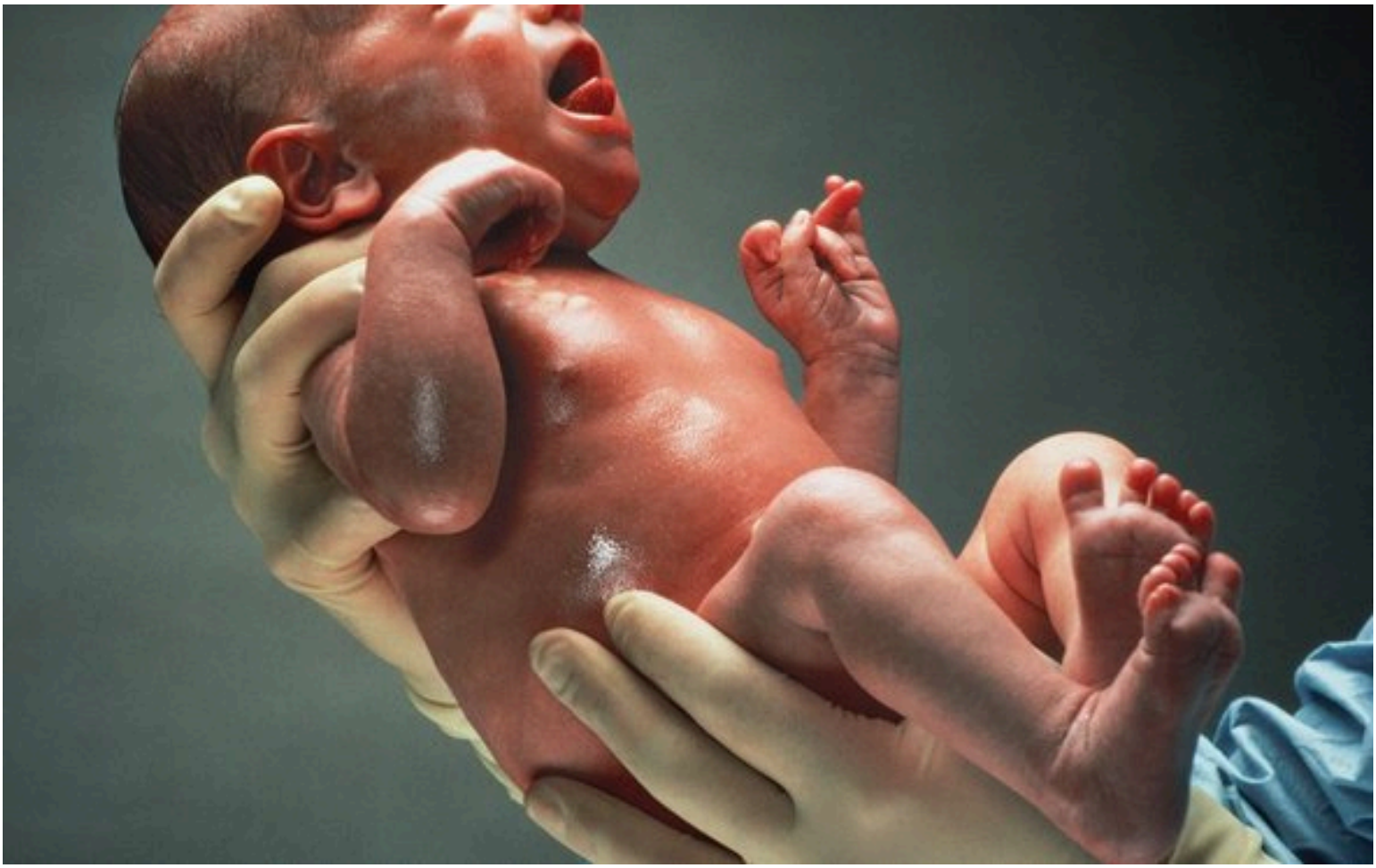
MEDICINE

Full Genome Sequencing for Newborns Raises Questions

Testing every newborn for a raft of known genetic risks is technologically feasible. Some worry the results could do more harm than good

