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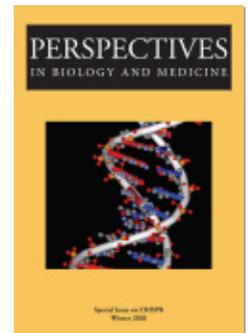
Genome Editing and Human Reproduction: The Therapeutic Fallacy and the "Most Unusual Case"

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GENOME EDITING AND HUMAN REPRODUCTION

*the therapeutic fallacy
and the “most unusual case”*

PETER F. R. MILLS

ABSTRACT In the current agon between those promoting and opposing the development of human reproductive applications of genome editing techniques, the bone of contention is often whether the prospective reproductive technologies answer an “unmet medical need.” Proponents often point to highly unusual cases of inherited genetic conditions as exhibiting that need. This essay argues that we ought to admit that the opponents are correct: human reproductive genome editing cannot be justified on medical grounds. Taking a deliberately provocative line, the essay suggests how inscribing such practices within a conventional model of biomedical research fails to take proper account of the interrelated interests in play, including those of the wider society and its future members. It also obscures important questions about how the public significance and value of human genome editing are produced through the dynamic encounter between science, technology, and social morality. This has certain discomfiting implications that will require both courage and humility to confront and—finally, perhaps—to embrace.

AMONG THE OBJECTIONS TO THE IMPLEMENTATION of what I will call “genome editing in human reproduction” (GEHR) is that it does not address any unmet medical need, and therefore fails to meet an important criterion for introducing an unproven procedure with potentially adverse consequences. To be clear: what I mean by GEHR is the use of any one of a number of related

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biological techniques, such as the CRISPR–Cas9 system, deliberately to modify a functional sequence of DNA in a cell of a human embryo (or human sperm or eggs, or their precursors), so that the modified sequence is replicated in the cells of a resulting child and may, without further intervention, be passed on to that child’s biological descendants. It is what some people call “germline” genome editing. The reason the objection is strong is that there appear to be potential harms that might result from the clinical use of such novel and unprecedented techniques. Some of these potential harms are individual, like an unpredicted negative consequence for the resulting child of editing a gene that has multiple functions; other harms may be social, like the disturbance of valued norms of interpersonal and intergenerational relations. In the absence of a pressing medical need, this consideration is assumed to create a strong presumption against GEHR that may be impossible to overcome.

There are at least two good reasons to be skeptical about the claim that GEHR can meet a pressing medical need. The first rests on the empirical observation that there are no (or very few) genuine candidates for the procedure in question (prospective parents) to whom no alternative course is available. The second rests on the judgment that, even if there are good candidates, their situation should not be regarded as one of “medical need.” I think both of these reasons are persuasive. Nevertheless, I do not think they will or should necessarily inhibit the eventual implementation of GEHR, and I therefore think that the task that lies ahead is to identify and explore conditions under which GEHR could be used beneficially and responsibly. I do not, however, think GEHR should be used now, and I do not think it should ever be used unless, as the result of a legitimate procedure that follows upon broad and inclusive societal debate, its use can be governed in a way that is consistent with the public interest. In this short essay I will attempt to explain this position.

THE MOST UNUSUAL CASE

Part of the objection to GEHR is that for all the possible outcomes that GEHR may be expected to deliver, there are existing reproductive technologies for securing these outcomes. If this is the case, and these established procedures do not entail the same risks or uncertainties that GEHR does, then introducing GEHR could not be a proportionate means to achieve the desired outcome.

What is this outcome? In most discussions of GEHR, this outcome is usually assumed to be the birth of a child with at least two preferred characteristics. The first is implicitly (although often only implicitly) the presence of a direct genetic link to both the prospective parents, which is achieved through the combining of their individual genomes, as happens in unassisted sexual reproduction. The second characteristic is the presence (or absence) of at least one other genetically conditioned feature that the combination of those genomes makes it unlikely (or

likely) that any resulting child will inherit. Such a characteristic might be the absence of a serious disease that has been diagnosed in the prospective parents, like cystic fibrosis. Disease traits of this kind are usually assumed to be good candidates for the second characteristic.

