



Reexamining the Ethics of Human Germline Editing in the Wake of Scandal

Karen M. Meagher, PhD; Megan A. Allyse, PhD; Zubin Master, PhD;
and Richard R. Sharp, PhD

Abstract

In November 2018, the announcement that genetically edited human embryos had been used for reproductive purposes caused international uproar; many observers argued that editing the human germline was unethical, particularly given the early stage of the science and the absence of appropriate oversight. We provide an overview of the implications of these events, focusing on the relevant ethical considerations for physicians addressing patient questions and concerns. The editing of the human germline for reproductive purposes should be understood against an historic backdrop of clinical research in assisted reproduction, as well as other exemplars of translational investigation. An important question raised by our growing capacity to genetically alter human embryos is how to understand the implicit social contract between science and society. To ensure that translational research continues to enjoy the historic trust placed in scientists and research organizations, it is critical that scientific and health care institutions proactively engage governments, patient advocacy organizations, and the general public in the formation of policies that guide gene editing.

© 2019 Mayo Foundation for Medical Education and Research ■ Mayo Clin Proc. 2020;95(2):330-338



For editorial
comment, see
page 221

From the Biomedical Ethics Research Program (K.M.M., M.A.A., Z.M., R.R.S.), Center for Individualized Medicine (K.M.M., R.R.S.), Division of Health Care Policy and Research (K.M.M., M.A.A., Z.M., R.R.S.), Department of Obstetrics and Gynecology (M.A.A.), and Center for Regenerative Medicine (Z.M.), Mayo Clinic, Rochester, MN.

In November 2018, just days before the Second International Summit on Human Genome Editing in Hong Kong,¹ a Chinese biophysicist named He Jiankui claimed to have used clustered regularly interspaced short palindromic repeats (CRISPR) to edit human embryos for reproductive purposes; the world reportedly has 2 gene-edited children living in it now, with reports of another on the way.² The twins—referred to as Lulu and Nana—were purportedly implanted via in vitro fertilization (IVF) in early 2018, after incomplete gene editing of the *CCR5* gene (for expansion of gene symbols, use search tool at www.genenames.org). No published data are available, but current information suggests that the edits were intended to make the girls resistant to HIV infection by inducing genetic variation similar to naturally occurring *CCR5* variants known to hinder infection by some predominant strains of HIV.^{3,4} Germline, or heritable, editing of *CCR5* has been possible for more than a decade through more thoroughly tested gene editing technologies⁵ but had

not been pursued clinically. As such, the safety and efficacy of these incomplete, novel edits are unknown.⁶⁻⁹

The announcement of the experiment was greeted with widespread consternation by scientists, ethicists, and the public. As the initial shock waves subside, the biomedical research community is taking stock of the implications. Because the results did not go through the peer review process, precise details about the experiment continue to emerge.¹⁰ The experiment as described involved contravention of genetic researchers' internal consensus that the science of the target gene was not ready. Moreover, the research transgressed globally shared research ethics norms and failed to comply with regulations governing research conduct. Since the announcement, several commentaries have outlined multiple violations of scientific and ethical norms and practices, including inadequate qualifications and training, a lack of experience among the investigators, and a failure to declare conflicts of interest.^{11,12} The

controversy has also generated debate about the obligation of, or mechanisms for, researchers to report when they know that unethical research is being performed.¹³ Given ongoing news coverage, patients may be aware of how a circle of scientific collaborators and colleagues tacitly encouraged, or at least failed to voice public concerns about, the research before it was made public.^{14,15}

The widespread coverage, in both scientific and popular press, of the alleged births has drawn renewed and intense attention to gene-editing and reproductive research. The result is a public whose increasing expectations of advances of genetics are being shaped by a mix of media narratives juxtaposing inspirational advances in curing disease¹⁶ with scientists portrayed as being rogue agents.¹⁷⁻¹⁹ Such impressions are reinforced whenever the few scientists determined to push boundaries too far make headlines, prompting professional societies to respond in the form of press releases and policy statements.²⁰ Against this backdrop, medical professionals should expect that patients may have questions about the current status of human gene editing, its promise and pitfalls, and the ethical considerations that will influence its development and possible adoption.

In this article, we provide an overview of the ethical implications of these recent events in reproductive gene editing in humans. Patients may start a conversation about advances in gene editing for several reasons—out of curiosity, concern, or a

medical need to parse their own family history. When these discussions emerge during a clinical encounter, health care professionals will need to determine when discussions of emerging genetic technologies are a distraction from other more pressing health needs, when genetic testing may be warranted, and when all that is desired by a patient is some medically informed insight about technology.^{21,22} Our aim is to prepare medical professionals to respond to patient and public questions about these matters.