By Bonnie Rochman on March 1, 2017



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Adapted from The Gene Machine: How Genetic Technologies Are Changing the Way We Have Kids—And the Kids We Have*, by Bonnie Rochman, by arrangement with Scientific American/Farrar, Straus and Giroux (US), China Renmin University Press (China).*

In 2010 in Texas, Jennifer Garcia had a baby, a little brother for her four-year-old son. She named him Cameron. Garcia had opted to do prenatal testing for conditions that included Down syndrome and cystic fibrosis with both boys. The tests came back fine. Once her sons were born, she did not think twice about having their heels pricked in the hospital and the resulting droplets of blood scanned for about 30 diseases that make up the

standard newborn-screening test administered to babies born in hospitals throughout the Lone Star State.

Months passed, and Cameron grew, lifted his head, smiled at his parents. He looked healthy and strong, hovering in the 90th percentile for height and weight for babies his age. He laughed at the family dog. He learned to logroll across a room to reach a toy. Then, at seven months old, he got pneumonia. In the hospital, he suffered seizures and had to be intubated. CT scans and MRIs followed, then EEGs, spinal taps and blood transfusions.

No one knew what was wrong. First, doctors thought Cameron had meningitis, then pertussis, then tuberculosis, so they plied him, just in case, with antiseizure medications, antibacterials, antivirals and antifungals. Specialists came and went, teams from critical care, pediatrics, neurology, epileptology, toxicology, immunology, infectious disease,

respiratory therapy. Ten days after he was admitted to a major medical center in Houston, an answer to what was ailing Cameron finally emerged: an immunologist suspected he had severe combined immunodeficiency, a genetic disorder otherwise known as bubble boy disease. Children with severe combined immunodeficiency, or SCID, do not have a functioning immune system, which was why Cameron was not getting better.

The diagnosis perplexed Garcia and her husband, John. They had no family history of SCID. In fact, they had never even heard of it. In any case, wasn't Cameron's newborn-screening test supposed to pick it up? Garcia started researching, and what she found left her in disbelief. Severe combined immunodeficiency is detectable via newborn screening, using the same dried blood spots that the Texas Department of State Health Services analyzes for the other diseases for which it scans. But Texas, along with most states at the time, did not screen for SCID. When SCID is identified early, before a baby falls seriously ill, a bone marrow transplant usually can cure the otherwise fatal condition, because it serves to replace the compromised immune system with a healthy version. More than 90 percent of babies who receive transplants in the first three and a half months of life recover. Cameron was already eight months old at his diagnosis, desperately ill and fighting for his life.

Understandably, Cameron's mother emphasizes the downsides of not screening for a disease if it is technically feasible. Cameron was born just one month after SCID had been added to the national list of recommended core newborn-screening conditions. Yet more than two years would pass before Texas would begin screening every baby for SCID. That was far too late for Cameron, who died on March 30, 2011. He was nine months old.

Since the night she left the hospital without Cameron in her arms, Garcia has become an activist who was ultimately instrumental in persuading Texas to include SCID among the diseases for which it screens. Knowing that all babies born in Texas hospitals are now

tested for SCID makes Garcia's loss marginally bearable. “I wanted his little life to have meant something not just to our family.... I wanted people to know this little baby changed things and opened eyes for a lot of people...,” Garcia said in a video about the importance of screening for SCID. “If we would have known Cameron had SCID, if we could have found that out earlier, before any infections, absolutely, 100 percent, Cameron would be here today.”

But what if we did not have to go through the time-consuming process of adding new diseases, one by one, to the list of disorders that newborn screening can detect? What if one test could look for many of the diseases that newborn screening identifies, plus lots more?