In such cases, however, GEHR is unlikely to be the only intervention available. There are reproductive technologies that involve the donation of sperm or eggs from third-party donors, thereby simply circumventing the genetic endowment from one parent. Since, however, these children would lack the first preferred characteristic (genetic relatedness), other approaches are also widely available in many (though not all) parts of the world. They involve genetic testing to select embryos for transfer (preimplantation genetic testing, or PGT) or to select pregnancies to carry to term (prenatal testing and termination of pregnancy, PNT/ToP).

It is true that these selective approaches often have their own distinctive limitations. While they could, in theory, offer people possible routes to the preferred outcome, the limited combinations of parental genomes and the limited throws of the dice that assisted conception treatment offers may mean that the chances of finding an embryo or pregnancy with the preferred characteristics are vanishingly remote. This is particularly the case if the aim is to find an embryo with two characteristics that assort independently. An example might be absence of an inherited condition like beta thalassemia combined with the capability of acting as an HLA-compatible tissue donor for an affected family member. In such a case, the parental link that can confer this compatibility may strengthen the case for GEHR. Added to these limited probabilities are the uncertainties and burdens of repeated treatment cycles and the broader impact of the treatments on individuals and families, particularly the risk to the prospective mother's health in repeatedly undergoing egg retrieval. Taking these circumstances into consideration certainly seems to strengthen the case for securing the preferred characteristics by GEHR, although it does not clinch it.

There are, however, some highly unusual cases in which no established alternative is feasible, although they are very rarely seen in clinical practice. They include cases such as those of couples where one parent is homozygous for an autosomal dominant condition (such as homozygous familial hypocholesterolaemia) or both are homozygous for a recessive one (such as sickle cell disease). Though rarely seen, these cases are not unknown and, despite the health difficulties that people in this position may be very likely to face themselves, it is not unreasonable that some of them should wish to become parents. Given, therefore, that in all other cases there are, arguably, alternative treatments available, and given the irreducible uncertainties associated with the use of GEHR, it is often imagined that the best argument for innovation must be found in one of these "most unusual" cases.

A Therapeutic Fallacy

There is, however, a second reason why even the most unusual cases—and a fortiori all other cases—would fail to meet the criterion of “unmet medical need.” It is that, even if there are prospective patients for whom there is no reasonable alternative other than GEHR, their claims do not meet the conditions of “medical need.”

Certainly, if GEHR were the “last best hope” of averting an imminent harm, compassion demands that it should at least be considered. Such an approach was relied upon in the case of the first person to be treated using genome edited cells—a baby girl with relapsed acute lymphoblastic leukemia, successfully treated with modified CAR-T cells at the Great Ormond Street Hospital in London in 2015 (Qasim et al. 2015). That, however, is plainly not the case with GEHR. What is at stake, first and foremost, is assisting a given couple to have a child. While the chosen approach involves some complex medical procedures, it would be a fallacy to assume that simply because GEHR involves a medical procedure, it necessarily has a therapeutic purpose.

The logical priority of procreation in this situation is why the purpose of GEHR was stated, above, as “securing preferred characteristics” rather than “avoiding unwanted characteristics.” Children do not just “come about”; prospective parents have to bring them about by doing something (albeit that different parents may, at different times, set to this task with different levels of forethought). In the case of GEHR, the process is, *ex hypothesi*, a deliberate one. In a conventional model of medical ethics, in which responsibilities must be assigned to individuals and alternative courses weighed, it is the circumstances of this choice that would appear to frame the evaluation of moral action.

A STRAW MAN?

The claim that there is an unmet medical need that could be addressed by GEHR is important, because this claim is quite often the one that supports arguments for GEHR research (for example, Deutscher Ethikrat 2019; NAS 2017). Thus, although it is a claim that is often seized on and challenged by opponents of GEHR, it seems to be more than merely a straw man (Lander et al. 2019). It is therefore worth examining the claim a little more carefully.

The Claim That the Medical Need Is “Unmet”

The claim that the medical need identified is unmet means that there is no currently available intervention that can feasibly fulfil it, at least in some cases (for example, the “most unusual cases” mentioned above). It is quite clear that the force of this claim is to support continued research in GEHR. (It is, coincidentally, a formulation that is gaining traction in relation to pharmaceutical research and innovation, albeit one without a settled definition; see Blumenrath and Heikkinen

2018.) The presence of an unmet need envisages the conditions for innovation of a radically new and potentially risky technology, since it refocuses the question of proportionality from a comparison with alternative treatments to a more fundamental weighing up of the bare need and the uncertainties involved. Hence the focus on redressing these uncertainties through the assembling of an evidence base built up from similar interventions in animal models (presumably up to and including large primates) and from human embryos that are not transferred to a woman (possibly having first increased knowledge of embryogenesis beyond the current 14-day horizon; Nuffield Council 2017). Such research purports to turn imponderable uncertainties into calculable risks. And, since risk appeared to be a technical matter, it is technical competence (not moral competence) to which we are encouraged to defer.

