VOICES OF THE PANDEMIC

Speaking science to power

A young disease modeling expert has found her voice during the pandemic

By **Kelly Servick**

In May, epidemiologist Caitlin Rivers made a rare outing amid coronavirus stay-at-home orders. She had been called for the first time in her career to testify before Congress—and she was intimidated. "You're looking at the dais and seeing all these eminent people. It's a really powerful experience," she says.

Then, questions about the U.S. response to COVID-19 started to fly, and Rivers was in her element. Five years out of graduate school, she is already well-versed in talking to policymakers about the science of pandemics. She has developed models to predict the spread of Middle East respiratory syndrome and Ebola, briefed the Department of Defense (DOD) on outbreak response, and tracked respiratory disease among Army service members. She's now at the Johns Hopkins Center for Health Security, a think tank that advises U.S. and international leaders on epidemics and disasters.

In formal reports, private conversations with congressional staffers and local officials, and a growing presence on Twitter and in the popular press, Rivers has emerged as a clear-eyed, tactful narrator of the unfolding pandemic. "One of my goals," she says, "is keeping the energy—the intention—around the bigger question, 'Are we headed in the right direction?'"

Rivers got interested in epidemiology as an undergraduate at the University of New Hampshire, inspired in part by Tracy Kidder's book *Mountains Beyond Mountains: The Quest of Dr. Paul Farmer, a Man Who Would Cure the World,* which describes the medical anthropologist's efforts to eradicate disease in developing countries. Rivers admired "the respect that he brought to the populations that he was working with," she says, "and just the vision—he was not about to let anything stop him."

Rivers majored in anthropology, and she brings an "anthropologist's understanding of how what seem to be totally different cultures can communicate with each other—the policy world and the modeling epidemiologists," says Stephen Eubank, an epidemiological modeler at the University of Virginia (UVA) who mentored Rivers during her graduate training in epidemiology and infectious disease at the Virginia Polytechnic Institute and State University (Virginia Tech).

Her Ph.D. coincided with the outbreak of Ebola in West Africa, and in the lab of Virginia Tech epidemiologist Bryan Lewis, she helped prepare weekly updates for experts at DOD. "Caitlin would often be emailing me at like three in the morning: 'I updated this to get this little thing in! You can put this on slide 12!'" Lewis, now also at UVA, recalls.

"We must not become numb. Those numbers represent ... people who were loved."

Caitlin Rivers, Johns Hopkins Center for Health Security

The demands of an epidemic are "well-suited to my personality," Rivers says. "I don't mind working hard, and I like having a purpose."

As she sat before an appropriations subcommittee in the House of Representatives in May, the country had made progress. Stay-at-home orders were starting to bring down new COVID-19 cases. But the nation was on the verge of widespread reopening that would put hard-won gains at risk. "We are in a critical moment of this fight," she told the representatives, warning that a clear national plan for testing, contact tracing, and strengthening health care systems was essential to prevent tens of thousands more deaths.

As early as March, Rivers, former Food and Drug Administration Commissioner Scott Gottlieb, and colleagues at the American Enterprise Institute had laid out criteria for safely reopening businesses, including waiting for a sustained reduction in cases. In her May congressional testimony, she urged the federal government to develop a national plan to eliminate test shortages and anticipate bottlenecks in the supply of reagents and materials.

Things might have gone differently if more people in positions of power had taken Rivers's advice. Four months later, the United States still logs tens of thousands of new cases per day and accounts for about one-fifth of the COVID-19 deaths documented worldwide.

"Things did not unfold as I would have liked them to, certainly," Rivers says of the U.S. reopening. "Politics can get so frustrating because it feels—not necessarily as an adviser, but as a citizen—like, 'Why can't you see it the way that I see it?'" But, she adds, she's sympathetic to the pressures that local decision-makers felt to restore their economies.

Laying blame and stirring controversy isn't productive for someone eager to influence policy, Eubank says, citing National Institute of Allergy and Infectious Diseases Director Anthony Fauci's aversion to publicly discussing his relationship with the Trump administration. Of course, Eubank adds, Fauci has decades of experience threading this needle. But Rivers understands it too, and is holding her own just a few years out of grad school.

"As a junior faculty, we don't have anyone helping. We don't have staff," says Natalie Dean, a biostatistician at the University of Florida who has co-authored editorials with Rivers on how to interpret antibody studies and the need for more detailed, transparent epidemiological data. "I think we're both adjusting to just having so many more people ask things of us."

ILLUSTRATION: KATTY HUERTAS

It's not just politicians who are turning to Rivers for clarity on the pandemic. On Twitter, which she previously used mostly to discuss new results with colleagues, she's made an art of giving a big-picture, 280-character view to her followers, who now number more than 140,000.

"Early in an outbreak, we often find only the most severe cases," she tweeted in February. "It seems like people are quite sick, which is scary. It's something of an illusion."

As some regions turned a corner in April, she predicted "growing agitation about whether staying home was necessary. Make no mistake, it is and was."

"We must not become numb," she urged in July as the United States passed 150,000 deaths. "Those numbers represent people, people who were loved."

