Conclusion

Clinical Implications

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On a sunny spring day, a hopeful couple goes through the paperwork they need to complete for the adoption agency they are working with. As they fill out the forms, they imagine the child that they will soon welcome into their family. They feel some fear but so much hope. What will the child look like? What characteristics did their birth parents have? Will the child look like the couple? Will they have the same skin tone, eye color, hair color and texture? Will others recognize their adopted child as theirs without question? How will their race affect their experience in the world? How may their health be affected by their race? What medical problems may their child face in the future?

Let us imagine some clinical encounters in this child's life. In the first, the newborn baby (like all babies) is screened for cystic fibrosis (CF) and sickle cell disease (SCD). In the second, what if this child has the misfortune to be diagnosed with a serious genetic disease? How might their perceived race or ethnicity affect how they are treated and what treatments are available? Third, imagine there is a new genetic therapy for the disease the child has. What barriers might the child face in accessing this treatment? Will such advances exacerbate inequity, or will they allow for more targeted interventions?

DIFFERENCES IN SCREENING

If this child is born in the present time in the United States, they will be screened for SCD and CF shortly after birth, regardless of their ethnicity. This was not always the case. For SCD, a national recommendation for universal newborn screening was made in 1987, but newborn screening did not become standard for all until 2006.[1] Universal newborn screening for CF was implemented in 2009. Both these diseases

are autosomal recessive single-gene disorders (meaning that one would have to receive a disease-causing variant of the relevant gene from each parent in order to develop the disease) with serious health consequences. There are, however, substantial differences in testing and treatment and in the funding for research on these diseases. This is in part because these diseases have historically been racially coded. SCD is more common in people with African ancestry, and CF is more common in those of northern European and Ashkenazi Jewish ancestry.

In the medical field, race has often been used as a proxy for genetic traits or variants.[2] One particularly clear example of this is the way in which SCD has been identified and treated in the United States. SCD is an autosomal recessive single-gene disorder of the red blood cells that causes them to change their shape under stress. SCD is characterized by recurrent vaso-occlusive crises, which occur when the deformed red blood cells block blood vessels, causing excruciating pain and damaging vital organs, which can eventually reduce life expectancy. This genetic trait is found in people from geographic areas where malarial disease is endemic. Since most African Americans have ancestors who were brought to the United States from parts of Africa where malaria is endemic, it was thought to be a disease of African Americans through most of the twentieth century. When a blood test was developed that could detect sickle hemoglobin in the 1960s,[3] only African Americans were screened for the disease. SCD, however, is also prevalent in people of Mediterranean, Middle Eastern, and Indian descent. Indeed, there is a village in Greece in which 1 in 5 people have the disease.[4] In comparison, the rate for African Americans is 1 in 365.

When SCD screening programs for African Americans were introduced in the 1960s, the test identified people who had the disease, but it also identified those who carried the trait, meaning that they had inherited the disease-causing variant from only one parent. Carriers are far more common than those with the disease; among African Americans, between 7 and 9 people per 100 carry the trait.[5] At the start, African American communities supported these testing programs, believing that they would allow people to make informed decisions about reproduction and health.[6] By the 1970s, however, these tests had become a tool of discrimination.[7] Fourteen states made the tests a condition for accessing public education and for getting married. For many people, a positive carrier test resulted in higher insurance costs, job discrimination, and job loss.[8] In this case, we see how racially targeted disease screening for SCD failed to identify non–African American carriers and resulted in what the legal scholar Dorothy Roberts has rightly described as a disaster for the people who participated in testing.

As we have discussed elsewhere in this volume, race is a *product* of social processes that, in turn, structures modes of understanding that *produce* social and political effects.[9] In the case of SCD, we can see how a genetic trait was weaponized as a tool of control and discrimination. If we compare SCD to other genetic diseases,

the differences in policies become very clear. For example, Tay-Sachs disease is, like SCD, an autosomal recessive single-gene mutation. A screening test for carriers was introduced in 1971,[10] around the same time as the SCD screening test. Genetic screening for Tay-Sachs was well received and popular in Ashkenazi Jewish communities (where 1 in 30 people is a carrier), and carriers experienced none of the punitive measures that marred SCD testing. For CF, screening tests were introduced in 1989. While this was later than many of the discriminatory practices outlined above, it is unlikely that a disease associated with northern Europeans would have resulted in anything like what happened with SCD.