The significance of this focus should not be underestimated. If it were possible to surmount the difficulty of innovation and demonstrate the risk profile of GEHR, then it would almost inevitably enter the repertoire of alternative treatments for a much wider range of indications, alongside the accepted treatments already in use. But this is not all: as GEHR could, in theory, enable the introduction of novel genetic features that are not available through selective technologies or natural reproduction, it is a potentially transformative technology, changing the horizons of possibility of human agency (Nuffield Council 2016). The “most unusual case” would therefore offer a bridgehead from which to extend the possible range of applications. But only up to a point.

The focus on innovation obscures a more important effect of the “unmet medical need” claim, namely to insinuate “medical need” as the presumptive criterion for any eventual use of GEHR. Curiously, in this regard, those promoting and opposing GEHR appear to be on the same side, albeit for different reasons. Medical need is a criterion that both sides can accept because it appears to offer a bulwark against the insidious expansion of uses of the technology.

The Claim That the Unmet Need Is “Medical”

The fact that the identified need is purported to be “medical” does not, strictly, strengthen the concept of need, although it is suggestive of a need that has authoritative and objective value (for example, in contrast to a subjective desire or whim). Its more obvious function, though, is to imply that the need deserves a distinctive kind of response. Placing the need within a medical context may imply, for example, that it demands the attention of medical specialists, the allocation of medical resources, the delivery of interventions through medical institutions, and the application of medical governance arrangements, according to medical norms. I have already drawn attention to the fallacy of concluding from the fact that medicine is applied, the object is a medical need. This is non sequitur as a result of the undistributed middle: we know that medical procedures treat medical conditions and that GEHR is (arguably) a medical procedure, but we

do not know (because it is not true) that medical procedures treat *only* medical conditions. We cannot therefore infer that any application of GEHR involves the treatment of a medical condition.

The “medical” framing also suggests characteristic standards for valuing interventions (in relation to how they redress or promote disease and health) and of appraising prospective interventions (in terms of relative probabilities of benefit and harms to individuals). Is the prospective parents’ need a need of this kind? Some genetic conditions may be contingently associated with clinical infertility, it is true, although assisted conception strategies characteristically circumvent, rather than treat, underlying infertility. It is acknowledged that the inability to conceive a child (or a child with or without certain features) can be a profound felt need. It might even be so profound as to affect the mental or physical health of people experiencing it in ways that are comparable to (other forms of) disease and disability. To treat it as a medical need, however, would seem to cast the child in the curiously instrumental role of a therapeutic agent, a means rather than an end in itself.

Does the prospective child have a “medical need”? Many genetic variants give rise to phenotypic states that are diagnosed medically. Some of these are treated by medical interventions. When it comes to the heritable single gene disorders that people usually have in mind when speaking of genetic disease (things like sickle cell disease, cystic fibrosis, or beta thalassemia), medical interventions are often for disease management and palliation, although gene therapy, enabled by the new genome editing techniques, is an exciting area of current development for some inherited conditions. But that is not what is in view here. The question is not about *treating* a condition diagnosed adventitiously but about *planning to bring about the creation* of a person with particular characteristics (or who is likely to be affected by such a condition). This makes all the difference in the world because of when and where the parents’ moral responsibility falls. In the first case, the parents’ responsibility is for how they respond to the unanticipated discovery that their child—another living human being—has a deleterious condition. In the second, their responsibility is for choosing the characteristics of a child they plan to bring into existence and putting that plan into execution. This holds as well if the child is conceived in the expectation that they would be treated in future, in utero, for example, or even by way of an intra-fallopian intervention on the preimplantation embryo. It is the epistemic context of the moral action that is relevant.