RESEARCH ETHICS AND REPRODUCTIVE MEDICINE

According to media reports, the experiment in China was conducted with considerable secrecy if not outright deception.²³ The implications of these revelations should be understood in light of the history of clinical research in assisted human reproduction. This history establishes clear prerequisites for responsibly investigating new interventions in reproductive medicine (Table). For context, early forays in IVF were seen as irresponsible human experimentation when Edwards, Steptoe, and Purdy announced the birth of Louise Brown in 1978.²⁴ In retrospect, it is clear that the process that led to Brown's birth violated many tenets of what we now consider requisite safeguards in clinical research. The experiments were not done under the auspice of any regulatory or research ethics body. The patients included in the experiment did not consent in ways we now consider meaningful to

TABLE. Case Studies and Prerequisites for Responsible Translation in Reproductive Medicine

| Variable | Case 1: In vitro fertilization | Case 2: 2018 gene-edited twins | Case 3: Uterine transplant |
|---|--------------------------------|--------------------------------|----------------------------|
| Animal research | ✓ | ✗ | ✓ |
| Preclinical embryo research | ✓ | ✗ | ✓ |
| Transparency with the public and scientific community | ✗ | ✗ | ✓ |
| Research oversight | ✗ | ✗ | ✓ |
| Fair patient selection | ✗ | ✗ | ✓ |
| Voluntary and informed consent | ✗ | ✗ | ✓ |
| Trial and long-term clinical safety monitoring | ✗ | ✗ | ✓ |
| Publication and peer review | ✓ | ✗ | ✓ |

ethical research; Lesley Brown was apparently not aware that she was giving birth to the very first baby born as a result of IVF.²⁴

As with many emerging reproductive technologies, there was uncertainty about whether children born as a result of IVF would face long-term health risks. It was not until 21 years later that it became clear that at least some of them would be able to reproduce naturally. Despite this uncertainty, millions of children have been born as a result of IVF procedures since the 1970s. Against a cultural tapestry in which reproduction, and particularly paternal bloodlines, has been prioritized for thousands of years, assisted fertility has been hailed as a medical triumph.²⁵⁻²⁷

Although the development of IVF may not have met the standards of responsible translation we might apply today, the procedure was based on considerable research on embryo development and IVF in animal models. A more recent comparison in responsible translation of reproductive medicine is the use of uterine transplant to alleviate absolute uterine factor infertility: the first live birth from a transplanted human uterus was reported in 2014.²⁸ Although the future health risks encountered by children born from a transplanted uterus may be similarly difficult to predict, the use of uterine transplant and subsequent implantation of an IVF embryo was founded on decades of animal models and transplant medicine.²⁹ The names and identities of the first cohort were kept confidential, but the experiment was done transparently in accordance with the scientific and clinical norms. The preclinical data were published in the scientific literature; the program was overseen by scientific regulators; and a large and diverse clinical team worked together to craft a protocol that was maximally protective of the health and well-being of women, their donors, and their future children. Furthermore, a detailed plan was in place, with the full consent and cooperation of the families involved, for long-term surveillance of the women and their children.³⁰

Based on the information publicly available, none of these prerequisites for responsible research were present in the experiments alleged in China. Although the use of CRISPR in human embryos for the purposes of basic science had some minimal precedence in the scientific literature, neither the procedure nor the mutations had been successful in other models.¹¹ Reports suggest that a lack of transparency marked much of this episode: HIV-negative blood samples were substituted for the blood of the actual fathers in order to evade Chinese restrictions limiting access to IVF; the reproductive endocrinologists were not told that the embryos had been edited; and the ethical approval document appears to have been forged.^{31,32} Additionally, the covert nature of the entire experiment raises questions about the extent to which there was a robust plan to monitor the long-term health of the women and children.

