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Genetic Immunisation

Tess Johnson, Alberto Giubilini

Suppose you could make sure that your child would be immune from some serious infectious disease, say CoVID-19 or measles. Here are three questions:

1) Would you do it?
2) Do you have a moral obligation to do it?
3) Should you be held accountable for not doing it?

These questions are intentionally vague. Many people would probably answer that it all depends. Maybe immunity is not the only thing that matters. How difficult would it be to achieve immunity? Would it be achieved through 'natural' means? Would the intervention be pre- or post-natal? Would it entail risk? Would it require an act or an omission?

Take vaccination, for example. Although most vaccines are, in an important sense, natural substances (for instance, when they contain viruses that have been weakened or had their disease-causing capacity removed), in another sense they are not, because they are produced in laboratories. People committed to natural lifestyles might reject vaccination on grounds of its 'unnaturalness'. The small risks from vaccines represent, to some people, sufficient reason to oppose them. Some parents would prefer their children were harmed as a result of an infectious disease (which is a consequence of non-vaccination, that is, an omission) than as a result of vaccination (an action). Finally, rather than vaccinate their children, some parents may prefer to rely on 'herd immunity'—that is, the protection from being in a population where enough other people are vaccinated that an infectious disease cannot spread. All these views will affect our answers to the three questions above, just in relation to vaccination.

But it gets still more complicated—what about immunity that isn't caused by vaccination after birth, but some pre-natal intervention? Suppose we discovered that some natural substance contained in apples, if consumed in large enough quantities, altered genes in the foetus in such a way that their future immune system became resistant to certain infectious diseases. Would women have a moral obligation to increase their intake of apples, if this avoided the need to vaccinate their children after birth? If we think that pregnant women have a responsibility to take folic acid (which protects babies against birth defects) during pregnancy, it seems plausible to conclude that they would have the responsibility to eat, say, two apples a day if that conferred immunity for their future children. The fact that the intervention would take place at the prenatal stage, and that it requires an action instead of an omission, hardly seems an important objection in this specific case.

Consider now a third type of intervention: gene editing at the embryonic stage - that is, modifying the DNA of an embryo that codes for aspects of the future child's immune system. These changes are inherited by following generations, because they are made before the embryo's sex cells have developed separately from the rest of the cells in the body. Suppose we could genetically engineer the same kind of alteration to the immune system as apples did in our previous example. Gene editing has already been used for immunity: it has produced cattle that are resistant to mastitis-causing bacteria, by adding genes that code for a protein that kills the bacteria. These advances may lead to gene editing that could in principle prevent some infectious diseases in humans, too. With immunity to certain diseases from birth, the need for vaccines and antibiotics would be reduced in both animals and humans—this would have the additional and positive side-effect of helping to combat

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'antimicrobial resistance', the resistance that evolves in certain infectious disease strains to drugs designed to kill them.

These interventions may sound like science fiction, but they are probably just around the corner. In fact, in 2018, gene editing was first used on babies brought to term, by Chinese scientist He Jiankui. He declared that he had managed to edit the embryos' genes to make them resistant to the HIV virus. The experiment was deemed both unsafe and unethical by the academic community—in part because of uncertainty about the risks involved by this modification—but it shed light on a new possibility: if we use gene editing to confer immunity, maybe we could eliminate infectious diseases that threaten our populations today. If gene editing technology was refined, properly ethically assessed, and made accessible to the public as a way of ensuring one's children's immunity, it might even become as important as, or even preferable to, vaccination. We will refer to such a technique as 'genetic immunisation'.

In this chapter we want to examine the ethics of genetic immunisation with reference to the three questions with which we began. We will compare vaccination and genetic immunisation to see whether these different interventions provide different answers to these three questions. If they do not, then parents who would undertake vaccination for their child, who see a moral obligation to vaccinate their children, and who think that policy should hold parents accountable for not vaccinating their children, would be able to argue that the same should apply to genetic immunisation.

If We Should Vaccinate, Should We Genetically Immunise Our Children?