The Claim That the Unmet Medical Objective Is a “Need”

Finally: what is the object of the need, or what is needed? It cannot be a need for GEHR per se, since this is only the means. To what is it a means, then? To the birth of a child. But not any child: a child with certain characteristics. The use of the term *need* here is clearly idiosyncratic. It expresses a particular kind

of claim, requiring a specific intersubjective context to be recognized. Though the nature of this claim is obscure, it is clearly a matter of great sensitivity and, perhaps for those reasons, seldom interrogated. For the time being, let me at least note that what *need* expresses is something that is widely accepted as being an interest of superlative importance for the individuals involved.

Who needs the child? The prospective parents. The prospective parents' need for a child is, however, relative to other important interests, most obviously the anticipated interests of their future child. So we should consider also what the child might need. (I am using the term *child* here to express the relation with the parents rather than life stage—it is important throughout to consider the future person as having a complete life course, however long that may be.) Future children cannot speak for themselves, nor could one child speak for all, but let me make the reasonable assumption that the child will need, as a minimum, the conditions of a life worth living. No doubt most people would go further: proposing to have a child who would enjoy a life barely worth living seems a poor parenting ambition (Parfit 1984). A “good enough” life, then, or conditions that are adequate in the circumstances, may be more reasonable expectations (O'Neill 1979). This is where GEHR comes in: it is assumed that GEHR can ameliorate these conditions, particularly in cases in which the conditions of the child's existence would not otherwise meet these standards. It could, however, also fail to do so. Troublingly, GEHR could have an adverse iatrogenic effect, making those conditions (by hypothesis) worse. Which of the possible outcomes will transpire is, on the basis of current knowledge, uncertain.

One thing that we can be certain about, however, is that (even if the parents “need” the child to exist) that child does not (*ex ante*) need to exist. In the context of the moral decision, the child is a prolepsis, an artefact of the imagination. We might, therefore, conclude as follows: if the child does not exist, then it can, a fortiori, have no further needs; if, on the other hand, the child does exist, then it will “need” the sufficient conditions of a “good enough” life; since there is some ineliminable uncertainty about whether the child will have these conditions as a result of GEHR, it will always be necessary to weigh this possibility against the parents' “need.”

This suggests, I believe, why the clinical trial model—by which a lot of the literature on prospective translational pathways for GEHR is implicitly informed—is inappropriate for introducing a radically innovative reproductive technology like GEHR. The intervention cannot be withdrawn or titrated. Most importantly, the trial model places too much weight on the consent and interests of patients, and it does not handle the interests of the future person well, independently of the prospective parents' interests in their existence. An institutional review board (known as a research ethics committee in the UK), competent to secure and protect individual interests, seems an inadequate measure to account for the interests of others who may be indirectly affected, let alone arbitrate the potential disrupt-

tion of societal norms. The prospective parents' consent (specifically that of the prospective mother) is primarily to a treatment that aims to give her a child. Even if the prospective child could somehow be said to have medical needs, the child's needs are conditional upon the fulfilment of their parents' (arguably) nonmedical needs: the child's need cannot make the treatment necessary for the strong and sufficient reason that the child's existence is not necessary.

Though I would argue that the innovation problem is therefore primarily a problem of the relation of interests rather than one of safety evaluation, I would nevertheless resist the suggestion that the anticipated consent of the future child is a relevant consideration. Such arguments do occur in the discourse, but the idea of a future child consenting to the circumstances of its own conception is plainly a nonsense, and it is nonsense on stilts to suggest that simply because such nonexistent people cannot consent to it, GEHR should therefore be prohibited.

A SKELETON

The claim that GEHR addresses an unmet medical need supports an argument for innovation; the counterclaim that GEHR does not address an unmet medical need is arguably a successful counter to that argument. But it is not necessarily a successful argument against the innovation. The discussion of "unmet medical need" has led down a narrow defile, but one that both proponents and opponents of GEHR seemingly want to pursue. In the remainder of this essay I will sketch out elements of a different approach and explore some of its implications. These will illuminate why the assumptions underlying the "unmet medical need" claim may have been so hard to relinquish. Such an approach may, nevertheless, offer reassurance so long as it is in step with broader societal values.

