to 3 million shots per day; on 23 March it announced that everyone over age 45 can get a shot starting 1 April. The AstraZeneca vaccine, manufactured by the Serum Institute of India, accounts for most of the shots delivered so far. The other locally produced vaccine, Covaxin, was developed by Bharat Biotech in collaboration with the Indian Council of Medical Research.

India has reportedly put on hold exports of the AstraZeneca vaccine to help meet domestic demand. Since January, India had exported 60 million doses to some 80 countries, through bilateral aid, commercial contracts, and the COVID-19 Vaccines Global Access Facility, a global scheme to increase access to the vaccine.

Vaccine coverage among the country's poor is lowest, because of low awareness and day workers' inability to take time off, social workers say. In Mumbai, authorities have begun to set up vaccination centers in slums. Also needed, says Arun Kumar, head of Apnalaya, a nonprofit that works in the city's slums, are "massive community-based programs to clear vaccine fears."

Some of those fears stem from Covaxin's hasty approval in early January, before data from phase 3 trials were available. "It created a doubt," says former federal health secretary K. Sujatha Rao. "Once trust is broken, it's not easily regained." (On 3 March, Bharat Biotech announced the vaccine had 81% efficacy, based on an as-yet-unpublished initial analysis of 43 cases.)

Reports of violations of informed consent in trials and inadequate transparency around adverse events may have also shaken confidence. On 16 March, a group of 29 doctors and researchers wrote a letter about reported deaths, about 100 so far, of vaccinees. Although the vaccines may not be responsible, the petitioners say, the government should investigate them and disclose its findings. Unlike at least 20 European countries, India has not paused use of the AstraZeneca vaccine after reports of serious clotting disorders (see p. 14); officials say they are reviewing the data.

In an attempt to slow the second wave, several states and cities have reintroduced curbs on social gatherings, imposed temporary lockdowns, and stepped up testing and tracing. In Mumbai, once again a hot spot of the pandemic, the city banned public celebrations of the spring festival of Holi. "We were lucky compared to what might have been," says epidemiologist Giridhar Babu of the Public Health Foundation of India. "But the story is not over. The virus keeps surprising us." ■

Vaishnavi Chandrashekhar is a journalist in Mumbai, India.

COVID-19

Pandemic scientists fight burnout

Running on empty at bedside, bench, and beyond

By **Meredith Wadman**

When not caring for COVID-19 patients—her latest was a man with bacterial lung and blood infections superimposed on SARS-CoV-2 pneumonia—Krutika Kuppalli has been helping oversee the rollout of pandemic vaccines at the Medical University of South Carolina (MUSC), where she's an infectious disease physician. She has also been meeting with vaccine-hesitant hospital staff, sitting on a committee that reviews all planned COVID-19 clinical trials at MUSC, applying for funding to study patients with Long COVID, and handling online harassment that has followed her numerous media appearances and two rounds of congressional testimony last summer.

Asked recently during a Zoom interview how she is doing, she paused for nearly 20 seconds, struggling to regain her composure. "We have been busting our butts for 12, 14 months," she says. "I just feel I'm empty."

Science's COVID-19 reporting is supported by the Heising-Simons Foundation.

From academic research centers to intensive care units (ICUs) to scientific journals to government agencies, scientists fighting the pandemic say they are hitting a wall, 15 months after the first report of a cluster of cases of pneumonia in Wuhan, China, introduced the virus that would upend their lives. "The pace that led to the incredible generation of knowledge on SARS-CoV-2 and COVID-19 has put enormous demands on the people who are expected to generate that knowledge," says David O'Connor, a viral sequencing expert at the University of Wisconsin, Madison, who has been tracking the spread of the virus, doing Zoom Q&A sessions with the vaccine hesitant, and helping neighborhood schools set up diagnostic testing. "This is a terrible time and we should all do what we can to help. But is it going to be sustainable?"