COMMON ETHICAL CONCERNS

In the decades since IVF was introduced, the ability to create embryos in vitro has given rise to a number of reproductive interventions. As genetic technologies improved, it became possible to remove DNA from in vitro embryos and assess them for genetic disease. The incidence of Tay-Sachs disease in the Ashkenazi Jewish community is a frequently cited example of how assisted fertility technologies can rescue families from the devastation of childhood disease; with a combination of community-based carrier screening and assisted fertility to avoid embryos affected with Tay-Sachs, the community dramatically reduced the frequency of the disease.³³ Other communities experiencing serious genetic disease have seen hope in reproductive gene editing, emphasizing the ability to avoid similar outcomes for their children.³⁴

However, these technologies also concern the ethics of procreation, including freedom to create one's future children and obligations to promote their interests.^{35,36} With greater editing capabilities have come fiery debates about what constitutes disease, disability, and a life worth living. While seeking to

eliminate lethal childhood conditions like Tay-Sachs was relatively uncontroversial, genetic conditions with more variable phenotypes and less immediate clinical impact are harder to categorize. In particular, the Down syndrome community has been vocal in raising concerns about how prenatal diagnosis can lead to the elimination of certain kinds of people labeled as deviating from a “healthy” norm.³⁷ Some communities, including those with hereditary deafness or dwarfism, have expressed concern about the categorization of their phenotype—which many regard as an essential element of their identity—as “diseased.”³⁸ At the same time, the use of these technologies to avoid conditions that do not manifest until late in life, or may not manifest at all, has been controversial. Individuals affected by late-onset genetic conditions have the opportunity to live productive, fulfilled lives. Should those lives be precluded on the basis of genetic risk?³⁹

These more foundational debates about the goals of reproductive research make the use of germline editing to create HIV resistance especially problematic. In the present case, HIV is an infectious disease that can be avoided through well-known protocols.⁴⁰ Transmission of the condition from parental serum is routinely avoided in assisted fertility by “washing” the gametes involved prior to fertility treatment. Moreover, using an elaborate and risky gene-editing procedure to offer even a chance of HIV resistance can send a telling message that life as an HIV-positive individual is sufficiently undesirable that it constitutes a life not worth living. Such research creates the very real possibility of exacerbating the stigma experienced by those living with HIV in China.^{40,41} None of the justifications for the use of either IVF or embryo editing appear to be justified by the target of the experiment.

KEY LESSONS FOR PHYSICIANS

There are several lessons to be learned from this case of gene editing research infractions. We outline 4 takeaways for physicians, some of which can facilitate conversations with patients who have questions about gene editing.

1. Carefully Scrutinize Current or Shortly Forthcoming Offers of IVF Gene Editing Services

First, physicians play a crucial role in communicating how genetic research is changing for both researchers and participants over time, including the challenges of establishing global accountability to share regulatory and ethical standards. Importantly, patients are likely to feel alone in navigating this expanding landscape of genetic technologies. Although a fringe industry of reproductive editing for patients is yet unknown, unscrupulous health care professionals or clinics prematurely commercializing the technology may spring up, similar to the situation seen with the offering of unproven stem cell therapies.⁴² Patients may even have read in continuing news coverage that medical tourism was a potential motivation behind the recent scandal.⁴³ Such marketing practices are likely to reflect disparate national and regional regulatory systems. If patients see advertisements for purportedly cutting-edge, innovative genetic reproductive options, physicians should be prepared to address their queries and correct any misinformation. Several patient populations can be vulnerable to such promises. In the CRISPR twins case, serodiscordant couples with the double stigma of infertility and one partner living with HIV were those who participated.

To prevent possible exploitation of vulnerable families, physicians can do the following:

- (a) Work to correct misinformation: continue to emphasize that the experiment was scientifically unfounded and unwarranted, and occurred without proper oversight. Physicians should explain how the science shows promise but needs further safety testing before reproductive gene editing is an option, if ever.
- (b) Explain the current state of gene editing for the patient’s genetic condition (or refer to a genetics specialist). Patients are unlikely to differentiate headlines about reproductive gene editing from advances in therapeutic gene editing.

Gene therapies from blindness to sickle cell anemia are also making headlines, and the state of science is distinct for each.^{44,45} For example, rigorous clinical trials for conditions like Leber congenital amaurosis are well supported by decades of research, and this somatic gene therapy would not pass to the next generation.⁴⁶

- (c) Seek what is motivating the patient's questions. A patient might be interested in genetics for any number of reasons including a direct-to-consumer encounter, a family history of disease, or unhappiness with current treatment. Limited time during a clinical encounter is a known barrier to integrating genetic services.⁴⁷ Identifying underlying concerns is a way to help patients feel heard while simultaneously determining whether genetic risk is the patient's main clinical need.²¹

2. Reinforce the Importance of Scientific Self-Governance and Counter Pressures That Contribute to Misconduct

Physicians will want to be aware of developing research regulations that could affect the pace of clinical translation. The future of regulatory oversight of reproductive gene editing is largely unsettled at the moment. Some commentators have called for stronger regulatory policies including a moratorium—if not an outright ban—on germline gene editing in humans.⁴⁸ Others contend that these efforts would reduce nations' competitive scientific edge and prevent the potential development of treatments and cures for millions of patients.^{49,50} Skeptics believe that tighter policies and enforcement surrounding gene editing will remain insufficient to capture the rare scientists who are driven to “go rogue.”¹⁹ A disconnect between idealized norms and the lived realities of research conduct may mean heavier oversight and restrictions on the autonomy of scientists or be cited to justify a moratorium until sufficient safety and ethical concerns have been addressed.

