. Nevertheless, both mothers are recognisably biological parents to the child.

The MST technique produces a further separation, between the woman who provides the nuclear genetic contribution, roughly equivalent to that provided by the male parent, and the woman who provides not only the mitochondria but the bulk of the egg (approximately 95% by volume) which, when fertilised, will form the body of the embryo. That the enucleated egg provides most of the matter may be true even in relation to DNA. In the debates over the proposed regulations it was frequently claimed that 'over 99% of our total DNA'[20] is in the nucleus, or that mitochondrial contain '0.1% of the total cell DNA'[21] but these figures are inaccurate, because they neglect the great number of copies of mitochondrial DNA. In fact the majority of DNA in the unfertilised egg may well be mitochondrial.[footnote ii]

It is important to recognise that the biological contribution of the egg is not limited to its nuclear and mitochondrial DNA. The egg is not merely a sack containing DNA. It has a strong influence over how the genes are expressed, which is why an egg can sometimes successfully 'reprogram' the nuclear DNA placed within it, as is evident in cloning by somatic cell nuclear transfer. The egg is a complex and highly specialised cell, no less specialised than a neurone or a white blood cell or a muscle fibre. The maturation of the oocyte is a complex process which we are still coming to understand. The egg has a unique role, which is to be fertilised by a spermatozoon so as to form an embryo. The egg is oriented, disposed, adapted to this activity. The first stages of division and development of the embryo are directed principally not by the DNA in the nucleus but by biochemical and structural factors already within the corpus of the egg (including what is termed 'maternal RNA'). It is for this reason that 'many animals - some fish and frogs under natural conditions, and experimentally, mammals - can produce embryos from the egg alone, without fertilization'.[22] Stuart Newman, Professor of Cell Biology and Anatomy at New York Medical College, therefore argues that, 'biologically speaking, the woman who provides the egg has a unique role in the reproductive process'.[22] In his view, she is *more* of a biological mother than is the provider of the nuclear DNA.

The generative power of the egg shows how far wrong Aristotle was in identifying the female with the 'matter' and the male with the 'form' and the 'efficient cause'. In fact whereas the female supplies the bulk of the matter, the form is inherited equally from both, and the efficient cause is also principally from the female. It is the egg that contains the active power which, post-fertilisation, first drives the development of the embryo, the developmental process that distinguishes an embryo from a gamete. This process, if it is the true development of an embryo of a particular species of animal,[footnote iii] must be shaped by the specific form inherited principally through the DNA. Nevertheless, in Aristotelian terms, any process requires not only a formal cause but also an efficient or moving cause and in mammalian reproduction this is found not in the DNA but in the vital activity of the ovum. In a multi-cellular organism, every cell contains DNA, and the great majority contain nuclear DNA, but it is only the ovum which, when fertilised, can generate a new organism. This is a very special cell and has a unique generative significance.

If an egg has been modified by MST, the resulting embryo will therefore have three biological parents: the biological father, the (nuclear) genetic mother, and the (enucleated) egg mother. Again, this separation strains the idea of biological parenthood, with a mother who does not provide the characteristic maternal contribution (materially and in relation to activity) which is the living egg, and a mother who does not provide the inherited characteristics passed on with the nuclear DNA. Nevertheless, both contributions are recognisably parental. If a surrogate mother were used to carry and give birth to the child, then the child would have four biological parents: one father and three mothers. However, if the birth mother were also the woman who provided the nuclear material, the child born by this procedure would indeed be a 'three parent' baby. The popular media description turns out to be apt, at least for one of the proposed techniques.[footnote iv]

The consistent stance of the British government has been that it 'cannot accept'[26] the validity of the language of three parent babies. The government responds that 'all available scientific evidence indicates that the genes contributing to personal characteristics and traits come solely from the

nuclear DNA, which will only come from the proposed child's mother and father'.[26] However, this response threatens to overlook the genetic contribution of the mitochondrial DNA, which may have effects 'on a range of important traits such as individual development, cognitive behaviour, and key health parameters'.[27, 28] The government's response also threatens to reduce biological parenthood to genetics and genetics to the sequence of the nuclear DNA.[footnote v] It assumes that the female biological contribution should be understood only on the model of the male. Against all this it should also be acknowledged that a 'surrogate' mother is undoubtedly a biological mother, even though her contribution is not genetic in character. It is argued here that, analogously, the egg mother who effectively provides the body of the embryo is also a mother per se, however much or little she also contributes to genetic inheritance.