Revaluing Reproduction

It was asserted above that the aims of GEHR are distinctively reproductive rather than therapeutic. Things are, in practice, inevitably somewhat murkier. Infertility is often a consequence of individual biology (although in the case of GEHR the prospective parents may not be technically infertile). However, little really hangs on the question of infertility. Many would maintain that the anguish experienced by people who are unable to conceive for whatever reason (or to conceive a child who will not perish in infancy, or who will not be affected with a lifelong impairment) is comparable to the suffering associated with (other forms of) illness or disability. The question is not whether this is a "medical" ground, but whether it offers good grounds for using GEHR.

In most societies, a very high value is placed on the protection of the procreative liberties of people of reproductive age, which should not be interfered with for any but the weightiest reasons. Nevertheless, the value, form, and scope of these liberties vary from society to society and from time to time. This suggests

that they are socially constructed to a significant degree, according to contingent moral, epistemological, and technological conditions. In particular, anthropological studies reveal the historical and cultural relativity of the value placed on the genetic link and other relations of kinship, and the acceptability of different kinds of intervention (Franklin 1997). For present purposes I observe only that if there is sufficient reason to think that the practices of procreation and the value placed on them are socio-technically conditioned, then these form an important part of the context for GEHR. We need to ask: how are the various procreative possibilities, including the prospect of GEHR, understood in *this* society, at the present time? Furthermore, how might realizing these possibilities reflexively affect these understandings?

I said above that, for most potential “medical” uses of GEHR, there are appear to be existing alternative technologies, but these substitute treatments are really only “alternatives” in some respects. Certainly, these technologies provide a path to parenthood. By some of these paths the child will be a direct genetic descendant of both parents but, by others, that child will be genetically related to only one of them, or to neither if dual gamete or embryo donation or adoption is chosen. Moreover, the paths to the superficially similar outcome may themselves be valued very differently: many people may want to draw a significant distinction between, for example, the acceptability of terminating a pregnancy (perhaps several) and allowing embryos to perish that have only existed in a laboratory. Therefore, if the value placed by the parents on the different procedures and outcomes are allowed to figure into the appraisal, the different approaches are no longer simply “alternatives.”

More subtly, it may also be the case that individuals’ preferences are influenced by prevailing social norms. This implies that their desires, or the way they formulate and represent those desires to themselves, may be influenced by values that are placed on them by society. These are, in all meaningful senses, real wants and desires, but their form and intensity are modulated by a feedback or “looping effect” between people’s inner motivations and how they play back to themselves through discourse and social experience (Hacking 1999).

Relationality and Identity

The discussion of interests engaged by GEHR has so far been highly individualized, with the interests of prospective parents set beside the interests of their proleptic offspring. The interests of professionals, service providers, and other members of society lurk in the background. The emphasis on weighing and balancing the interests of different individuals distracts, however, from the extent to which these interests are interrelated and interdependent. We have already acknowledged the extent to which parents’ welfare may be affected by their children, but this is at least as much the case in reverse. The parents who care for, nurture, and educate a child are arguably the most significant factor contributing

to that child's welfare. They provide the context by which their welfare-affecting experiences are both formed and bounded, at least in the early part of their lives.

It is worthy of note that, from the point of view of lived experience, what is important to children are their own potentialities and limitations. Insofar as these are bound up with the conditions of their existence decided (deliberately or unwittingly) by their parents, it is difficult for them to reprove their parents without arguing against their own existence. This does not mean that prospective reproductive choices should be a matter of indifference. But it does suggest that parents and their offspring value their own lives through a self-relation that is structured as narrative, that these structures interweave, and that judgments are contextualized by this complex interweaving. This implies that prospective parents' responsibilities towards their future children with regard to their future welfare at the time of reproduction have a satisficing rather than maximizing character, and should be appraised in relation to their reasonable good faith rather than their consequences (Mills 2019a).

Revaluing Disease?

It is also true that the social environment contributes significantly to the life experience. One must be careful not to overstate this in the case of clinical disease. There is a large literature on the social construction of disability, which can be applied to a number of genetic conditions. Material and social conditions, however, may make little difference when a condition involves high levels of physical pain, mental impairment, and dependency, particularly when it is lethal in infancy. There is, nevertheless, an indeterminate range of conditions, including progressive conditions and those of late onset, where social and material circumstances make a considerable difference to lived experience, both in clinical and psychosocial terms.