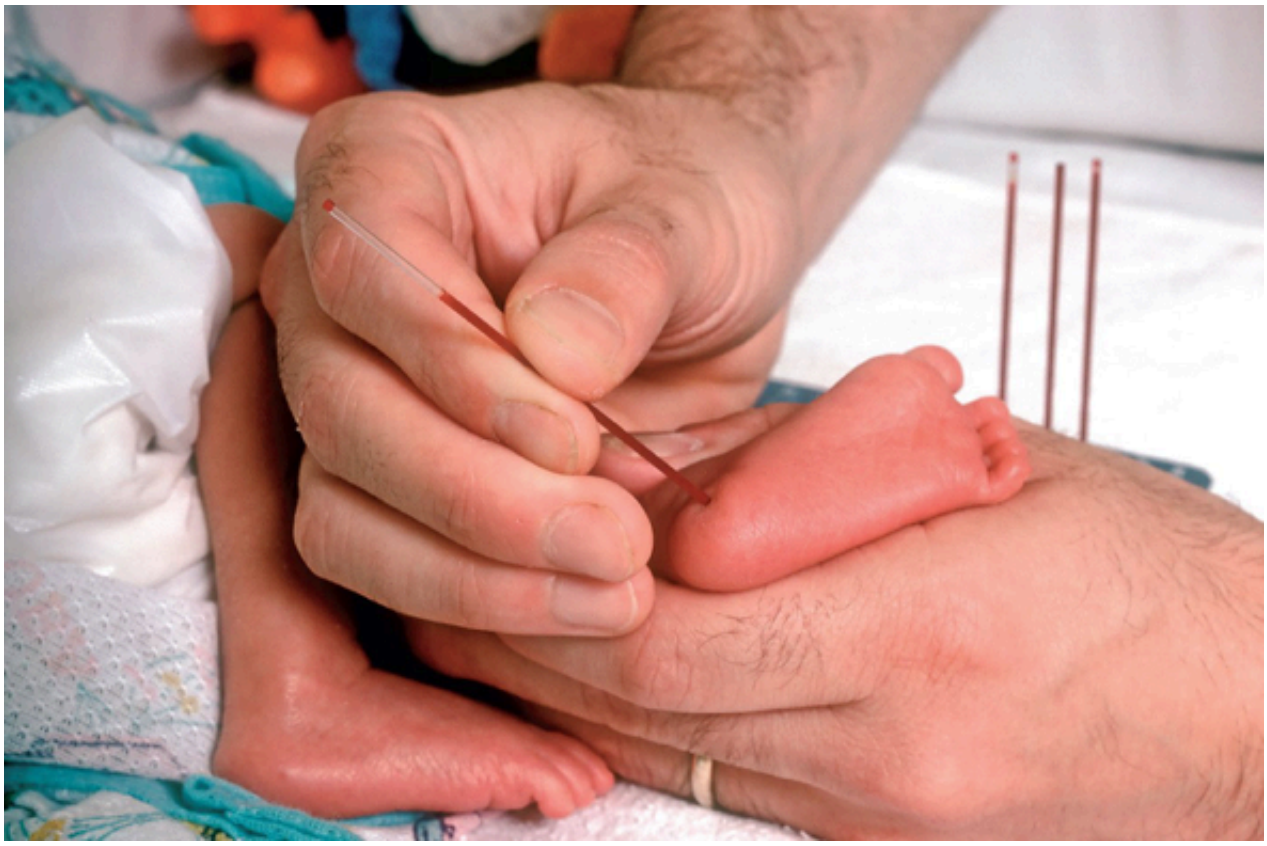
The question is not hypothetical. In highly anticipated research that stands to overhaul what we know about health from the first moments of life, the National Institutes of

Health has charged four university medical centers with studying the medical, behavioral, economic and ethical implications of using genome sequencing to map out the entirety of babies' genetic code. Would it be wise to sequence every baby's genome?

A THORNY ISSUE

There are obvious benefits. Far more children who are at risk could be identified, allowing earlier treatment for someone whose life, like Cameron Garcia's, hinged on early detection. But inevitably, some parents will have to cope with finding out about health problems that cannot be mitigated and about the genetic missteps called variants of uncertain significance whose impact is unclear: they could indicate a problem, or they could simply be a string of DNA gobbledygook.