The egg mother would have a real biological relation to the offspring even if there were no genes that were traceable through the female line, through the mitochondria. The fact that such genes are transmitted is not essential to this biological relationship but rather, is *expressive* of it. The genetic contribution of the egg mother allows a child to trace her female lineage, at least to some extent and in relation to groups and movements of peoples. It is by mitochondrial DNA, through the female line, that the human race has traced its evolutionary history back to the African Eve.[29,30, 31] The significance of these mitochondrial genes is thus not only that they are associated with heritable characteristics.[27, 28] In addition to this, the enduring presence of these genes is a reminder of the significance of the egg from which the embryo is formed.

Some ethical implications

An implication of the language of mitochondrial 'donation', 'transfer' or 'replacement' is that it suggests that the egg is modified by the transplantation of healthy mitochondria. Once the misleading language is set aside it can be recognised that MST 'modifies' an egg (the egg from the egg donor) that is *already healthy*. The reason for the modification is not to replace defective mitochondria but to replace the nuclear DNA of the egg mother with that of another woman.

It is therefore inaccurate to say that the aim of the regulations is 'is to ensure that mothers who carry damaged mitochondria can have children with the confidence that they will be born without the devastating and often deadly conditions that can be caused by serious mitochondrial disease'.[33] MST presupposes the use of a donor egg, and the use of a donor egg already ensures that the child does not inherit mitochondrial disease, with or without further modification of the egg by MST (indeed MST may introduce a risk of transmission of affected mitochondria). It is more accurate to say that the techniques 'could allow women who carry disease-causing mutations in their mitochondrial genes to give birth to *genetically related children* free of mitochondrial disease.'[34]

It is understandable that couples wish to conceive and (in the case of the woman) bear children who are genetically related to both of them. This is a very natural desire. Equally, it is no doubt true that for many women who carry a mitochondrial disorder 'the idea of having a child to whom they are not genetically linked is… difficult to accept'.[35] It is no part of the argument of this paper to suggest that a woman *should* bear a child to whom she is not genetically related, or indeed should bear a child at all. The point is only that the promised benefit of this technique is to enable parents to satisfy 'a preference to have genetically-related children'.[36] MST is not a treatment for mitochondrial disease. The egg that is to be modified does not carry this disease. MST is a form of IVF which uses an egg donor and does not add to the safety or efficacy of standard IVF with an egg donor. What it adds is a desired genetic connection, albeit of a very unusual kind.

The lady vanishes,[footnote vi] **again**

The most important feature of the terminology of 'three parent' embryos from an ethical perspective is that it draws attention to *the other woman*, the egg mother. The approval of regulations that would allow MST in clinical use represent only the latest in a series of biotechnological innovations that rely on past, present, and future use of women's bodies. 'Any increase in research or treatments involving MST or PNT would increase the demand for egg

donors'.[37] The 'harvesting' of human eggs to supply these technologies involves significant health risks,[38, 39] 'with its hormonal induction treatment causing manifestations of ovarian hyper stimulation syndrome in up to one third of treated women. Severe forms requiring hospitalisation and potentially life-threatening are less common but by no means rare'.[40] Furthermore, in order to increase the supply of eggs, regulations now permit 'donors' to be 'compensated' at up to £750 a time,[41, 37] and the Wellcome Trust Centre for Mitochondrial Research has already advertised that it will pay women £500 'for a completed donation cycle'.[42] This in effect encourages poor women to sell their eggs.

Another means of increasing the supply of human eggs is to pay for fertility treatment in exchange for taking some of a woman's eggs; this is known, euphemistically, as 'egg sharing'. If the eggs are then used in assisted conception (either in standard IVF or with MST), this could lead to a woman becoming the biological mother of a child to whom she will not have access. In the case of MST, the regulations that have been passed would also deprive any resultant child of the choice about whether to contact her.