Clinically diagnosed genetic conditions are, however, only a subset of conditions that could potentially be affected by GEHR. The experience of conditions in this wider range, which includes things like resistance to endemic disease and to environmental stresses, are likely to be much more relative to circumstances. In some cases, those conditions might profoundly affect life experience, in others hardly at all. The point is not that circumstances are more important than genetic endowments, but that they are (unsurprisingly) interrelated, which means that the question of whether there are good reasons to intervene with GEHR cuts across the question of clinical ontology. "Medical" reasons are not necessarily good reasons; good reasons are not necessarily "medical."

Societal Interest

The discussion so far has only been on a micro-level, that of individuals and their intra-familial relations. As well as the future offspring, the actions of individuals may represent a challenge or a threat to other members of society or to

the norms of society itself. These “externalities” may be insidious and difficult to evaluate, just because they exist on a different scale. Low-impact, high-prevalence effects, such as stigmatization of parents of children with certain “avoidable” conditions, are notoriously difficult to compare with high-impact, low-prevalence effects, such as the “most unusual cases” described above. Such externalities might include increasing inequality in a way that is corrosive to society, for example as a result of certain families obtaining access to advantages denied to others, or the cumulative social effects of normalizing certain interventions on those in positions of vulnerability (Nuffield Council 2018).

Here, it is important to recall that norms are constructed both to support certain reproductive projects and to protect others, especially those in positions of vulnerability, from the consequences of the unbridled exercise of reproductive choices. This certainly supports the societal interest in the forms and bounds of reproduction available to individuals. There is, however, a more abstruse but ultimately important reason for societal interest in reproductive norms, which arises from the potentially disruptive effect of reproductive technologies for the integrity of public values subtending the broader, more or less coherent (if dynamic) system of norms that regulate interpersonal relations and conduct. The disruptive effect of sociotechnical evolutions is potentially to restructure rather than simply supplement implicit normative frameworks. After all, the way societies value reproductive freedoms cannot be wholly distinct from the way they value other kinds of liberties, and norms must negotiate tensions and find consistency with each other while accommodating or repudiating technological change.

CONCLUSION

The line of thought I have sketched out in the second part of this essay may lead to a number of discomfiting implications, at least for those involved in GEHR research. The displacement of GEHR outside a “medical model,” where the criterion of “unmet medical need” holds sway, implicitly challenges the self-image of the researcher as engaged in an inherently noble Baconian project, one that is essentially about bringing relief to those affected by disease and disability. Instead these noble purposes are confused in practice with a wider range of human desires and preferences including, in particular, the imperative for having genetically related offspring. Researchers must confront the ethical questions that can neither be settled nor avoided by simply categorizing their work as legitimate biomedical research, questions that are not technical but moral in nature, and public rather than private. The researcher is necessarily implicated in these questions’ resolution as a matter of good faith, but implicated as a supplicant rather than an arbiter.

A second implication is that the objective of GEHR now appears to be to enable choices about what kind of people may exist in the future. This is a different and difficult discourse. It is perhaps for this reason that researchers have been

among the most willing to justify using GEHR by adopting a medical model rather than pursuing the debate into the territory of population health.

Evolution and Enhancement

Adopting the medical model has pushed the target for GEHR innovation towards the “most unusual case” in a way that makes it seem to have little relevance to most people. The questions about the circumstances under which it is appropriate to use GEHR have thus been treated as if they were a continuation of questions about the use of the selective embryological technologies that preceded it. GEHR, however, potentially breaks from the former limits of these questions, because it can offer genetic relatedness without having to work within the combinatory constraints of the prospective parents’ genetic endowment. On the one hand, we find the question of what is a good reason for using GEHR is freed from the assumption that the reason must be a medical one. On the other, it potentially opens up a wider range of uses and targeted characteristics that would make the efforts and attention that have been given to GEHR more explicable than if they were all for the relief of the “most unusual cases” (Baylis and Robert 2005).

To accept the criteria of medical use conveniently reduces questions of human “enhancement” to border skirmishes between conservatives and progressives around the limits of legitimate medical practice. Liberating GEHR from the medical assumption, however, raises the question of “enhancement” and the horror of function creep—the diversion of the technology to purposes other than those for which it was initially developed. If all uses are arguably “nonmedical,” and “nonmedical” uses cannot be ruled out in principle, some other means of moral discrimination must be found.