Throughout higher education many are feeling a strain from campus closures, remote teaching, disrupted research, work-from-home challenges, and more. For example, a survey of more than 1100 U.S. faculty members found 55% had seriously considered changing careers or retiring early because of the pandemic. The survey, conducted in October 2020 by *The Chronicle of Higher Education* and Fidelity Investments, also found that 69% of respondents felt stressed, 68% felt fatigued, and 35% felt angry—more than double the 2019 numbers. An international survey by the publishing house De Gruyter found a similarly bleak picture among medical and life scientists, specifically, although the numbers were small: Of 116 respondents, 76% said the pandemic had impacted their well-being; 30% said the impact was "severe."

Physicians have borne much of the burden, says Mona Masood, a Philadelphia-area psychiatrist and founder of the Physician Support Line, a free call-in service staffed by volunteer psychiatrists. The help line has fielded calls from more than 2000 people since it launched 1 year ago; calls have peaked during pandemic surges, Masood says. Some are from doctors on the front lines—for example, an ICU physician who had just lost his 20th patient and broke down on the phone after a 48-hour shift. Others come from physician-scientists who, despite their work on vaccines or variants, feel guilty that they are not caring for COVID-19 patients alongside their colleagues.

For junior scientists, the crisis has magnified stresses already present in the academic system. "Everyone is working nights, weekends, every spare minute of their lives. There's no extra pay. There's no guarantee of any extra recognition," says Emma Hodcroft, a computational biologist and postdoc at the University of Bern who has been tracking SARS-CoV-2 evolution for the project Nextstrain. "I am precariously employed; I don't have a long-term job. I feel a lot of pressure that this is my opportunity and I cannot waste that," says Hodcroft, who has been an author on 18 SARS-CoV-2 papers and preprints since February 2020.

Some academic scientists—especially those with young children—say their institutions have done little to alleviate their stress. "A few 'atta-boys' are tossed by the Provost to thank faculty for their flexibility with coping with challenging times, but no real differences implemented," one senior lecturer commented in a recent National Academies of Sciences, Engineering, and Medicine report that found a disproportion-

ate, deleterious impact of COVID-19 on the careers of women in academic science, technology, engineering, math, and medicine.

The demands of reviewing or editing an unceasing glut of coronavirus papers have also been backbreaking for some. "They did replace me with two people. That tells you what my workload was," says one biology manuscript editor who recently left a top-tier journal and asked not to be identified for fear of career repercussions.

Scientific societies have, in some cases, tried to step into the breach. The American Association for Anatomy (AAA) in October 2020 launched a website of self-care resources called THRIVE in response to "cries for help" from members, largely Ph.D. anatomists who teach and conduct research in medical schools, says Shawn Boynes, AAA's executive director and the prime mover behind THRIVE. The website, which is open to all, has had roughly 3000 monthly visitors, but Boynes says it is at best a Band-Aid. "Why isn't more of this addressed at the institutional level on a regular basis? The pandemic pulled the curtain back and you can see how unbelievably challenging it really is with people who choose academia as a career."

The challenges extend beyond academia. At the Centers for Disease Control and Prevention (CDC), for example, the burden of being the front-line agency responding to the pandemic has taken a major toll. "This question of burnout, personal and professional, is the No. 1 thing I talk about with friends" at the agency, says a senior CDC epidemiologist who has worked at a high level in the pandemic response. Some mid-career CDC scientists are talking about early retirement—a choice that was almost unheard of before COVID-19, they add.

Still, other scientists grappling with the pandemic say that despite the pressure, they have never felt more fulfilled. These past 15 months have been "the hardest of my life," says Sarah Schmedes, lead bioinformatician at Florida's Bureau of Public Health Laboratories. Schmedes is adjusting to being a single mother to a 1-year-old son after her husband died of a heart attack in December 2019. "It definitely helps that I love my job. Being in this field at this time is incredibly rewarding. I'm very honored."

Marion Koopmans, chief of the viroscience department at Erasmus Medical Center in Rotterdam, Netherlands, says she has been working at least 8 a.m. to 11 p.m., 6 or 7 days a week since the pandemic began. Recently, she traveled to Wuhan as part of a World Health Organization team investigating the pandemic's origins (see p. 10), while still managing a 150-person lab in Rotterdam. "I don't feel like I'm burning out," she says. "I can actually do things that contribute to getting through the pandemic. At least that's what it feels like. And that helps." Still, she says, she is taking measures to protect a modicum of personal time so she can watch *Anne with an E* on Netflix or share a nightcap with her husband. "I ask the strictest secretary to block my calendar and route my emails through her."