Depending on the state the child is born in, they might first be given a test that measures blood levels of trypsinogen (a precursor to the enzyme trypsin) to screen for CF. If this precursor is elevated, they will be given a genetic test for CF. The child's genetic results will likely be evaluated using the CFTR2 database, which contains 159 variants that are implicated in CF. The database is fairly homogeneous in term of ancestral lineage—95 percent of the people who contributed are of European ancestry, which results in a test that is less likely to detect disease-causing variants that are more prevalent in people with non-European ancestry, such as the girl described in the chapter by Tina Rulli.[11] Moreover, different variants of CF have slightly different clinical indications. This means that symptoms from less common variants may not be recognized as being associated with CF because doctors tend to look for the symptoms of variants that are more common in European populations. A larger possible consequence is that future treatments will be designed to address symptoms more common in those of European ancestry and, thus, may be less effective in alleviating symptoms for patients with different variants.

DIFFERENCES IN TREATMENT

If the couple's child has CF or SCD, what kind of medical care might they expect? Both diseases are associated with complications that affect the quality of life and lead to a shortened lifespan for patients. Children with CF or SCD are frequently admitted to the hospital for more aggressive medical care than they can get at home. Patients with CF are frequently hospitalized for breathing difficulties and recurrent infections. The complications associated with CF include sinusitis, diabetes, pancreatic insufficiency resulting in difficulty with weight gain, growth and vitamin deficiencies, abdominal pain, liver dysfunction, bowel obstruction (distal intestinal obstruction syndrome, or DIOS), infertility, and others. Patients with SCD are hospitalized with painful crises and infections, often starting in infancy. They suffer from chronic pain throughout their lives. They also suffer from damage to many of their organs secondary to the sickling of their red blood cells and blockage of the blood vessels that supply oxygen to all the organs of the body.

Complications of SCD include strokes, recurrent infections, avascular necrosis of bone (death of bone cells), blood clots, kidney disease, vision loss, and others.

People of African or Indigenous American ancestry often face significant inequities in the management of their pain. To illustrate this, a study of children evaluated in the emergency department for abdominal pain found no racial differences in the testing done to evaluate the source of the abdominal pain—a symptom of both CF and SCD—but determined that significantly less pain medicine (particularly opioids) was administered to Black and Hispanic children compared with non-Hispanic white children. This is not just a matter of older physicians being trained at an earlier time, when racism may have been more common in medical practice. A study of misconceptions among medical trainees regarding biological differences between Black and white patients demonstrated that 25 percent of residents believed Black skin is thicker than white skin. Those who held these false beliefs were more likely to show bias in how much pain they perceived white people with the same condition experienced compared to Black people and thus were more likely to undertreat pain in Black patients.[12]

DIFFERENCES IN RESEARCH SUPPORT

Two early drug therapies—Pulmozyne, which thins mucus in the lungs, and TOBI, an aerosolized antibiotic specifically for CF—were the result of intentional directed research funded by the Cystic Fibrosis Foundation.[13] In 2019, the Food and Drug Administration approved gene modulation (cystic fibrosis transmembrane conductance regulator, or CFTR) therapy for CF for patients older than 12 years of age.[14] This was later expanded to include children over 2 years of age. The use of these therapies for this population of patients has been found to improve their lung function and decrease their need for hospitalizations. Treatment for CF has improved through targeted therapies, but these treatments are not effective in all patients, and there is still no cure, only some alleviation of symptoms.

While CF has benefited from sustained, directed, well-funded research, there are disparities in research funding when it comes to SCD. SCD is three times as common as CF, but the two diseases have received the same amount in federal funding. When private funding is factored in, the disparity increases exponentially. For example, in the period from 2013 to 2016, CF research received 971 times more funding than SCD.[15] This discrepancy has resulted in fewer research articles and fewer drug approvals for SCD. There have also been innovations in treatment for SCD, but these discoveries have been more accidental than intentional.[16] For example, one of the most common medications prescribed to relieve symptoms, hydroxyurea, was initially used in chemotherapy, but starting in the 1980s, physicians began using it for SCD. It took until 1998 for hydroxyurea to be approved by the FDA for adults with SCD. The only curative treatment was discovered when a patient with leukemia was given a hematopoietic stem cell transplant, which also

cured their SCD. While these transplants do cure SCD, it is difficult to find matching donors, and there is a serious risk of adverse effects.[17]

TECHNOLOGICAL PROMISE AND ECONOMIC ACCESS

More recently, however, gene therapies targeting variants that cause CF and SCD have been developed. These biotechnologies have the potential to radically improve outcomes, especially for those with SCD. As of November 2023, the FDA has indicated that it will likely approve a gene therapy for SCD developed using the CRISPR technology, the first approval of a therapy that uses the new genetic medication technique.[18] The treatment works by removing the bone marrow cells and modifying the gene that governs the production of red blood cells. The patient then undergoes chemotherapy to eradicate the remaining cells that still have the genetic mutation for SCD.[19] The cells with the modified genes are then infused back into the patient's body. This treatment does not work by fixing the mutation; rather, it uses a compensatory mechanism to stimulate the production of fetal hemoglobin cells.[20] These new cells are able to carry oxygen through the body more effectively than sickled cells.[21] Although there are currently no similar gene therapies for CF, research is underway to develop them.

