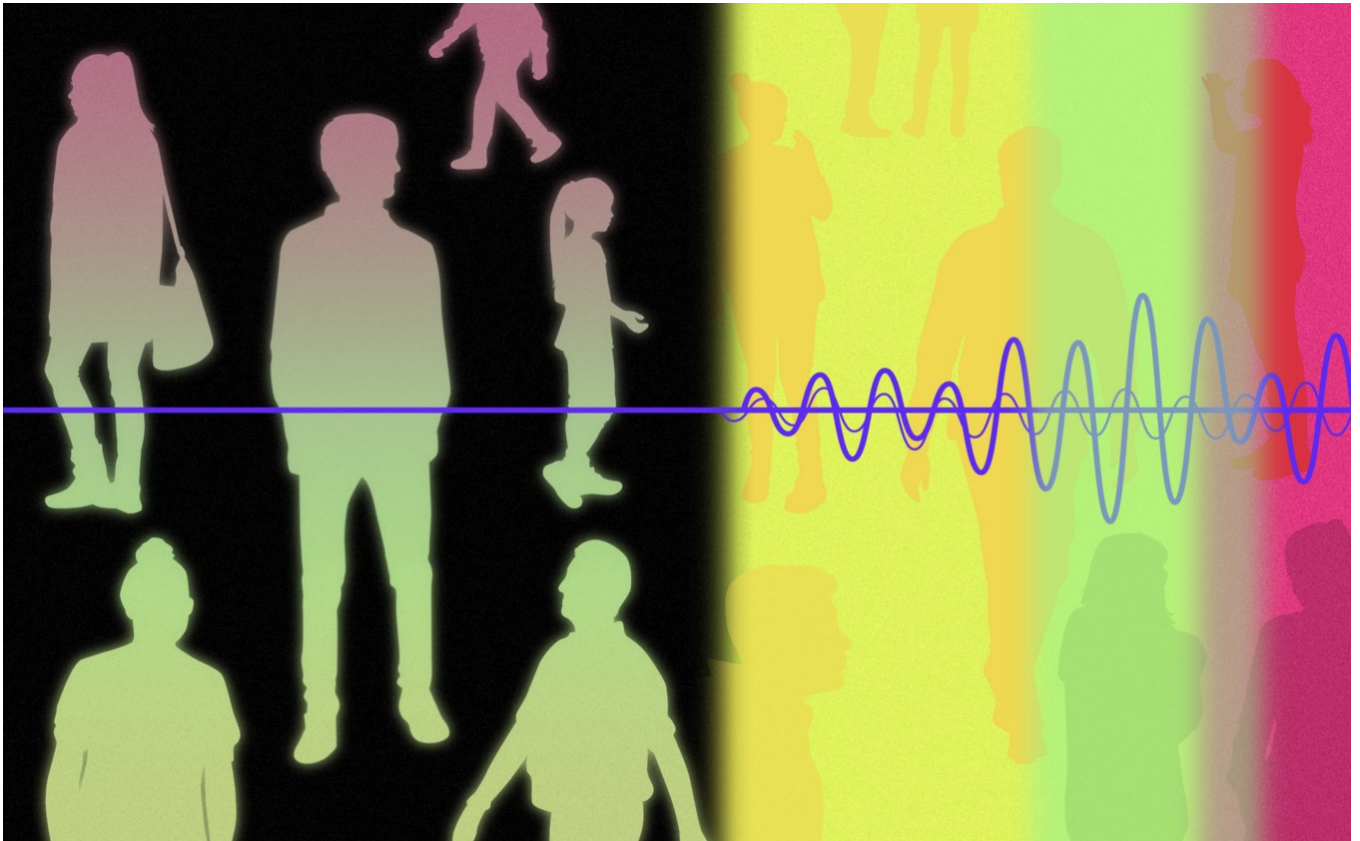


Gene Therapy Could End Deafness. Should It?

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The End of Deafness

Tweaking a person's DNA could provide hearing to those born without it, but not everyone thinks deafness needs to be 'cured'

When Jessica Chaikof was born in February 1995, doctors at an Atlanta hospital placed a pair of headphones on her, piping sounds into her newborn ears while an electrode stuck to her tiny head measured her brain's

response to the noise. Her parents, Melissa and Elliot, held their breath.