When, in 2008, scientists were proposing to use admixed human-nonhuman embryos for research,[40] this was advocated in part on the basis of providing an alternative to the use of human eggs. At that time it was acknowledged that there were 'legitimate concerns about whether it is appropriate to encourage young women to undergo invasive and potentially harmful procedures without any direct medical benefit'.[43] However, since the political success and scientific failure of that avenue of research, public expressions of this 'legitimate concern' have largely ceased. The contemporary situation is just as it was in 2006 when Donna Dickenson remarked that 'the women from whom the ova are taken have virtually disappeared from view',[44] or in 2008 when Francoise Baylis observed that 'their eggs are regarded as mere receptacles and their reproductive labour is taken for granted.'[45]

The failure to acknowledge the third parent, the (enucleated) egg mother, is not accidental. The whole rationale of MST is to replace the genetic identity of the egg mother as far as possible with the identity of the nuclear transfer mother. The concomitant of this is that the identity of the egg mother is all-but erased so as to deny her real biological contribution and her link to the child. It is this same rationale that is in play when the regulations remove the right of the child to identifying information about the (enucleated) egg mother – misleadingly described in the regulations as the 'mitochondrial donor'[3]. A further motive for removing the right of a child to identifying information about the egg mother may be to increase the supply of egg 'donors', as 'the removal of anonymity from egg and sperm donation in 2005 is widely cited as being a contributory factor to the current shortage of donors for reproductive purposes'.[37]

If, as argued here, the common public language of 'three parents' is broadly accurate then the attempt to restrict knowledge about the third parent is a major ethical concern. Twice in the relatively recent past governments have come to recognise the unnecessary suffering caused by denying children the opportunity to know about their biological parents, first in relation to adoption, and later in relation to IVF with sperm or egg 'donors'. This process should not need to be repeated a third time. It is not for the State but for the offspring to decide whether they will see it as important or significant to know about an unacknowledged biological parent and perhaps to make contact.

Why would someone not be curious about this unacknowledged third parent? How could they not wonder what characteristics they might otherwise have inherited had her nuclear DNA not been replaced? Thoughts about 'what would have been' in this context are philosophically slippery, as it is arguable that the circumstances of our origins determine our identity.[46] In this case it would not be accurate to say that *my* genetic inheritance was changed for, without MST, the fertilisation of the donor egg would not have been my conception, but that of a different person. Nevertheless, it is natural to be curious about one's biological origins and one's biological parents. If I had come to be

in this way I might well want to meet this other woman, from whose modified egg I came to be. Furthermore, if I think this then there will certainly be others who think this, even if not everyone thinks in this way. 'If a child gets DNA from 3 or more parents this will lead to desires to want to know the identity of the donor parent. Reasons could vary from thankfulness, curiosity, identity confusion, or desperate need to be loved.'[47]

Public opinion on three parent embryos

The power to enact these regulations was clearly and explicitly provided for in the primary legislation, the Human Fertilisation and Embryology Act 2008.[2] However, the provisions relating to future regulations were inserted into the primary legislation with little if any public engagement on the issue. In 2005 there had been an extensive Department of Health consultation which informed the Review of the Human Fertilisation and Embryology Act presented in December 2006.[48] The Review ran to 45 pages and did not include the word 'mitochondria' at any point.

There was therefore no public discussion prior to the provisions appearing in the draft bill of 2007.[49] Furthermore, subsequent to the publishing of the draft bill, public discussion of the bill was dominated by the proposal to permit the creation of hybrid embryos[40, 50] and consultation exercises were conducted principally on this issue.[51, 52, 53, 54, 55] There were a few other issues that emerged in public and political debate, such as whether the law should recognise a child's need for a father, but there was no proactive consultation by government, and no interest or awareness within the media or among the public about provisions for future regulations relating to 'mitochondrial donation'.

