Sequencing a person's DNA is now a routine task. That reality has left doctors looking for ways to put the technology to work.

A decade ago, a top federal scientist said, "Whether you like it or not, a complete sequencing of newborns is not far away." Dr. Francis Collins, who made that statement, has been head of the National Institutes of Health for the intervening decade. But his prophecy hasn't come to pass, for both scientific and practical reasons.

Scientists have found that, so far, a complete genetic readout would be a poor substitute for the traditional blood test that babies get at birth to screen for diseases.

Even when genetic testing provides useful information, it also can raise unsettling questions.

One of the big concerns about running gene scans on newborns is how families will receive and make sense of the results.

Christine Kim, a graduate student who studies international health, volunteered for a study at the University of North Carolina at Chapel Hill to explore that issue.

"I think when it's your first [child], you want to be as prepared as possible, even though there's no way to actually prepare for the experience," she said.

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After her baby girl was born, the infant had the standard blood test to screen for rare genetic disorders. The baby got a cheek swab as well, so researchers could sequence all her genes. (This test is called exome sequencing, which decodes about 2% of a person's

DNA, the part that contains the actual genes but not, for instance, the code that regulates gene expression.)

Both the blood test and the gene scan gave the baby a clean bill of health. But the next question was trickier: Should Kim and her husband learn about genes that could affect their child later in life?

"On the chance they did identify something, would we need to put it in her medical records?" Kim wondered. "What does that mean for future health insurance?"

It's currently illegal to base health insurance coverage on genetic information, but Kim and her husband worry about efforts to weaken those protections. Life insurance and long-term care insurance could also be at risk.

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They thought about the ethics of prying into another person's genes. "Should we have access to that information?" she wondered. On the other hand, learning about their baby's genes would also tell them something about their own. "Maybe that's selfish, but I was very curious about that too," she said.

And that information turned out to be eye-opening. Kim said the couple's baby carries a genetic variant that puts her at elevated risk of a disease as an adult. For privacy reasons, she didn't want to be more specific. And Kim learned if the baby has that variant, then she has it too. That has made her more vigilant about her own health.

"I have given that information to my family, and it was suggested that my sisters and my mom also get tested," she said.

This wasn't the point of the newborn genetic screening, but it's certainly a consequence. And it plays into the conversation over whether to make DNA sequencing of newborns routine.

Dr. Cynthia Powell at UNC helped run the study, whose results were published in June in *The Journal of Pediatrics*. She concluded that parents must get a chance to make an informed choice about how much information to receive — just the basics relating to

their newborn or everything that could be actionable in the coming years. (Parents didn't learn about genetic variants that are difficult to act on, such as those that increase the risk of developing Alzheimer's disease.)

"We found that most people who were allowed that choice, about 70% of individuals, wanted information in all of the categories that we offered," Powell said. That proportion may be high because the research team recruited people who were curious to begin with, but it's clear there is a hunger for this information.

But Powell's study and others show that, despite their high-tech gloss, genetic tests are actually much worse than the standard heel-prick test at picking up metabolic disorders like phenylketonuria. Those conditions are the main reason newborns get a blood test at birth.

The simple and inexpensive blood tests detect the actual biochemical defect that is a sure sign of these metabolic disorders.

In many cases of genetic testing, it's not that straightforward to identify the underlying genetic flaw. A disorder can be caused by any of a number of genetic variants, and those variants can be on different genes. Many have yet to be cataloged.

Scientists discovered an even deeper problem. Just having one of these problematic variants isn't necessarily enough to determine whether a child actually develops a metabolic disease.

It turns out that other variants can sometimes come into play in ways that scientists have yet to understand. "It really opens a new can of worms," said Dr. Jennifer Puck at the University of California, San Francisco.

So DNA tests aren't going to replace the standard testing without a lot more research.

Still, there are reasons to consider the DNA test as a routine add-on.

"There are other conditions that we have no screening test for," Powell said. "Conditions that could predispose a child to cancer or other neurological conditions that are potentially treatable."

Powell and Puck spoke at a meeting in late June organized by the NIH to review the prospect of genetic screening for newborns.

Dr. Robert Green, from Brigham and Women's Hospital in Boston, voiced one view about doing that: "If sequencing reveals health risks at any point in life, and if that's good, then it's better to do it early."

Why wait to find out potentially useful information, he asked his colleagues.

One reason not to go all in for genetic testing at birth is that, unlike the blood tests, these genetic tests can be freighted with worries about privacy and personal preferences, as Kim discovered.

And Puck said it would be a mistake to bring all those thorny issues to newborn screening programs that are now so widely embraced that parents aren't even asked about them.

"The newborn screening programs we have enjoy a huge amount of public trust," she said at the NIH meeting. "And we have to preserve that trust."

Supplemental DNA screening would also be discriminatory, she argued, because it is not covered by government health insurance for the poor.

"We can't now follow up everyone," she said, "and I don't think it's right to have only wealthy people followed up and have the rest of our population left behind."

Scientists at the meeting did agree that there can be good reasons to sequence genes if a child is sick and doctors don't know why. That's the story Patricia Bass of Greensboro, N.C., told me about her son, Aiden.

"For the first eight weeks of his life, he wasn't gaining weight correctly, and we kept going back to the doctor," she said. "And finally my husband and I kept looking in his eyes, and we noticed a white opaqueness. We knew it would probably be cataracts."

That condition required emergency eye surgery. Aiden also had other troubles, including hearing loss and poor muscle tone. At age 2, it seemed he might have a rare disease.

"So we had him seen by a geneticist locally, and they didn't find anything," she said.

The Basses learned of the genetic testing study over in Chapel Hill, and they signed up.

Aiden's test revealed that he has a serious genetic condition called Lowe syndrome, which could have a potentially devastating effect on everything from his kidneys to his intellect.

It's not clear why his previous genetic test missed the diagnosis.

The diagnosis was bad news, but at least they had an answer.

"You grieve a life that you thought was going to be something different than what it is," Bass said. "So that was very hard. Very hard."

As a result of the diagnosis, she has added more specialists to Aiden's list of doctors. But more significantly for the family, the diagnosis has changed her outlook.

"I decided to say it happened *for* us instead of *to* us," she said. "And that one powerful word has really changed my life. Because I think of it as I was blessed and given an opportunity to love such a special soul, who has changed so many people that he's met with such positivity."

Aiden lives his life with so much joy, she said.

"I think I used to worry more," Bass said. "Now I'm just living in the moment every day."

That revelation is a far cry from the aspiration that genetic testing will transform care of children, but it is a step in that direction.

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