Newborn hearing screenings wouldn't become widespread in the United States for a few more years, but Jessica was considered at high risk for deafness. Her older sister, Rachel, was born with profound hearing loss and went completely deaf at 18 months old.

In the hospital, the couple waited while the audiologist tried the test on Jessica again and again. After several attempts, the doctor still couldn't get a response in either ear. Her parents knew what that meant — their second daughter was deaf, too. Experts had told the Chaikofs that Rachel's deafness was brought on by a viral infection, but Jessica's diagnosis meant that the cause was genetic. At three weeks old, Jessica was outfitted with hearing aids, but she never responded to sound.

The Chaikofs wanted to help Jessica as soon as possible since the first few years of life are thought to be critical for language acquisition. When Jessica was 14 months old, the family flew to New York to find out whether she would be a candidate for a cochlear implant, an electronic device that provides a modified sense of sound. The following month, Jessica underwent surgery, at the time becoming the youngest child in the country to get a cochlear implant.

"It's given me the opportunity to communicate with the world, get to know people, be fully mainstream, and identify very much with the hearing world," says Jessica, who's now 25.

A cochlear implant receives and processes sound and speech but doesn't provide natural hearing. Jessica needed years of intensive training to learn how to listen to and interpret spoken language with her cochlear implants, and though they're made to be long lasting, they sometimes break and need to be replaced. Even with the device, Jessica is still deaf.

In the future, parents of deaf children may have alternatives that don't

involve surgery or an electronic device prone to failure. Now, researchers are developing ways to retain hearing by altering a person's genetic code. These genetic treatments could be given to children when they first show signs of hearing loss or before it even begins. Eventually, they could even be administered in the womb so a baby is born with the ability to hear. A single shot could preserve hearing for the rest of a person's life. As a new era of potentially deafness-eradicating treatment begins, the choice that people like Jessica face is: Should we?

"Deafness is a difference. It's a disability. It's not a disease."

If these so-called gene therapies work, they could address the wishes of some families with deafness-causing genes, like the Chaikofs. They may even have the potential to end inherited deafness in humans altogether.

The promise of such a treatment is no doubt immense. In the United States, [two to three](#) out of every 1,000 children born have hearing loss in one or both ears. About half of those cases have a genetic cause. But the ability to eliminate deafness — or any disability — by changing a person's DNA creates unprecedented ethical issues.

Many deaf people don't view deafness as a condition that needs to be "cured," and some see the attempt to do away with deaf people as a modern form of eugenics. They worry that genetic treatments could erode Deaf culture and lead to more discrimination against deaf people.

"Deafness is a difference. It's a disability. It's not a disease," says Jaipreet Viridi, PhD, an assistant professor at the University of Delaware who studies the history of medicine, technology, and disability. Viridi lost her hearing at age four to bacterial meningitis. "Many deaf people consider themselves as part of a community with a strong identity and language."

These genetic treatments are still years from reality, but as science gets closer to reversing hearing loss and deafness, future parents may face the

choice of whether to change their child's DNA to give them the ability to hear. With that choice comes the threat of eradicating a minority group with a rich culture and language.

Hearing is a complex process. Sound enters the ear, moves through the ear canal, and makes the eardrum vibrate. This vibration ripples through three tiny bones in the middle ear, agitating fluid in the snail-shaped inner ear, or cochlea. Thousands of sensory cells called hair cells activate, converting the movement of the fluid into electrical pulses. The auditory nerve, nestled next to the cochlea, transmits this information to the brain to interpret into sound.

For people with hereditary deafness and hearing loss, this process is impeded by damage to the ear cells caused by mutations in certain genes. Wade Chien, MD, an otolaryngology surgeon and scientist at the National Institute of Deafness and Other Communication Disorders, says more than 120 genes have been associated with inherited deafness and hearing loss.

"With each one of these genes, there are multiple mutations in the gene that could lead to hearing loss," Chien says.

Chien is one of several scientists pursuing genetic treatments to prevent hearing loss and deafness in people born with these DNA alterations. He says these treatments, injected into the inner ear, could provide more natural hearing than hearing aids and cochlear implants, which are far from perfect.