Widespread public awareness of the issue can be dated to a series of announcements on 19 January 2012, and to the media interest that followed. In the first place the Wellcome Trust announced its decision to grant £4.4 million to Newcastle University to fund research 'to prevent transmission of mitochondrial diseases'.[56] On the same day, the Nuffield Council on Bioethics, which is part-funded by the Wellcome Trust, announced that it would conduct an ethical review of these

techniques.[57] Also on the same day, the Secretaries of State for Health and for Business, Innovation and Skills tasked the Human Fertilisation and Embryology Authority (HFEA) to seek public views on the techniques.[58]

In relation to the language of 'three parent' embryos the conclusion of the Nuffield Council working group was as follows:

> Although the perception of the personal and social relationships created by egg or embryo reconstruction would remain a matter for the individuals concerned, it is the view of the Working Group that 'motherhood' is not indicated either biologically or legally by virtue of mitochondrial donation.[59]

The apparent respect given here to the perspective of the individuals concerned is immediately qualified by rejecting any view which would imply that the relationship to the egg donor was as to a 'third parent'.[60] On the basis of the argument presented in this paper, that qualification rests on a mistake. The mistake is not in the requirement that subjective perspectives be constrained by an understanding of the biology. On the contrary, the appropriateness of subjective emotional responses can and should be assessed in relation to the best available objective (or inter-subjective) account. The mistake of the working group was that its discussion of biological parenthood focused too narrowly on the extent of the mitochondrial genetic contribution to personal identity. Had the working group acknowledged that the bulk of the embryo was from the donated egg-cell, and had they recognised the unique generative capacity of that cell, then they would perhaps have recognised the procreative significance of the egg per se. They might have then recognised also that MST is a nuclear transfer technique, centrally and purposefully concerned with altering the genetic identity of the resulting child. The Nuffield Council Report was thus a missed opportunity for critical reflection on the fracturing of biological parenthood: a fracturing seen not only in relation to MST but already in relation to standard IVF with an egg donor.

The conclusions of the Nuffield Council helped shape the consultation exercise conducted by the Human Fertilisation and Embryology Authority.[61, 62] Unfortunately, the representative survey, which would offer the most reliable guide to current opinion, did not ask whether participants regarded the egg donor as a 'third parent', nor did it ask whether the child conceived should have a right to identifying information about the egg donor.[63] The question about the right of the child to information was asked in the open consultation questionnaire, but that suffered from two problems. In the first place the nature of an open consultation is to be self-selecting, and to give prominence to the views of those who are engaged with the issue and have already formed their opinions. In the second place, this particular questionnaire was framed so that respondents who were opposed to the technique were not given the opportunity to express an opinion about the access of the child to identifying information.[64] A number of respondents expressed frustration with this restriction which further limits the usefulness or meaningfulness of the data. Nevertheless, the deliberative meetings did openly solicit views in relation to the child's access to information, and compared these before and after discussion.

Prior to discussion, opinion expressed by the participants was roughly equally divided between those in favour of a right to identifying information, those against, and those undecided, with a slight preference for access to such information (34% for, 30% against).[65] After guided discussion those against providing identifying information had risen to 44% while the number in favour was very little changed (32%). This shift of opinion was shaped at least in part by the information and guidance that was provided. 'Many participants took into account the comparison made by experts, between mitochondrial donation and blood transfusion or bone marrow donation. This perhaps provides some explanation for the decrease in the proportion of participants concerned about the child having DNA from three people'.[66] If the argument of the present paper is valid then the comparisons provided by experts were not in fact apt but were rather misleading. In the light of this possibility, it is noteworthy that while some participants accepted these analogies, at the end most

remained either unconvinced or actively opposed to them, and the number who thought the child should have access to identifying information was virtually unchanged.

When the government issued a consultation on the draft regulations, a similar picture emerges. The government asked 'Do you agree that people donating eggs and embryos for the purposes of mitochondrial donation should not have the same status as those donating eggs and embryos for use in fertility treatment but rather regarded more like organ or tissue donors, so should not be identifiable to young people born as a result of the treatment?'[67] The way in which this question is framed clearly shows the official preference for the analogy of tissue donation over the analogy of gamete donation (and thus biological parenthood). The result of the consultation was that 143 people agreed with the government and 146 were against.[67] Though this consultation exercise was not a representative poll, this split is very similar to the initial views given in the HFEA deliberative survey, fairly evenly divided but with a slight preference for providing identifying information. The government response to the consultation also noted that 'a number of respondents who supported the principle of mitochondrial donation, and agreed with most or all of the other consultation questions, disagreed with this proposal'.[68] Not only the split of responses but also this combination of views should perhaps have given cause for a reassessment of the government's position.