Previous examples of scientific self-regulation, such as the 1975 Asilomar conference, are often depicted as having helped

researchers address public and regulatory concerns about the potential for recombinant DNA to create new pathogens by collaboratively creating a system of scientific self-regulation.⁵¹ This process might be repeated for gene editing technologies.⁵² For instance, Jasanoff and Hurlbut⁵³ suggest that more than just scientists and regulators need to be involved in the global conversation, proposing a “global observatory” to be more inclusive in who develops an ethical framework for heritable gene editing. Several international efforts are under way to develop such guidance.^{54,55}

In the meantime, however, there is an important question about how we will revisit the relationship between the institutions of science and society more generally. Historically, scientific researchers, and in particular medical researchers, have been granted a large range of latitude and comparatively light regulation on the assumption that their pursuit of knowledge constitutes a social good. The creation of gene-edited twins outside norms of scientific conduct can be considered a violation of this social contract. How can scientists and clinicians work together toward restoring faith that the medical scientific complex is responsible, is regulated, and can be trusted with the health and well-being of current research participants and future generations? By recognizing that scientists themselves have interests, we acknowledge the societal and institutional forces that can jeopardize the scientific ideals of disinterestedness and open sharing of research findings.⁵⁶ A hypercompetitive environment of biomedical research leads to competition for a few resources.⁵⁷ Conflation of scientific achievement and being “the first” can contribute to lack of transparency, including operating under a shroud of secrecy.⁵⁸ As scientists and clinicians, we have mutual duties to acknowledge and counter these forces wherever possible.

3. Acknowledge the Emerging Role of Shared Governance

It is important to note that a wider variety of voices are not always being deliberately excluded from these conversations.

Stakeholders are increasingly interested in ways to include patient and public voices but often lack the prior experience and knowledge to do so effectively. In communicating how times have changed, physicians can draw from the history of medicine and bioethics, in which a paradigm of shared decision making has replaced deference to clinical authority.⁵⁹ Analogously for researchers, past decisions made primarily by groups of scientific and academic elites may not be morally or socially sufficient to develop satisfactory research ethics policy today.⁶⁰

Referencing the ancient Greek god of medicine Asclepius, bioethicist Howard Brody once appealed to this power of healing and its attendant authority, as those inside the profession are positioned as arbiters, “to say what is or is not an appropriate exercise of the craft.”⁶¹ Yet the exclusivity of this power is fading with increasing public skepticism of the primacy of expertise. Including social perspectives in developing a gene editing ethical framework is one way to avoid the insularity of scientific self-governance. Physicians will often serve as crucial links between patients and researchers as more inclusive or democratic visions of scientific policy formation emerge. Questions about who should be at the table remain,⁶² but calls for inclusion of affected communities and public voices are likely to continue.

4. Name the Moral Ambiguities That Are Independent of Recent Scandal

Finally, we should keep in mind that research ethics scandals are especially confusing for the public when they combine blatant research infractions with ongoing moral indeterminacy. It can be difficult for all involved to sort out the multiple sources of controversy. Although preventing “bad actors” in research is currently the focus of attention, gene editing researchers will also need to address underlying concerns about the moral permissibility of heritable editing and how such social conversations should take place.^{62,63} One thing that remains is the need to capture a broad array of perspectives on the ethical issues of heritable gene editing and determine the best course of action to minimize patient

injury and dignitary harms, while permitting the science to continue. Disagreements about the moral permissibility of heritable gene editing are also likely to continue; an examination of public and expert perception studies on gene editing shows no real consensus on the different applications of gene editing.^{64,65}

Although agreement on ethical principles and practices could facilitate policy development, consensus in and of itself is not a requirement for creating more appropriate research ethics policies.⁶⁶ For example, a consensus may not adequately represent minority opinions, especially the views of those with less power. Consensus may also stifle further moral reflection and deliberation on a given topic, considering the issue to have been “dealt with.” Moral reflection and discourse on heritable gene editing should continue even in the presence of a large social consensus or an agreed upon set of norms.