Hearing aids, which are typically prescribed to people with mild to moderate hearing loss, only amplify sound. They don't help much if a person can't understand or interpret those sounds to begin with. Cochlear implants, meanwhile, are given to people with more severe hearing loss when hearing aids don't work. They allow sound to bypass the nonfunctioning cochlea and stimulate the auditory nerve directly, but they don't provide sound in the same way that hearing people experience it. For someone with a cochlear

implant, speech can sound robotic or mechanical. Implantation also involves making a small hole in the skull behind the ear to place the device, which is generally safe but can sometimes cause swelling, infection, bleeding, or ringing in the ear.

Within two months of getting an implant on her left side, Jessica began to respond to spoken language, but it took years of auditory-verbal therapy to learn how to listen with it and speak. When she was nine, she got a second implant for her right ear. Hearing with it took several more years of tedious training and practice.

"I hated hearing out of that right implant," Jessica says. "I could barely hear anything at first." She spent hours a week trying to differentiate between sounds. It wasn't until she was a teenager that she could hear equally well from both implants. Now, many children get implants on both sides at an early age, but that wasn't always the case.

In high school, Jessica's first implant stopped working in the middle of midterm exams. She had to push through using just her right implant until she could undergo surgery again.

Genetic treatments could be a device-free alternative that doesn't require surgery. One approach that Chien is working on is called gene therapy, which involves replacing a mutated copy of a deafness-causing gene with one that isn't mutated.

"For patients who are not interested in having something implanted in their head, we think a gene therapy or gene editing approach could be a good option."

Jeffrey Holt, PhD, a Harvard Medical School professor of otolaryngology and neurology at Boston Children's Hospital, is using gene therapy to restore hearing in "Beethoven" mice — named for the composer who famously lost his hearing — which are bred to have a mutation in a gene known as *TMC1*.

The same mutation causes progressive hearing loss in people, culminating in deafness by the mid-twenties. Beethoven mice typically go completely deaf at around six months old.

The *TMC1* gene, which Holt has been studying for about a decade, makes a protein that's crucial for converting sound into electrical signals inside the inner ear. It's one of the top 10 most common genes that can cause hearing loss when mutated, he says, estimating that it affects between 4,000 and 8,000 people in the United States.

In 2015, Holt and his colleagues [restored hearing](#) in mice using an engineered virus to deliver a healthy copy of the *TMC1* gene to ear cells. Electrodes placed on the back of mice's heads measured their brain activity in response to sounds played into their ears. Deaf mice produced no brain activity in response to the sound, but those treated with gene therapy did. In an even simpler test, the researchers placed the mice in a "startle chamber," a small box equipped with speakers. When they played sudden loud noises, mice treated with the gene therapy jumped, but the deaf mice didn't.

Holt thinks gene therapy will work well for people with recessive deafness, like Jessica Chaikof, who became deaf because they inherit two copies of a mutated gene — one from each parent. The idea is that the new, working copy should be able to compensate for the mutated gene. For dominant forms of deafness, where just a single copy of an altered gene is enough to cause deafness, Holt and his team are using a newer method known as CRISPR.

As the researchers described last year in [Nature Medicine](#), they used the gene-editing tool CRISPR to snip out the deafness-causing gene in Beethoven mice. Holt thought that if they could eliminate the mutated copy of the gene and leave the nonmutated one, it would be enough to preserve hearing. The treated mice could hear sounds at about 45 decibels — the level of a normal human conversation — which untreated mice couldn't detect. Six months after the treatment, the gene-edited mice still had near-

normal hearing, while the untreated mice had gone completely deaf.

There's still work to do, though: The editing didn't correct 100% of the hair cells with the *TMC1* mutation. A year after the treatment, some of the unedited cells died off, leading to some decline in hearing. Holt and his collaborators at the Broad Institute of MIT and Harvard are now refining their approach with a more precise form of gene editing called [base editing](#).



Image for post

"For patients who are not interested in having something implanted in their head, we think a gene therapy or gene editing approach could be a good option," Holt says. "We don't think it's ever going to replace the cochlear implant, but we think it could be an alternative for patients who prefer that."

