Evolving policy with science

Albert Schweitzer, physician and Nobel laureate, wrote: “The first step in the evolution of ethics is a sense of solidarity with other human beings.” The evolution of U.S. policy governing heritable human germline modification reflects this observation, and a “Human Genome Editing” consensus study committee of the U.S. National Academy of Sciences and National Academy of Medicine (NAM) concluded last month that clinical trials for heritable editing, under strict regulations, may eventually be permissible for parents hoping to prevent serious diseases in their children.

In a 1975 meeting in Asilomar, California, scientists recommended strict safeguards against environmental risks from recombinant DNA research. Their caution was rewarded, and the work has become routine. They also noted in passing (as it was still entirely infeasible) that the human germ line should not be modified. Over time, other reproductive technologies developed, such as prenatal diagnosis and preimplantation genetic diagnosis, each grounded in a desire for genetically related, healthy children. Some feared this might lead to intolerance for disability, but public commitment to accommodation and acceptance of disabilities actually increased. Some feared children would be viewed as commodities, but this did not happen either. Regulators strengthened quality control over cell-based and reproductive therapies, and long-term follow-up showed that risks, while present, were small.

The prospect of eventual germline modification is now more real. In 2016, a NAM consensus study concluded that concerns about the social harms of using healthy, donor mitochondria to circumvent mitochondrial DNA defects were speculative, and that safety risks could be managed with tightly controlled, long-term studies. Even so, the report cautiously recommended restricting clinical trials to male embryos, thereby allowing only nonheritable germline alteration. After extensive public consultation, however, the United Kingdom, in 2016, authorized heritable mitochondrial replacement in female embryos. Yet even then, a distinction was drawn between replacing mitochondrial DNA and editing nuclear DNA.

With CRISPR-Cas9 technology, genome editing is easier than ever before, and routes to germline modification of nuclear DNA are becoming conceivable. In 2015, a meeting modeled loosely after Asilomar counseled prudence, and organizers of an international summit concluded that heritable alteration of nuclear DNA should not proceed without more research on its risks and more opportunities for public engagement and discussion about its implications.

The 2017 Human Genome Editing study committee evaluated the rapidly advancing science and ongoing public debates in various countries. It found that much further research is needed to make germline editing reproducible and safe in humans, but that off-target effects are becoming more manageable, and animal research on edited gametes suggests that editing embryos (with its accompanying problem of mosaicism) might be avoidable. It also found the regulatory systems in the U.S. and some other countries well positioned to manage future clinical trials. With input from patient and disability rights advocates, clinicians, scientists, ethicists, and public engagement specialists, the committee concluded that it is time to move heritable germline modification to prevent serious diseases from the category of “never” to the category of “maybe, but only if...” The committee listed stringent criteria that would need to be met. Preclinical data must be robust. Regulatory agencies will need to exercise tight control over eligibility and ensure that germline editing is used solely when it is the only effective or acceptable option. Regulatory bodies and the public must define the serious conditions that could be grounds for germline editing and ensure that it does not extend to uses beyond prevention of serious disease. Protocol design must incorporate long-term, even multigenerational monitoring, suggesting the need for collaboration with other agencies that specialize in surveillance. With these measures, the ethics and policy may evolve alongside the science.

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