The disagreement about whether, and how, to vaccinate children is often based on members of the public holding different and sometimes incorrect factual beliefs. The vast majority of people, from anti-vaxxers to those more informed about science and the benefits of vaccines, think that parents have a moral responsibility to protect their children's health. The disagreement is about how to achieve this. Some think that vaccines are ineffective or harmful, or that some infectious diseases are not particularly dangerous. Yet, most people agree that parents have a responsibility to preserve their children's health. If so, then given negligible risks and significant benefits of vaccines, failing to protect one's child against certain infectious diseases through easily-available vaccination is like failing to provide children with adequate nutrition to prevent them from developing certain health conditions. One might go further and say that non-vaccinating parents are morally blameworthy even if the child does not get the infectious disease, because they have put their child at preventable risk of serious illness. Parents fulfil responsibility for their child's health once they make sure the child enjoys either direct (through vaccination) or indirect (through herd immunity) protection.

Parents are often encouraged to fulfil their responsibilities through social pressures or forms of non-coercive government action. For instance, even where vaccination is not mandatory, most governments promote vaccination uptake, if only by providing accurate information or subsidising certain vaccines. The existence of parental responsibilities and the encouragement of their fulfilment via government policy can be explained by appeal to 'paternalism', that is, the principle according to which certain individuals (in this case, children) ought to be protected regardless of whether they consent to it (direct paternalism) or whether those responsible for them consent to it (indirect paternalism). But there is another reason: we want parents to provide for their children's health not only because that is in their children's best interests, but also because we want to protect and promote public health. Arguably[1], vaccinating one's children constitutes a fair contribution to maintaining herd

[1] see, e.g. Giubilini 2019; Giubilini 2020

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immunity. This shared duty to contribute implies a *prima facie* duty to vaccinate our child for the sake of the community, even beyond our individual duty to our child as a parent.

Does the same moral requirement hold for genetic immunisation?

Vaccination and Genetic Immunisation: Similarities and Differences

1. Aims

The aim of vaccination policies is to protect individuals and reduce the spread of certain infectious diseases in society. These contribute to individual and public health but also to productivity and the economy. A pandemic of simple seasonal flu could cost a country like the USA around $45.3 billion in lost gross domestic product (GDP) with low vaccination rate; this number could come down by at least $10 billion with higher vaccination rates[2].
Genetic immunisation could achieve the same result as vaccination and would be aimed at the same target—reducing the spread of disease by improving the ability of our immune cells to respond effectively to infection.

2. Nature of Intervention: Genetic modification and enhancement

Genetic immunisation involves direct genetic modification (which we assume will be safe). Is parental responsibility and responsibility to society any different for direct modification as opposed to a vaccine, or eating apples to cause immunity? Whether the apples work by changing gene expression or the foetus' immune cells doesn't appear to be morally relevant. And if that's right, the directness of genetic modification doesn't seem a *morally relevant difference* when we compare genetic immunisation with vaccination.

What about whether each of the two interventions constitutes an 'enhancement' or a 'preventive measure'? Some people believe that an enhancement is either not permissible at all, or else less permissible than a treatment. Depending on how one understands the concept of 'human enhancement', vaccination could be taken to be either a preventive treatment or an enhancement. Vaccinations are preventive measures in that they do not treat a disease but create a new capacity for preventing certain diseases. In that sense, both vaccination and genetic immunisation count as preventive measures. But vaccination might also be termed an enhancement if we focus on the fact that the capacity does not exist in the natural, pre-vaccination population, unless they have acquired immunity by getting infected. In this sense, genetic immunisation is an enhancement, too. If the catagorization of vaccination as a form of enhancement does not make it morally unacceptable, the same holds true for genetic immunisation.

Worries that genetic immunisation is a form of enhancement might be a proxy for a different kind of concern, namely that genetic immunisation is 'eugenics'. This concern was voiced when He Jiankui announced the birth of the two first gene-edited babies[3]. More generally, the eugenics rhetoric is one of the most common strategies used to oppose human enhancement[4]. The rhetoric suggests analogies between the enhancement practices proposed today and the kind of practices carried out in Nazi Germany and elsewhere in the first part of the 20th Century. Because of this dark history, the

[2] Prager et al. 2017
[3] Huang 2018
[4] e.g. Kass 2008: 301

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term 'eugenics' now carries a negative connotation, although the term itself is not inherently negative, if we look at its literal meaning ('good birth'). Making humans 'better' in certain respects, by exploiting our knowledge of genetics and heritability, is by definition a good thing. The disagreement is on what 'good' and 'better' mean (e.g. whether people with certain disabilities can have a good life) and on which means may permissibly be used to make humans 'better'. Where eugenics involves expressing disvalue toward those without a certain desired characteristic, for instance, ethical problems arise. They arise too if a process is enforced using state power to impose a certain way of life or to deprive citizens of individual liberties regarding reproduction or even life (as was the case in Nazi Germany).