With so many genes associated with deafness, mutations in different genes

could make deafness come on sooner or later. Scientists want to figure out how big of a window of time they have to give a treatment. To do that, the National Institutes of Health is [launching a study](#) to follow families with dominant forms of genetic deafness. Many types of dominant hearing loss start out later in life, whereas recessive forms of deafness affect children very early in life. Chien, who will lead the study, says one of the goals is to learn whether gene editing might be a treatment option for these people.

Human trials of genome editing for [sickle cell disease](#) and a type of [genetic blindness](#) are already underway, but Chien says it will be a few more years before researchers attempt gene editing for deafness in people. The NIH study, he says, will lay the groundwork for those trials.

One day, a genetic treatment could be given before hearing loss even begins — perhaps before a baby is even born. For families like the Chaikofs, who know they carry a deafness-causing genetic alteration, that option could mean having children who are born with their hearing intact.

For Melissa and Elliot, Jessica's cochlear implant surgery couldn't come soon enough. Their older daughter, Rachel, got an implant at two and a half years old, in 1989, as part of a clinical trial, but at the time, giving one to such a young child wasn't yet the norm. Fortunately, by the time Jessica was born, in 1995, the FDA permitted surgeons to use their own discretion to implant even younger children; Jessica received hers at 15 months old. Now, infants as young as nine months can get the device.

The Chaikofs have become proponents of early cochlear implant surgery after observing the difference it made for Jessica, who they say picked up spoken language faster than her older sister. Melissa recalls an audiologist who once teased her about her enthusiasm for early treatment, saying, "If it were up to you, we'd do them in utero!" Now, the possibility of treating deafness in the womb is on the horizon.

"In many forms of human hearing loss, by the time the person is born, there

is already irreparable damage to the inner ear," says John Brigande, PhD, a neuroscientist in the Oregon Hearing Research Center at Oregon Health & Science University, who has hearing loss. "Intervening before birth is going to be a prerequisite if we want to try to establish a hearing outcome."

Doctors sometimes treat certain conditions, like spina bifida, before a baby is born, but no one has ever attempted altering the genes of a developing human fetus in the womb. Brigande, however, is developing a treatment known as antisense therapy that could prevent deafness from happening before birth. The approach doesn't permanently change DNA but instead influences the expression of a gene. In this case, the therapy aims to "silence" a genetic mutation that causes Usher syndrome, a type of genetic hearing loss that's often accompanied by gradual vision loss and balance problems. Brigande [has shown](#) that delivering this therapy to the developing inner ear of fetal mice with Usher syndrome can correct the expression of the mutated gene and recover hearing.

The Food and Drug Administration has approved a handful of antisense drugs, the effects of which typically last several months, but none are given before birth.

Before any of these genetic approaches can be tried in people, scientists must first test them in animals whose ears more closely resemble those of humans. Brigande is working with a team at the Oregon National Primate Research Center to breed monkeys with some of the same deafness-related mutations as people; a team at Harvard and Massachusetts Eye and Ear is pursuing similar efforts in pigs.

Genetic treatments for deafness may also open the door to a future in which we make lasting changes to the human race. One scientist is already forging ahead with a controversial plan to do so. Denis Rebrikov, PhD, a Russian biologist, wants to use CRISPR to [edit DNA in embryos](#) from deaf couples so that their babies will be born with the ability to hear.

Editing embryos is fraught with safety and ethical issues. For one, using CRISPR in embryos is known to cause [unintended DNA changes](#), some of which may be harmful to a resulting baby. Furthermore, any genetic changes made at the embryo stage would be passed on indefinitely to any children, removing the choice from future generations of whether they want to remain deaf.

Experts have declared that gene editing [isn't yet safe enough](#) to be used in this way and, even when it's advanced enough to do so, should be used only to prevent serious diseases from being passed on. Not only is the technology too immature, they say, but using it in this way could lead to a slippery slope of creating genetically modified babies with other "enhancements." Rebrikov says he's [forging ahead](#) nevertheless.

Many deaf people don't view their deafness as a disease or even a disability but as a cultural identity. In the Deaf community, some feel cochlear implants are an affront to that culture. Genetic treatments raise new concerns since they involve changing a person's genetic makeup.