The Social Production of Moral Norms

A critical examination of the claims both for and against GEHR addressing an “unmet medical need” reveals their dependency on a number of assumptions, such as those about the reasons for and purpose of GEHR, the relative social value of genetic relatedness, the strength of entitlement to treatment, and the relationship between technical development and moral norms. Such assumptions are both made and refashioned by discursive processes: by the exchange of knowledge, understanding, and meaning as they are relevant to different people’s interests and responsibilities. These are necessarily public processes, because norms belong to a wider and more-or-less integrated system that patterns human interactions beyond reproduction.

These processes need both a medium and a venue, both of which are difficult to realize. It is difficult for public discourse to incorporate new knowledge and new technologies that originate in the private spaces of laboratories and exam

rooms. Assembling a venue for the expression of an interest that can be articulated as a public policy is particularly challenging now, when democratic states are experiencing a decimation of the public sphere through a combination of self-reinforcing social media interactions and identity politics. For some time, the public sphere in many countries has comprised only the most impoverished, transactional engagements. For all its scientific excellence, there are reasons to think that the US might not be the right place to implement GEHR if tensions over reproductive rights become exacerbated in a way that could make it more difficult to regulate in the public interest.

The Need for a Geo-Ethics

There is a further discomfiting implication. While the nation state under the rule of law is the natural horizon of public policy and of the authoritative exercise of governance, any settlement on how GEHR should be used is contingent on the local interplay between social and technical developments and developments in the wider global context. On the one hand, a given society's reproductive norms are continually under challenge from dynamics of internal dissent and subterfuge. On the other, there is the possibility that other societies might arrive at contradictory settlements or more-or-less accommodating ways of life. It is unfortunate that this has turned the initiatives of some researchers into threats to others and, for some, given the practice of scientific research the character of a race or contest.

In recent time, and particularly since November 2018 (when the birth of genome-edited twins was announced in China), a fairly obvious polarization has emerged between those who want to forge ahead, who see the primary obstacles to be overcome as technical, and those who see the most immediate obstacles as moral ones. The first group speak in terms of a pathway along which technology can be trusted to develop by regulated steps, to the point where the question becomes not "Why?" but "Why not?" The second group speak in terms of the need for consensus or, at least, explicit consideration of what differences of approach can be tolerated, before any such steps are taken. It is notable, however, that Jiankui He, who was sentenced in December 2019 for his lead role in producing genome-edited babies in China, arguably followed an "entrepreneurial approach" that was radically different from the "medical" or "consensual" approaches of his orthodox critics (Mills 2019b).

If we are sensitive to the dynamics by which evolutions in technical knowledge and public morality inform each other, it will not be a matter of indifference which of these directions is taken (Baltimore et al. 2018; Lander et al. 2019). The first of these represents not an arrogation of authority to one nation state, but potentially to one cadre of practitioners, what might be called the "Republic of Science." Hence the need for both a public ethics, to align technological and social norms, and what I have called a geo-ethics of GEHR, to define the terms

of tolerable coexistence between polities that may wish to preserve and evolve different values and ways of life. The practices that can help to realize this goal are varieties of discursive exchange that all involve opening up the venues within which decisions about the governance of GEHR are made to attend to broader interests, a process that also recognizes the interdependency of these decisions and of the fields on which those decisions bear. Three such venues are the convocations of the elite scientific research community, international human rights institutions, and the public sphere of national debate and policy formation (Mills 2019c).

Let's Not Get Carried Away

Before we get carried away, however, it is appropriate to recall that there are many uncertainties about what GEHR might achieve, if it achieves anything at all. Even to identify potential targets, there are technology problems (sequencing and managing data), information problems (having sufficient research data to draw on), and utility problems (being able to use the knowledge to make desirable edits without unintended collateral effects owing to pleiotropy) to overcome (Nuffield Council 2018). The most likely cases in which GEHR could be effective, based on present knowledge, are probably those of well-characterized disorders, conditioned by a simple, orthogonal, and highly penetrant underlying genetic factors, such as many of the known single-gene disorders for which the existing “alternative” treatments were developed (Horton and Lucassen 2019). There may be other cases that are technically tractable for genome editing but not by selective interventions, including those that are not associated with inherited disease. What we may ultimately be able to achieve with GEHR, and what the consequences will be, are uncertain at the present time and in the present state of knowledge. The only thing that we can say is that these things will depend substantially on what we do next.

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