Patients, patient advocates, and the public, among other interested parties, should be included at the broad governance level, but specialist physicians are more likely to encounter requests to link patients to specific gene-editing protocols. Physicians are encountering reproductive gene editing controversy at the advent of its clinical translational potential and in the midst of a turn toward more participatory models of scientific governance and research.^{67,68} Their patients could be approached not only as potential participants but also as test cases for partnership in more engaged approaches to research, presenting physicians with an opportunity to inquire about community engagement practices within any project. Those projects with social science research aims, ethics collaborators, or community engagement elements can supply physicians with some evidence of quality—as one way of assessing genetic researchers’ commitment to not only minimal but the highest research ethics standards. As clinical trials proceed, more local engagement efforts also offer researchers the opportunity to be responsive to the diversity of genetic conditions and the experiences of patients most affected by these conditions and those who

care for them.⁶⁹ As physicians advocate for their patients confronting rare diseases, their own experiences can also help move research forward ethically.^{70,71} When encountering gene editing research projects that likely await us in the future, physicians can advocate for patients, and their practices, by encouraging genetic researchers to pursue project-specific forms of engagement that recognize the relevance of stakeholders' perspectives to smoother translation to clinical practice.

CONCLUSION

As the face of biomedical institutions, health care professionals will play a major role in shaping public understanding of gene editing. Gene editing techniques and other emerging genetic technologies continue to push the envelope of what is medically possible. Careful reflection and inclusive problem solving are needed to ensure that high ethical standards, not scandal, lead the way forward in gene editing research. In the meantime, the lessons learned and outlined here can help physicians and their patients navigate the rapidly changing landscape of genetic medicine together.

Abbreviations and Acronyms: CRISPR = clustered regularly interspaced short palindromic repeats; IVF = in vitro fertilization

Grant Support: Support for this research was provided by the Center for Individualized Medicine and the Center for Regenerative Medicine at Mayo Clinic.

Potential Competing Interests: The authors report no competing interests.

Correspondence: Address to Karen M. Meagher, PhD, Biomedical Ethics Research Program, Mayo Clinic, 200 First St SW, Rochester, MN 55905 (Meagher.Karen@mayo.edu; Twitter: @MayoBioethics).