Readers gravitate to these level-headed summaries even when the news is bad, says Dean, who describes Rivers as her "pandemic pal." Their friendship was born on Twitter, she says, where they connected over the struggle of caring for young children while working from home. (Rivers has 19-month-old twins and a 6-year-old.)

Rivers admits the demands of the pandemic have been "a lot to manage," but she also sees opportunities, including the chance to revive a proposal that would better prepare the country for the next viral threat. While she was in graduate school, Rivers and colleagues proposed creating a National Infectious Disease Forecasting Center, akin to the National Weather Service, that would put a coordinated team of epidemic modeling experts inside the government.

Currently, academic experts largely volunteer their time. "There is no other capability of national strategic importance that we handle like that," she says. "We don't let the military self-organize. We don't let the national hurricane center be academics in various universities who volunteer."

In 2015, the proposal seemed to have a chance. Rivers, with colleagues including biodefense adviser Dylan George, then at the White House Office of Science and Technology Policy, discussed the idea at a White House meeting on epidemic preparedness. But it never advanced to a formal initiative or a line in the federal budget. "We hit the budget cycle at the wrong time," says George, who is now at the national security investment firm In-Q-Tel.

COVID-19 has put new momentum behind the effort. Rivers says she has been meeting with congressional staff about it, and she is hopeful that the past efforts laid the groundwork even though they didn't pay off in time to help with COVID-19. She wishes the initiative had been launched in 2015, she says, "but the second best time is now." ■

BIOMEDICINE

Narrow path charted for editing genes of human embryos

Panel outlines most justifiable uses if safety is ensured

By **Jon Cohen**

When He Jiankui announced the creation of the first gene-edited babies in 2018, the work was widely seen as dangerous, unethical, and premature. Two years later, an international committee has concluded that the dangers remain too great for anyone to follow in He's footsteps. But its report, released last week, also lays out rare circumstances that might justify "heritable human genome editing" (HHGE) and calls for a global scientific body to help countries assess future proposals.

The committee, organized by the U.K.'s Royal Society and two branches of the U.S. National Academies of Sciences, Engineering, and Medicine, reviewed the latest on CRISPR and other ways to modify DNA and consulted scientists, physicians, ethicists, and patient groups. Its report, which Harvard University genome-editing researcher David Liu calls "thoughtful, balanced, and well-bounded," emphasizes that making heritable genome changes remains too risky for now. "There are a lot of gaps in our knowledge and further research is needed," says Kay Davies, a geneticist at the University of Oxford who co-chaired the commission.

> **"It is a ban on editing the genome of the embryo in principle."**
> **Denis Rebrikov**, Pirogov Medical University

But Liu is uneasy with the report's analysis of when and how embryo editing might be implemented. "I continue to struggle to imagine plausible situations in which clinical germline editing provides a path forward to address an unmet medical need."

The report largely steers clear of the complex social and ethical implications of creating gene-edited babies. But it does call for an international panel of scientists to assess proposed uses of HHGE, provide regular updates about related technologies, and review clinical outcomes if an edited embryo implanted into a mother is born.

It also categorizes uses of HHGE into a hierarchy ranging from potentially justifiable to strictly off limits. The most justifiable use, the commission said, would be helping those rare couples who, even with in vitro fertilization (IVF) and screening of embryos before implantation, have little or no chance of having a baby that does not inherit a genetic condition leading to "severe morbidity or premature death." A couple in which one partner is homozygous for the Huntington disease mutation is an example; without intervention, their children will inherit the mutation and develop the fatal disease.

Genetic diseases that have less serious effects and can be corrected or treated in other ways, such as deafness, rank lower. At the bottom—most taboo in the eyes of the panel—is the use of HHGE for genetic enhancement, creating children who are smarter, better at sports, or resistant to HIV, which was the goal of He's experiments.

If HHGE is allowed, the panel said, any embryo edit should only "specifically change one DNA sequence into a specific desired sequence" that is common in "the relevant population." This means the simplest, most frequently used form of CRISPR, which can cripple genes but does not fix them, should never be used in embryos. The panel also noted there may one day be a way to avoid the danger of unintended "off-target" DNA changes. Scientists have proposed editing the stem cells that produce human sperm or eggs before any embryo is created. Those gametes could then be tested for off-target changes before they are used for IVF.

The report's criteria for future use of HHGE are so stringent that "it is a ban on editing the genome of the embryo in principle," says Denis Rebrikov of Pirogov Russian National Research Medical University, who has pursued a project to correct a deafness mutation in embryos of couples who each have the aberrant gene. (Rebrikov has not moved forward because he is not yet satisfied he can safely edit a human embryo.)

Fyodor Urnov, a CRISPR researcher at the University of California, Berkeley, is glad the commission was so restrictive. "The careful guidelines laid out in this report show that the list of problems that could be addressed by such editing is, in fact, quite small," he says. "It is an open secret in the gene-editing community that human reproductive editing is a solution in search of a problem." ■

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Science **369** (6509), 1282-1283.
DOI: 10.1126/science.369.6509.1282