But consider vaccination and genetic immunisation. Expressing disvalue toward certain groups is neither the goal nor a side-effect of inducing disease immunity, whether that be through vaccination or genetic modification. Nobody would say that when a state introduces a measles vaccination policy, it sends a negative message against those with measles. And immunising children against infectious diseases through gene editing would not express any negative attitude against people who are not immune any more than vaccinating children does.

The point about state use of power is more problematic. Certainly, we can see how compulsory genetic immunisation may be justified on the same grounds as vaccination, at least when it's relatively cheap and easily available to prospective parents already intending to use IVF. And it might be argued that this would constitute a coercive, imposing or liberty-threatening practice.

To this concern we have two replies.

Firstly, if our major worry is about state imposition and limitation of individual liberties, then the simple response would be to accept that genetic immunisation, although a good thing in itself and perhaps even a moral obligation (the second question with which we started), should not be made compulsory (the third question)—nor for that matter should vaccination, on the same grounds. Of course, many people would still be willing to genetically immunise their children (first question) without there being a legal obligation, out of a sense of parental responsibility.

Secondly, not every form of state imposition is wrong, even if it does infringe individual liberties. Quarantine, vaccination, rationing allocation of scarce health resources, and taxation are a few examples of what are normally regarded acceptable forms of liberty infringement. The real problem arises when the state uses its power to impose certain types of substantive values or norms on others—for example, values about what counts as a good life or a good human being. This is not consistent with the values of liberal, democratic societies. In such societies, the state should create conditions that enable individuals to develop and pursue their own values and life goals, so long as these are consistent with equal rights and liberties of others.

Would either compulsory vaccination or genetic immunisation impose states' values on its citizens? Even if we thought herd immunity and a decent level of public health are intrinsically good, they are also—and we would say, mainly—preconditions for citizens' abilities to pursue their own goals and values. Freedom from infectious disease is a health-related good that serves the pursuit of other goals. If that is right, then the eugenics objection loses its force.

3. Stage of Intervention

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Perhaps an ethically relevant difference is between pre- and post-natal intervention. We might ask, for instance, whether parental responsibilities are affected by genetic immunisation's status as a pre-natal intervention.

However, assuming genetic immunisation is easily available and not too costly in the future, parents would seem to have as pressing a responsibility to pursue genetic immunisation as women would to eat disease-preventing apples during pregnancy. Equally, so long as the pre-natal intervention is safe and does not impose significant costs to the woman undertaking it, there doesn't seem to be a relevant moral distinction between the apples (pre-natal) and vaccination (post-natal) interventions.

The important costs caveat may, however, limit the scope for implementing genetic immunisation. Genetic immunisation would require prospective parents to use IVF to conceive a child. This involves invasive operations and over-stimulation of the ovaries to produce eggs, costs that for many prospective mothers may be morally significant. If so, then we should limit our investigation of genetic immunisation to cases where prospective parents already choose to undertake IVF.

4. Continuity of Intervention

We should also consider the continuity of the intervention. Genetic immunisation would be a form of *heritable* modification, with changes passed on to future generations. We are assuming that the kind of genetic immunisation we are concerned with would be safe and that the only change would be to an individual's and their descendants' immunity to a certain disease. Suppose there was high uptake of genetic immunisation, so that a few generations down the line significant parts of the global population would be immune from, say, measles—is this future problematic, somehow, compared to the same effect of a vaccination programme that eradicates measles a little later? The ultimate ambition of a vaccination policy is permanent immunity against certain infectious diseases. A safe heritable genetic immunisation producing the same outcome, but for multiple generations, seems at least morally equivalent to vaccination, if not better.

5. Bodily Integrity

Bodily integrity is a principle typically advanced against vaccination, especially compulsory vaccination. The claim is that forcing somebody to have a vaccine violates their bodily integrity - crudely, that is the right not to have one's body interfered with in ways that are considered too invasive.

Even if this charge has some merit, it is not necessarily a decisive principle. One could plausibly argue that the benefits of vaccination outweigh the slight invasion of a jab. In any case, for the purposes of this discussion, the real question is whether vaccination and genetic immunisation pose differing levels of threat to bodily integrity.