Depending on what results are returned to parents, many moms and dads will wind up finding out that the bulk of their child's genome is still incomprehensible. Michelle Huckaby Lewis, a trained pediatrician and lawyer who researches genetics policies at the Johns Hopkins Berman Institute of Bioethics, worries that could cause problems. “The genetics and subspecialty workforces will not be staffed adequately to meet the growing demand,” she wrote in a commentary in *JAMA Pediatrics*. “Moreover, coveted appointments with subspecialists may be filled by children whose conditions may not manifest until later in life making access more difficult for those whose needs are more urgent.”



NEWBORNS are already tested for a range of genetic conditions with a heel stick. The stick could also provide enough blood to screen for many more such disorders. Credit: Dan McCoy *Getty Images*

Regardless, it seems to be the direction in which health care is headed. “We are moving to a world where the technology will get so good and the cost will get so low that it will be very appealing to apply sequencing to not only sick people but well people,” says geneticist Robert C. Green. Green co-leads the BabySeq Project, a newborn-screening study taking place in part at Harvard University–affiliated Brigham and Women's Hospital and Boston Children's Hospital, one of the four federally funded study sites.

BabySeq is examining how parents and doctors can use genomic data to improve children's health care. Green and his co-leader, Alan Beggs, are studying 240 sick and 240 healthy newborns. They are randomly sequencing half of each group to assess whether parents of sick kids respond differently to sequencing results than do parents of healthy

babies. Do parents of sick babies find the additional information helpful while parents of babies deemed healthy find it overwhelming? Does either group prefer the more limited picture provided by conventional newborn screening? What is the best way for doctors to incorporate this wealth of data into caring for the youngest and most vulnerable patients? The intent, Green says, is to answer some questions: “Is this scary or not? Is this useful? Is this likely to confuse the hell out of people or not?”

In a lead-up to the study, Green and his colleagues surveyed parents soon after their child's birth to ask if they would want to sequence their baby's DNA. They found a groundswell of interest in newborn sequencing. Three months later they went into greater detail, explaining to parents exactly what kinds of data that genome sequencing could generate about their children—cancer risk, for example, or predisposition for Parkinson's disease.

The percentage of parents who remained interested hardly budged. “This suggests there is a gigantic appetite out there for this, even in healthy babies,” Green says. “It is going to be hard to resist.”

Still, sequencing a baby and “vomiting the results out to the family,” as Green characterizes it, “feels like it's very dangerous.” The combination of anxious parents and doctors trying to interpret uncertain results seems particularly volatile. “People are a bit more sanguine about finding out stuff about themselves than they are about their kids,” Green notes. “The salient question is harm. Depending on whom you talk to, there are all these theories about harm—about anxiety, distress, misconstruing information. All these questions are heightened when talking about babies because they aren't able to have a choice. This is a first opportunity to look for harm.”

MODELING THE FUTURE

When I visited Boston in the spring of 2015, the project was on the cusp of recruiting its first infant. I thought I would meet with one researcher, maybe two, but was greeted by half a dozen people—neonatologists, geneticists, genetic counselors—in a hospital conference room. It takes a village to raise a child—and to hash out the details of sequencing that child. They explained that BabySeq (which, by late 2016, had enrolled about 100 families) would limit the results it returns to parents to only those gene changes that are linked to diseases that take root in childhood. The infants' parents and their pediatricians would also be enrolled in the study, with the goal of assessing medical outcomes and impact on parent-child bonding, as well as whether the data are useful and how they are incorporated into a child's health care. In other words, does the massive influx of information from genome sequencing translate into better health care for a child? Does the benefit justify the costs, financially and emotionally?

“If you imagine a world where every baby could be sequenced quickly, how would that information be used by their doctors to facilitate their care, to make a diagnosis, to prescribe medication?” Green asks. “We're trying to model that situation at a time when it's not really easy or cheap to sequence and doctors aren't used to dealing with it. We're trying to model the future.”

But not a speculative, far-off future, if Green's predictions are correct. “In five years, I am suggesting that sequencing will be given away as a freebie,” he asserts.

ABOUT THE AUTHOR(S)

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Bonnie Rochman is a journalist covering science, health and parenting. She formerly worked as a columnist for *Time* magazine and has written for the *New York Times Magazine* and the *Wall Street Journal*, among others.

Credit: Nick Higgins