If the couple adopting this child has good health insurance and a relatively high income, they will most likely be able to benefit from these innovations. If not, these new interventions may be out of reach. In our largely for-profit medical system, novel and expensive treatments tend to exacerbate existing health inequalities. Gene therapies similar to those that may soon be available for SCD carry a price tag of up to $3.5 million per patient; researchers have speculated that the price for the new SCD therapy will be between $4 million and $6 million.[22] This price will go down as the technology advances, but it is unlikely to become anything close to affordable in the foreseeable future. This will likely be true of future genetic therapies for CF, although racialized health insurance and wealth gaps[23] will affect availability: studies have shown that extremely expensive medical treatments like this one are hard for people to access because of "discriminatory insurance coverage, onerous reimbursement payee issues, and severe copay burdens."[24] For now, even if the cost is somehow mitigated, these therapies will be available only at major medical research facilities, which also makes them geographically difficult to access for most people.

GENES AND ENVIRONMENT

Throughout this conclusion, we have been discussing single-gene mutation diseases, which follow a clear, Mendelian inheritance process. Most diseases do not adhere to such a clear pattern. While there may be genetic components to susceptibility to diseases and the kinds of symptoms and outcomes people experience, there is considerable evidence that environment and health access are more

determinative in the context of health. Take, for example, asthma, a complex disease affecting 8 percent of American children,[25] which seems to have a hereditary component but is also substantially influenced by a child's living environment. For example, as a group, Puerto Ricans have one of the highest rates of asthma at 14.9 percent.[26] Puerto Ricans also have ancestry lineages that are quite distant from one another. Even though there is a range in terms of ancestry-informative genetic markers,[27] researchers have sought evidence of a founder effect, which would mean that Puerto Ricans are descended from a limited number of individuals, one or more of whom had asthma-causing variants.[28] Medical geneticists have suggested that studying communities with these kinds of founder effects might be an effective tool in identifying patients at higher risk for diseases that might not be identifiable with standard population groups.[29] In other words, given that Puerto Ricans have diverse ancestral lineages but are descended from a smaller number of people, researchers expect that using a Puerto Rican dataset to examine disease risk would be far more effective in identifying the variants associated with asthma than using existing datasets that use broader population labels.

Undoubtedly, the availability of more diverse and more fine-scaled genetic databases, combined with standardized electronic health records, could benefit a broad range of people, allowing them to take health precautions or start early treatment of diseases. There is a risk, however, that when diseases are coded as genetic, then researchers and practitioners give less attention to nongenetic factors. Even though asthma seems to have a genetic component, environmental factors—such as living in a household with a smoker, air pollution, and allergens—play an enormous role in the development of disease.[30] In fact, when researchers compared Puerto Ricans living in New York with Puerto Ricans living in Puerto Rico, where fewer people smoke, the air is less polluted, and allergens linked to asthma are less common, they found far lower rates, between 6.4 and 7.7 percent[31] as opposed to 14.9 percent. In such cases, attributing the asthma to genetics can mask the effects of environment and, importantly, the effects of racial disparities in health-care access and access to healthy living conditions.[32]

We began this volume with the process of selecting gametes and embryos and how these decisions are shaped not simply by the hopes and desires of the prospective parents but also by systems, institutions, and practices already in place. Many of the chapters addressed the ways in which people are racialized and the ways racialization is reproduced socially and scientifically. In a racialized society, we are all assigned a racial identity—a process in which, as the chapter by Alice B. Popejoy shows, we may or may not have much agency—and those identities structure our relationships, opportunities, and experiences. These racialized identities also affect how patients are tested and diagnosed, how they are treated by health professionals, and ultimately how funding is allocated for biomedical research. Given this history, we suggest that future medical research ought to adopt fine-grained genetic analysis based on a continuous model of ancestry, rather than one using

continental clusters. More importantly, we also hope that any genetic approach to medical research or practice takes seriously the effects of social inequalities and racial discrimination.

NOTES

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