REFERENCES

- Regalado A. Chinese scientists are creating CRISPR babies. *MIT Technology Review* website. <https://www.technologyreview.com/s/612458/exclusive-chinese-scientists-are-creating-crispr-babies/>. Published November 25, 2018. Accessed August 21, 2019.
- Stubble P. Second woman pregnant with gene-edited baby, say authorities in China. *The Independent* website. <https://www.independent.co.uk/news/science/gene-edited-baby-china-woman-pregnant-investigation-he-jiankui-a8739946.html>. Published January 22, 2019. Accessed August 21, 2019.
- Ryder SP. #CRISPRbabies: notes on a scandal [published correction appears in *CRISPR J*. 2019;2:64. <https://doi.org/10.1089/crispr.2018.29039.spr.comex>]. *CRISPR J*. 2018;1(6):355-357.
- Sampson M, Libert F, Doranz BJ, et al. Resistance to HIV-1 infection in Caucasian individuals bearing mutant alleles of the CCR-5 chemokine receptor gene. *Nature*. 1996;382(6593):722-725.
- Perez EE, Wang J, Miller JC, et al. Establishment of HIV-1 resistance in CD4+ T cells by genome editing using zinc-finger nucleases. *Nat Biotechnol*. 2008;26(7):808-816.
- Peikoff K. In IVF, questions about 'mosaic' embryos. *The New York Times* website. <https://www.nytimes.com/2016/04/19/health/ivf-in-vitro-fertilization-pregnancy-abnormal-embryos-mosaic.html>. Published April 18, 2016. Accessed August 21, 2019.
- Wei X, Neilsen R. CCR5-Δ32 is deleterious in the homozygous state in humans [Retraction Note published in *Nat Med*. 2019;25(11):1796]. *Nat Med*. 2019;25(6):909-910.
- Cahill ME, Conley S, DeWan AT, Montgomery RR. Identification of genetic variants associated with dengue or West Nile virus disease: a systematic review and meta-analysis. *BMC Infect Dis*. 2018;18(1):282.
- Zhang S. A mutation that resists HIV has other harmful consequences. *The Atlantic* website. <https://www.theatlantic.com/science/archive/2019/06/what-we-still-dont-know-about-the-gene-edited-in-the-crispr-babies/590815/>. Published June 3, 2019. Accessed August 21, 2019.
- Regalado A. China's CRISPR babies: Read exclusive excerpts from the unseen original research. *MIT Technology Review* website. <https://www.technologyreview.com/s/614764/chinas-crispr-babies-read-exclusive-excerpts-he-jiankui-paper>. Published December 2, 2019. Accessed December 19, 2019.
- Krimsky S. Ten ways in which He Jiankui violated ethics [letter]. *Nat Biotechnol*. 2019;37(1):19-29.
- Nie J-B, Cheung ATM. He Jiankui's genetic misadventure, Part 3: what are the major ethical issues? *The Hastings Center* website. <https://www.thehastingscenter.org/jiankui-genetic-misadventure-part-3-major-ethical-issues/>. Published January 10, 2019. Accessed August 21, 2019.
- Greely HT. How should science respond to CRISPR'd babies? *Issues Sci Technol*. 2019;35(3):32-37. <https://issues.org/how-should-science-respond-to-crispr-d-babies/>. Accessed August 21, 2019.
- Belluck P. Gene-edited babies: what a Chinese scientist told an American mentor. *The New York Times* website. <https://www.nytimes.com/issue/todayspaper/2019/04/14/todays-new-york-times>. Published April 14, 2019. Accessed December 10, 2019.
- Choi C, Marchione M. Chinese scientist told UMass Nobel laureate about gene-edited babies. *WBUR radio* website. <https://www.wbur.org/commonhealth/2019/01/28/chinese-scientist-told-umass-nobleist-about-gene-edited-babies>. Published January 28, 2019. Accessed December 10, 2019.
- Kolata G. Sickle-cell patients dreamed of a cure: enter gene therapy. *The Philadelphia Tribune* website. http://www.phillytrib.com/nyt/sickle-cell-patients-dreamed-of-a-cure-enter-gene-therapy/article_543dc8c6-68d6-51ae-8c0b-d4373c06f6c8.html. Published January 28, 2019. Accessed August 21, 2019.
- Malik K. Don't dismiss gene editing on account of one rogue case. *The Guardian* website. <https://www.theguardian.com/commentisfree/2018/dec/02/dont-dismiss-gene-editing-on-account-of-one-rogue-case>. Published December 2, 2018. Accessed August 21, 2019.
- Grossman D. Russian scientist wants to use CRISPR to genetically edit infants. *Popular Mechanics* website. <https://www.popularmechanics.com/science/health/a27954572/russian-scientist-crispr-baby-gene-editing/>. Published June 12, 2019. Accessed August 21, 2019.