In the case of genetic immunisation, the 'body' that is interfered with is an embryo; it's not clear that embryos even have a 'body', or one whose integrity can be meaningfully violated. It may be argued that changes from genetic immunisation are carried through in the child's DNA, violating the child's body in the process. But even if this claim is granted, the genetic changes in the child seem equivalent to the changes incurred through vaccination. The only difference is that the former involves changes to DNA and the latter to cells. Genetic immunisation is no more a violation of bodily integrity than vaccination.

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5. Alternative Measures and Cost

Genetic immunisation and vaccination may differ in cost and availability. At first glance, vaccination seems a more efficient means to cause immunity, given the portability of vaccines and the lack of equipment and expertise required. Genetic immunisation requires IVF and many associated costs, equipment, and qualified personnel. However, vaccines are not always an alternative option to achieve immunity, even in high income countries where they are easily available. Some people have adverse reactions (e.g. allergies) to certain vaccines, some are too young to be vaccinated and so cannot enjoy direct protection for a few months or years, and no vaccine is 100% effective. In that case, being born with immunity may be preferable to having to acquire immunity through vaccines.

What about the costs of each intervention? On a per-intervention basis, genetic immunisation is predictably more costly than vaccination. However, the cost of genetic immunisation will probably come down in future, and since immunity will be passed down to subsequent generations, the cost will be spread among the immune descendants of an edited individual, potentially making it comparable, or lower than, vaccination when considered per immune individual. What's more, such intervention may in the long run reduce the need for antibiotics, thus reducing, too, the impact and costs of antibiotic resistance.

6. Effectiveness

Although immunity from genetic immunisation would be heritable (unlike vaccination), this may not increase the effectiveness of the intervention, compared to vaccination. Disease strains evolve over time, so if diseases change significantly between one generation and the next, genetic immunisation may become obsolete. But this is the same with vaccines. New vaccines frequently need to be developed for fast-evolving disease strains such as flu viruses. Meanwhile, for slow-evolving diseases, we would still see the benefits of multiple generations inheriting immunity. For example, let's consider multi-drug resistant tuberculosis (MDR TB). One of very few viable vaccines still effective against (non-pulmonary) MDR TB is neonatally-administered bacilli Calmette-Guérin. This was first used in 1921 and has remained effective for 100 years. Although, like vaccination, genetic immunisation may not remain effective against fast-adapting diseases, we can assume it would show the same effectiveness at producing immunity per generation as vaccination.

What Do These Similarities and Differences Mean?

If vaccination is a moral obligation and should be compulsory, then our discussion suggests that parents would and should genetically immunise their children. However, any compulsory policy would have to be limited to those already undertaking IVF—otherwise too great a burden would be imposed on prospective mothers. As for the increased costs of genetic immunisation, this would seem to be balanced by its continuity into future generations. One might think that individuals have a moral responsibility to look after their own health, but that the state has no business in forcing them to live up to such moral responsibilities toward themselves or their children, especially when this is costly. But the cost issue is eliminated entirely if we consider the idea of publicly subsidised genetic immunisation, similar to the way we currently implement vaccination programmes. This may mean that parents undertaking IVF can be held accountable for not genetically immunising their future children.

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When it comes to availability, we need to be realistic: it's unlikely that genetic immunisation will be an option for people in some areas of the world. This doesn't make it less morally required for those for whom it is available, but it does mean we need to make sure that vaccine development and distribution is not neglected *in favour of* a complete switch to genetic immunisation. Vaccine development will continue to be important for many years to come, and is a necessary alternative to genetic immunisation for those prospective parents not already intending to undertake IVF.

Is Genetic Immunisation the New Vaccination?

So is genetic immunisation the new vaccination? If parents would and should vaccinate their children, and if they should be held accountable for not doing so, does the same hold for genetic immunisation?

Overall, we think that genetic immunisation is *not* 'the new' vaccination. It must not replace current vaccination. However, with some caveats, it *is* a promising and morally-justifiable new alternative to traditional vaccination. Vaccination must continue to be supported, but for parents who are already undertaking IVF, genetic immunisation may become the new vaccination. If so, it should be accompanied by the same aspects of parental responsibility and accountability—to the benefit of both individual future children, and society at large.

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Recommended additional reading:

Giubilini, Alberto (2019). *The Ethics of Vaccination* (Palgrave MacMillan)