Melissa Chaikof and her husband, a doctor, got cochlear implants for their daughters because they didn't want any opportunities to be closed off to them because of their deafness. More than 90% of deaf children are born to hearing parents, and in a world that caters to the hearing, many parents choose hearing aids or cochlear implants for their deaf children instead of raising them with sign language. Melissa figured her daughters could always learn American Sign Language (ASL) or stop using their implants if they wanted to.

"It wasn't that I wanted my kid to talk. I want my kid to have language."

But when Jessica was 11 and Rachel was 19, a routine eye exam revealed that Rachel was going blind. Both Rachel and Jessica were eventually diagnosed with Usher syndrome, the rare genetic disorder causing deafness and blindness that Brigande is attempting to treat in mice. The

family was devastated. The particular mutation that Rachel and Jessica have is so rare that Melissa and Elliot founded a nonprofit, the [Usher 1F Collaborative](#), to fund research on it. Melissa feels that getting a cochlear implants for her daughters was the right decision since they will eventually lose their peripheral or side vision and their ability to see at night.

Like many deaf children of hearing parents, Jessica and Rachel weren't given a choice about whether they wanted a cochlear implant. In contrast, Rachel Coleman, executive director of the American Society of Deaf Children, let her son Liam decide. In 1998, when she and her husband found out that their 14-month-old was deaf, she threw herself into learning sign language, desperate to help Liam communicate. To her, sign language was the obvious choice.

"It wasn't that I wanted my kid to talk. I want my kid to have language," she says. The way she sees it, speech doesn't come naturally to a child born deaf.

Coleman was amazed at how fast her child picked up signing. By the time Liam was a toddler, they (Liam uses they/them pronouns) knew thousands of signs. While other kids cried and threw tantrums, Liam could sign when they wanted something. Eventually, Liam's vocabulary surpassed that of their hearing peers. Coleman and her husband had heard of cochlear implants but didn't think Liam needed them.

"I had no interest in it," she says. "We were proof that sign language works."

As Liam grew older, Coleman noticed that hearing children and their parents didn't invite them to parties or playdates. She figured it was because they didn't have any experience interacting with deaf people. Tired of Liam being left out, she and her sister created the colorful kids' TV show [Signing Time!](#) to help hearing children learn sign language. Liam was a regular on the show, along with their cousin Alex, who is hearing but learned sign language from infancy to communicate with Liam.

Coleman and her husband had at first planned to let Liam decide to get a cochlear implant at age 18. But after meeting deaf people who got implants as adults and felt they would have been able to use the devices more fully if they were implanted at a younger age, they let Liam choose at age six.

Liam signed yes. With the cochlear implant, they gradually learned to use spoken language, but the Coleman family never stopped using sign language at home.

Now, Liam uses a combination of ASL, spoken English, and their implant to communicate. Some signing deaf people choose not to get hearing aids or cochlear implants at all and lead fulfilling lives without them. Others decide to stop using their implants. In the future, if a parent decides to get their child a genetic treatment, that child will not be able to make these choices for themselves.

Researchers working on genetic treatments for deafness insist that they want to provide families and individuals with more choices, not eradicate deafness. "We want to provide options," Holt says. "It's really going to be up to the patients to decide whether they want to pursue those and embrace these potential therapeutics. It's not anything we would ever want to push on anyone." For deafness that comes on later in life, older children and young adults may also be presented with the choice of whether to change their genes.

But what if all those individual choices lead to fewer and fewer deaf people? What kind of society do we become when we eliminate people with a disability?

The possibility isn't as far off as it sounds. In Iceland, the number of babies born with Down syndrome has [nearly reached zero](#) since prenatal testing became available in the early 2000s. In Denmark, the termination rate of Down syndrome pregnancies is [around 95%](#); in the U.K., it's [about 90%](#). In many parts of Europe, these tests are more widespread because of national

health care, and abortion is also more accessible and less divisive than it is in the United States. As a result, the vast majority of women in these countries choose not to carry a Down syndrome pregnancy to term.

Jackie Leach Scully, PhD, a bioethicist at University of New South Wales in Australia who is deaf, says it's important that individuals have bodily autonomy and freedom of choice. But she points out that decisions made around gene therapy and gene editing will have ripple effects beyond the person getting the treatment. "When you're looking at these sorts of technologies, there are consequences for the Deaf community," Scully says. "There are consequences for society as a whole."