19. Charo RA. Rogues and regulation of germline editing. *N Engl J Med*. 2019;380(10):976-980.
20. Common statement between the Association for Responsible Research and Innovation in Genome Editing (ARRIGE), the Genome Writers Guild (GWG) and the Japanese Society for Genome Editing (JSGE). Japanese Society for Genome Editing website. http://jsge.jp/wp-content/uploads/2019/06/common_statement_Arrige_GWG_JSGE.pdf. Published June 14, 2019. Accessed August 21, 2019.
21. Ofri D. The fallout of a chance medical finding. *The New York Times* website. <https://well.blogs.nytimes.com/2013/01/17/the-fallout-of-a-chance-medical-finding/>. Published January 17, 2013. Accessed August 21, 2019.
22. Arnold C. Mosaic. The uncertain future of genetic testing. *The Atlantic* website. <https://www.theatlantic.com/science/archive/2017/07/the-uncertain-future-of-genetic-testing/534045/>. Published July 19, 2017. Accessed August 21, 2019.
23. Larson C. Gene-editing Chinese scientist kept much of his work a secret. Medical Xpress website. <https://medicalxpress.com/news/2018-11-gene-editing-chinese-scientist-secret.html>. Published November 27, 2018. Accessed August 21, 2019.
24. Marantz Henig R. *Pandora's Baby: How the First Test Tube Babies Sparked the Reproductive Revolution*. Woodbury, NY: Cold Spring Harbor Laboratory Press; 2006.
25. Dow K. 'Now she's just an ordinary baby': the birth of IVF in the British press. *Sociology*. 2019;53(2):314-329.
26. Dow K. 'The men who made the breakthrough': how the British press represented Patrick Steptoe and Robert Edwards in 1978. *Reprod Biomed Soc Online*. 2017;4:59-67.
27. Wilson D. In vitro fertilization, infertility, and the 'right to a child' in 1970s and 1980s Britain. In: Davis G, Loughran T, eds. *The Palgrave Handbook of Infertility in History: Approaches, Contexts and Perspectives*. London, UK: Palgrave Macmillan; 2017:565-587.
28. Brännström M, Johannesson L, Dahm-Kähler P, et al. First clinical uterus transplantation trial: a six-month report. *Fertil Steril*. 2014;101(5):1228-1236.
29. Favre-Inhofer A, Rafii A, Carbonnel M, Revaux A, Ayoubi JM. Uterine transplantation: review in human research. *J Gynecol Obstet Hum Reprod*. 2018;47(6):213-221.
30. Castellón LAR, Amador MIG, González RED, et al. The history behind successful uterine transplantation in humans. *JBRA Assist Reprod*. 2017;21(2):126-134.
31. Cyranoski D. CRISPR-baby scientist fired by university. *Nature* website. <https://www.nature.com/articles/d41586-019-00246-2>. Published January 22, 2019. Accessed August 21, 2019.
32. Symons X. He Jiankui fired, accused of forging ethics review. BioEdge website. <https://www.bioedge.org/bioethics/he-jiankui-fired-accused-of-forging-ethics-review/12944>. Published January 28, 2019. Accessed August 21, 2019.
33. Edelson PJ. The Tay-Sachs disease screening program in the U. S. as a model for the control of genetic disease: an historical view. *Health Matrix Clevel*. 1997;7(1):125-133.
34. Smith DG. The case for CRISPR babies. *Elemental* website. <https://medium.com/s/story/the-case-for-crispr-babies-4d4e0a6fbfdb>. Published January 23, 2019. Accessed August 21, 2019.
35. Lavazza A. Parental selective reproduction: genome-editing and maternal behavior as a potential concern. *Front Genet*. 2019;10:532.
36. Liao SM. Designing humans: a human rights approach. *Bioethics*. 2019;33(1):98-104.
37. Skotko BG. With new prenatal testing, will babies with Down syndrome slowly disappear? *Arch Dis Child*. 2009;94(11):823-826.
38. Parens E, Asch A. Disability rights critique of prenatal genetic testing: reflections and recommendations. *Ment Retard Dev Disabil Res Rev*. 2003;9(1):40-47.
39. Horn R, Parker M. Opening Pandora's box? ethical issues in prenatal whole genome and exome sequencing. *Prenat Diagn*. 2018;38(1):20-25.
40. Subbaraman N. HIV researchers slam the scientist who made genetically engineered babies. BuzzFeed News website. <https://www.buzzfeednews.com/article/nidhisubbaraman/hiv-crispr-china-twins>. Published November 26, 2018. Accessed August 21, 2019.
41. Zhang C, Li X, Liu Y, et al. Emotional, physical and financial burdens of stigma against people living with HIV/AIDS in China. *AIDS Care*. 2016;28(suppl 1):124-131.
42. Hawke B, Przybylo AR, Paciulli D, Caulfield T, Zarzeczny A, Master Z. How to peddle hope: an analysis of YouTube patient testimonials of unproven stem cell treatments. *Stem Cell Reports*. 2019;12(6):1186-1189.
43. Regalado A. Disgraced CRISPR scientist had plans to start a designer-baby business. 2019, Aug 1. MIT Technology Review website. <https://www.technologyreview.com/s/614051/crispr-baby-maker-explored-starting-a-business-in-designer-baby-tourism/>. Published August 1, 2019. Accessed August 21, 2019.
44. Grossman D. CRISPR testing will challenge inherited blindness. *Popular Mechanics* website. <https://www.popularmechanics.com/science/health/a28539000/crispr-testing-will-challenge-inherited-blindness/>. Published July 29, 2019. Accessed August 21, 2019.
45. Stein R. Sickle cell patient reveals why she is volunteering for landmark gene-editing study. Copyright 2019 National Public Radio. WAMU American University Radio website. <https://wamu.org/story/19/07/29/sickle-cell-patient-reveals-why-she-is-volunteering-for-landmark-gene-editing-study/>. Published July 29, 2019. Accessed August 21, 2019.
46. Kumaran N, Smith AJ, Michaelides M, Ali R, Bainbridge J. Gene therapy for Leber congenital amaurosis. *Expert Rev Ophthalmol*. 2018;13(1):11-15.
47. Mikat-Stevens NA, Larson IA, Tarini BA. Primary-care providers' perceived barriers to integration of genetic services: a systematic review of the literature. *Genet Med*. 2015;17(3):169-176.
48. Lander ES, Baylis F, Zhang F, et al. Adopt a moratorium on heritable genome editing. *Nature*. 2019;567(7747):165-168.
49. Daley GQ, Lovell-Badge R, Steffann J. After the storm—a responsible path for genome editing. *N Engl J Med*. 2019;380(10):897-899.
50. Master Z, Bedford P. CRISPR gene editing should be allowed in Canada, but under what circumstances? *J Obstet Gynaecol Can*. 2018;40(2):224-226.
51. Gregorowius D, Biller-Andorno N, Deplazes-Zemp A. The role of scientific self-regulation for the control of genome editing in the human germline: the lessons from Asilomar and the Napa meetings show how self-regulation and public deliberation can lead to regulation of new biotechnologies. *EMBO Rep*. 2017;18(3):355-358.
52. National Academies of Sciences, Engineering, and Medicine. *Second International Summit on Human Genome Editing: Continuing the Global Discussion; Proceedings of a Workshop—in Brief*. Washington, DC: The National Academies Press; 2019. <https://doi.org/10.17226/25343>.
53. Jasanoff S, Hurlbut JB. A global observatory for gene editing. *Nature*. 2018;555(7697):435-437.
54. National Academies of Sciences, Engineering, and Medicine. New international commission launched on clinical use of heritable human genome editing. National Academies of Sciences, Engineering, and Medicine website. <http://www8.nationalacademies.org/onpinews/newsitem.aspx?RecordID=5222019>. Published May 22, 2019. Accessed August 21, 2019.
55. World Health Organization. WHO expert panel paves way for strong international governance on human genome editing [press release]. World Health Organization website. <https://www.who.int/news-room/detail/19-03-2019-who-expert-panel-paves-way-for-strong-international-governance-on-human-genome-editing>. Published March 19, 2019. Accessed August 21, 2019.