But O'Connor emphasizes the need for the community to take broader steps. "A year into this, we need to assess: What does the future look like? Does it look like the same workforce being asked to do twice as much as they were doing before? I don't know what the right answer is, but the number of times recently I've heard 'I'm just done with this' uttered in frustration from friends and colleagues is really concerning."

Kuppalli for her part does not foresee an end to her own exhaustion, in part because whenever she is asked to do one more thing to fight the pandemic, "I don't feel like I can say no. Because it's larger than me and I feel lucky to be in a position to contribute." ■

With reporting by Charles Piller.

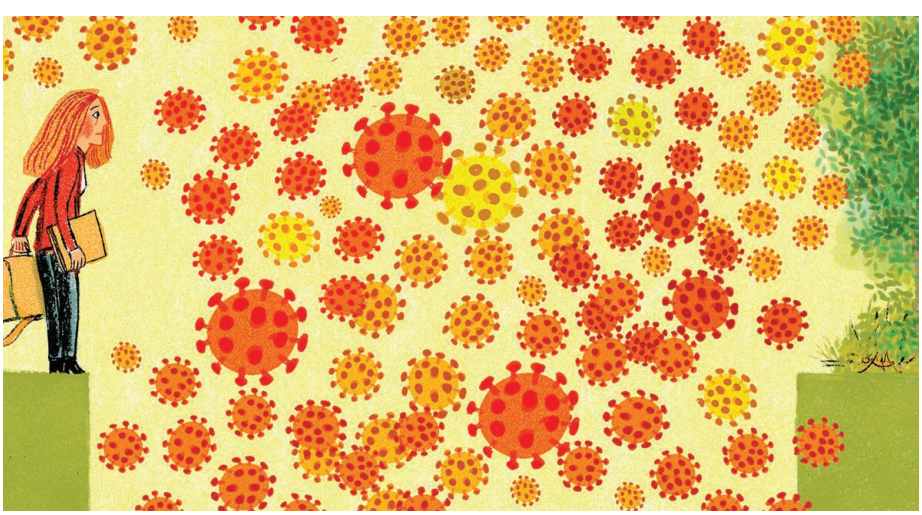

ILLUSTRATION: ROBERT NEUBECKER

COVID-19

Side effect worry grows for AstraZeneca vaccine

Some nations limit shot to older people, as probe of clotting disorders continues

By **Gretchen Vogel** *and* **Kai Kupferschmidt**

It's been one step forward, two back for AstraZeneca's COVID-19 vaccine. Even as the company rebutted criticism of its efficacy claims last week, a bigger problem loomed for the vaccine and the many millions depending on it. Evidence continues to accumulate that an unusual clotting disorder seen in dozens of European recipients is a real, albeit rare, side effect. A preprint has detailed a proposed mechanism, and multiple scientific groups have said the worry is legitimate and must be seriously weighed against the vaccine's COVID-19 protection.

This week, Canada and Germany joined Iceland, Sweden, Finland, and France in recommending against the vaccine's use in younger people, who seem to be at higher risk for the clotting problem and are less likely to develop severe COVID-19. The approach makes sense given that other vaccines are available, says Sandra Ciesek, a virologist at Goethe University Frankfurt. "We do not have just one vaccine. We have several."

AstraZeneca's vaccine incorporates the spike gene from SARS-CoV-2 into another, nonpathogenic virus. Last month, many countries suspended its use following initial reports of the clotting issues in recipients, which have led to at least 15 deaths in Europe. Some researchers dismissed the cases as normal background levels of blood clots. And most countries resumed vaccinations after the European Medicines Agency (EMA) said the vaccine's benefits outweigh any risks, even though it couldn't rule out that the clotting symptoms were connected to the vaccine.

In parallel, the company's initial report of results from a key vaccine trial in the Americas drew unexpected criticism. In a press release, AstraZeneca claimed the trial had shown the vaccine had 79% efficacy in pre-

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Science **372** (6537), 13-14.
DOI: 10.1126/science.372.6537.13