For many people, the idea of ending deafness brings to mind eugenics, a movement that emerged in the late 19th century that sought to improve humanity by breeding out disabilities and other undesirable traits. In Nazi Germany, deaf people were sterilized or sometimes killed. In the United States, deaf people were initially listed as targets of sterilization but were ultimately spared from state eugenics efforts.

"The world needs to embrace deaf people for who they are instead of trying to fix and cure us."

"Such use of genetic technology is a form of genocide and shifts humanity towards the creation of master peoples, which was the goal of Nazi Germany during World War II," says Howard Rosenblum, CEO of the National Association for the Deaf, a Maryland-based nonprofit that advocates for deaf rights. "The world needs to embrace deaf people for who they are instead of trying to fix and cure us."

Virdi, the historian at the University of Delaware, says the attitude that deafness and other disabilities need to be "fixed" took hold in the Victorian period. In her new book, [Hearing Happiness: Deafness Cures in History](#), she explores various cures for deafness touted throughout American history. Before cochlear implants and hearing aids, there were dubious treatments

like electrotherapy and skull hammering. Virdi argues that gene therapy and gene editing are just a new version of the same old idea, only with even more profound implications.

"Improvements in science don't necessarily mean that we need to eliminate human variety, especially human conditions that are not life threatening, like deafness," she says.

Efforts to develop genetic treatments assume that deaf people want to be hearing and that deafness is something that needs to be corrected.

"Changing the bodies and genes of deaf people and disabled people keeps the focus on 'curing' individuals," says Teresa Blankmeyer Burke, PhD, a deaf philosopher and ethicist at Gallaudet University in Washington, D.C., the only liberal arts college for deaf and hard-of-hearing students.

Burke is concerned that society may rush into genetic technologies as a solution to the perceived "harm" of deafness. Hearing people and deaf people have different notions of what this harm is, she says. Many hearing people assume the biggest harm or impairment for deaf people is their lack of hearing. But for many deaf people, the greater harm is discrimination and the lack of accessibility in society.

The Americans With Disabilities Act, a major civil rights law passed in 1990, prohibits employment discrimination against people with disabilities and imposes accessibility requirements. But Burke says deaf people still struggle with basic issues of access.

In the future that Burke is worried about, fewer deaf people in society could lead to further discrimination and marginalization of deaf people, a loss of schools and other services for deaf people, and an erosion of sign language.

Ultimately, the decision that could lead to such a future will be made by worried parents like the Chaikofs, who only want to provide the best opportunities for their children. When the first human trials of these genetic

treatments begin, they will have to consider the risks, which are currently unknown. If parents bank on gene therapy or gene editing working and it fails, a child could carry the stigma of knowing their parents sought to “cure” them.

Even if some of these treatments are successful, Brigande, the researcher at Oregon Health and Science University, doesn’t think hereditary deafness will ever be completely eliminated, because there are so many genetic causes. Genetic treatments might work better for some types than for others, he says.

Scully, the bioethicist, isn’t convinced that gene therapy or gene editing will be a “cure” for deafness, at least not at first. An existing [gene therapy](#) reverses vision loss in people with a type of genetic blindness, but it doesn’t provide perfect vision, and the effects vary from person to person. Nevertheless, Boston startup [Akouos](#), which is developing gene therapies for inherited deafness, plans to begin its first clinical trial in 2022.

While her day vision is good, Jessica has trouble seeing at night or in dim lighting, and she can’t drive. She knows that her vision loss will only get worse over time.

Jessica hopes genetic treatments for both deafness and blindness will be available in the near future. Her parents’ organization, the Usher 1F Collaborative, has partnered with researchers to pursue a gene therapy for vision loss caused by Usher syndrome.

For her, the choice to pursue gene therapy to treat deafness would be easy. She says if a genetic treatment is available when and if she decides to have children, she would want them to get it.

“I would rather not see my child experience what I experienced,” she says. “I’d rather they have an easier path than me.”

Future Human is a new science publication from the OneZero editorial team at Medium. Read more about it [here](#).