56. Martinson BC, Anderson MS, de Vries R. Scientists behaving badly. *Nature*. 2005;435(7043):737-738.
57. Alberts B, Kirschner MW, Tilghman S, Varmus H. Rescuing US biomedical research from its systemic flaws. *Proc Natl Acad Sci U S A*. 2014;111(16):5773-5777.
58. Getz LJ, Dellaire G, Baylis F. Jia Kui He: a sorry tale of high-stakes science. The Hastings Center website. <https://www.thehastingscenter.org/jiakui-sorry-tale-high-stakes-science/>. Published December 10, 2018. Accessed August 21, 2019.
59. Rothman DJ. *Strangers at the Bedside: A History of How Law and Bioethics Transformed Medical Decision Making*. New York, NY: Basic Books; 1991.
60. Hurlbut JB. Human genome editing: ask whether, not how. *Nature*. 2019;565(7738):135.
61. Brody H. *The Healer's Power*. New Haven, CT: Yale University Press; 1992:176.
62. Matthews KRW, Iltis A. Are we ready to genetically modify a human embryo? or is it too late to ask? *Account Res*. 2019; 26(4):265-270.
63. Knoppers BM, Kleiderman E. "CRISPR babies": what does this mean for science and Canada. *CMAJ*. 2019;191(4):E91-E92.
64. McCaughey T, Budden DM, Sanfilippo PG, et al. A need for better understanding is the major determinant for public perceptions of human gene editing. *Hum Gene Ther*. 2019; 30(1):36-43.
65. van Dijke I, Bosch L, Bredenoord AL, Cornel M, Repping S, Hendriks S. The ethics of clinical applications of germline genome modification: a systematic review of reasons. *Hum Reprod*. 2018;33(9):1777-1796.
66. Trotter G. Bioethics and healthcare reform: a Whig response to weak consensus. *Camb Q Heathc Ethics*. 2002;11(1):37-51.
67. Rose KM, Korzekwa K, Brossard D, Scheufele DA, Heisler L. Engaging the public at a science festival: findings from a panel on human gene editing. *Sci Commun*. 2017;39(2):250-277.
68. Aungst H, Fishman JR, McGowan ML. Participatory genomic research: ethical issues from the bottom up to the top down. *Annu Rev Genomics Hum Genet*. 2017;18:357-367.
69. Juengst EJ. Crowdsourcing the moral limits of human gene editing? *Hastings Cent Rep*. 2017;47(3):15-23.
70. Paneque M, Tuchetti D, Jackson L, Lunt P, Houwink E, Skirton H. A systematic review of interventions to provide genetics education for primary care. *BMC Fam Pract*. 2016; 17:89.
71. Falahee M, Simons G, Raza K, Stack RJ. Healthcare professionals' perceptions of risk in the context of genetic testing for the prediction of chronic disease: a qualitative metasynthesis. *J Risk Res*. 2018;21(2):129-166.