A significant proportion of the population, even among those supportive of the techniques, regard the relationship between the child and the (enucleated) egg mother in the case of MST as similar to that between the child and egg mother in standard IVF with donor gametes. If a significant proportion of people think this then, if the techniques successfully give rise to children, at least some of these children will share this opinion and will wish to have access to identifying information about the person referred to here as the 'other woman'. Where such a desire is not supported by law, 'experience has shown that few donor conceived people have been told the truth about their conception by their heterosexual parents and doubtless fewer still will be told the exact nature of

the preimplantation changes made to their embryo form at the laboratory stage.'[69] This would be an injustice.

Due acknowledgement of 'the other woman'

This paper has not attempted a comprehensive ethical analysis of MST, nor has it explored the degree to which PNT is analogous to MST, biologically and/or ethically. This paper has set to one side questions such as the ethical status of the human embryo, the implications of these techniques in relation to effects on the germline, and the adequacy of the evidence of safety or efficacy. Its focus, rather, has been to explore the main terms in which the public debate has been conducted, and to draw out some ethical implications from the exploration of these terms. It has concluded that, whereas the term 'mitochondrial donation' is misleading, the language of 'three parents' is broadly accurate, at least for one technique. This in turn helps highlight a set of ethical concerns, in regard to 'the other woman' and the child of this woman. The woman who is, at least with MST, the third (or fourth) biological parent must not be erased from the ethical picture, nor hidden from her child. It is her egg that is modified. Furthermore, it is modified not to improve its health or the health of the resulting child but to change its genetic identity so as to make the resulting child less 'difficult to accept'[35] by the commissioning woman. It is the (enucleated) egg mother who effectively provides the body of the embryo. She takes risks with her health in order to provide this egg and gives it voluntarily, financial inducement notwithstanding. Without her, *this* embryo simply would not exist. In relation to the significance of her contribution, William Harvey's words seem apposite: *ex ovo omnia*.

Footnotes

i. The example of mitochondria might seem to be an exception to this rule, for it seems most probable that these structures developed from what were once independent organisms existing symbiotically within a host organism. So these 'parts' did exist before the 'whole'. However, the transition here from endosymbiotic organisms (whole-to-whole relationship) to organelles (part-to-whole relationship) is utterly unlike manufacture. The parts were not produced separately, as parts, immediately prior to the assembly of the whole. Rather the new kind of living organism evolves from previous living organisms (a whole evolving from wholes). In any case mitochondria are now well-integrated parts of a whole, as they have been for well over a billion years. They are not organisms that could exist independently outside a cell.

ii. The egg contains approximately 300,000 copies of the 16,569 base-pair mitochondrial genome compared to one copy of the 3,031,042,417 base-pair nuclear genome. I am indebted to Neville Cobbe for pointing this out to me.

iii. Because other processes may mimic, but be distinct from, true embryological development, the task of distinguishing embryos from gametes and from 'pseudoembryos' may not always be straightforward.[23, 24, 25]

iv. This paper focuses on MST because there are further complications in relation to PNT. For whereas MST starts with three gametes, combines elements of the two eggs, and generates one 'three parent' embryo by fertilisation, PNT starts with four gametes, generates two embryos by IVF, and then deconstructs these embryos. The PNT embryo is not itself generated by fertilisation, directly from gametes, but by reconstruction from two embryos, in a process very similar to somatic cell nuclear transfer (that is, cloning). PNT thus strains our understanding of biological parenthood perhaps to breaking point,

notwithstanding that the embryo produced is very like an embryo generated by the 'three parent' MST technique.

v. On some problems with genetic reductionism see [32]

vi. The title of this section is taken from an article by Donna Dickenson [44]

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