



## From Vaccine Nationalism to Vaccine Equity — Finding a Path Forward

Ingrid T. Katz, M.D., M.H.S., Rebecca Weintraub, M.D., Linda-Gail Bekker, M.D., Ph.D., and Allan M. Brandt, Ph.D.

The global effort to develop safe and effective Covid-19 vaccines has yielded remarkable results, owing in part to early, decisive investments in clinical discovery through efforts such as

Operation Warp Speed. These achievements highlight the payoff of stable, long-term support of basic research and immunology: our scientific community was prepared to act. Now, as the global community faces scarce supply, we confront a distressing reality: our current global vaccination rates of roughly 6.7 million doses per day translate to achieving herd immunity (70 to 85% of the population having received a two-dose vaccine) in approximately 4.6 years. Vaccine distribution remains nonexistent in many of the poorest countries, and experts anticipate that 80% of the population in low-resource settings will not receive a vaccine this year. Although investment in discovery is critical, the long-term neglect of public health and global delivery strategies has left us poorly equipped to end this pandemic.

The complex bottlenecks in allocating and disseminating new-

ly approved vaccines require urgent attention. They include ensuring production capacity, supply chains, human resources, and health infrastructures to deliver vaccines safely, effectively, and quickly. Barriers to vaccine uptake are augmented by mistrust, misinformation, and historical legacies affecting vaccine confidence.<sup>1</sup> Even wealthy countries have faced formidable obstacles and made critical missteps in implementing mass-vaccination programs.

Furthermore, the early competitive procurement of vaccines by the United States and purchases by other high-resource countries have fed a widespread assumption that each country will be solely responsible for its own population. Such vaccine nationalism perpetuates the long history of powerful countries securing vaccines and therapeutics at the expense of less-wealthy countries; it is short-sighted, ineffective, and

deadly. Ultimately, wealthy countries have a critical interest in assisting global vaccination, especially in countries that will need supportive partnerships to ensure supply and delivery. Moreover, an uncoordinated patchwork of immunity could exacerbate the rise of escape variants that could alter vaccines' effectiveness.

These inequalities reveal a fundamentally flawed view of global health, and our global economy more broadly, in which vaccines and essential medications are treated as a market commodity rather than as a public good. We have seen similar policies enacted during past pandemics. During the height of the HIV epidemic, for example, most low-resource countries could not access life-saving antiretroviral therapy because of the prohibitively high prices set by the pharmaceutical industry and the belief within United Nations agencies and among major donors that the focus in these settings should be on prevention instead of treatment. The commodification of global public goods reinforces widespread inequities in access and

exacerbates vast disparities in health and economic well-being. Ultimately, addressing critical constraints is both a moral issue and one of national security that requires bold, decisive action to ensure expansion of supply, distribution, and delivery of Covid-19 vaccines.

The United States, under the Biden administration, and the G7 nations have committed support for global vaccine procurement through the Covid-19 Vaccines Global Access (COVAX) program, which supplies vaccines to low- and middle-income countries, but this funding alone remains inadequate. Currently, COVAX plans to vaccinate at least 20% of the population of participating countries by the end of 2021.<sup>2</sup> Though this would be a substantial achievement, it falls far short of the goal of securing global herd immunity in a timely fashion.

The United States has an opportunity to lead by building on past effective efforts and investing in strategies with proven success. The challenges of delivering costly HIV therapeutics to low-resource settings inspired the creation of programs such as the President's Emergency Plan for AIDS Relief (PEPFAR) and the Global Fund to Fight AIDS, Tuberculosis, and Malaria, which have been critical to ensuring global scale-up of antiretroviral therapy for populations that previously lacked access. Reflecting on the impact of PEPFAR, which was approved with bipartisan congressional support in 2003, Anthony Fauci noted on the program's 15th anniversary that "PEPFAR has done as much as or more than any other program in enhancing the humanitarian image of the United States and has firmly established it as a key player in the response to a historic global health crisis."<sup>3</sup>

The United States could build on PEPFAR's success by committing to what some experts have dubbed a President's Emergency Plan for Vaccine Access and Relief (PEPVAR).<sup>4</sup> Such a program could integrate global health needs into ongoing funding priorities, augment funding for vaccine production and delivery, and assist in building critical health infrastructures, while providing the Biden administration an opportunity to rejoin the global diplomatic community.

PEPVAR could use strategic lessons from the global responses to HIV, H1N1 influenza, and Ebola by engaging with multinational organizations such as the World Health Organization, as well as governments, ministries of health, and affected communities. The program could help accelerate distribution of Covid-19 vaccines, working with national governments and multilateral organizations. Unlike COVAX, whose mission is primarily to increase and improve vaccine delivery to countries that are most in need, PEPVAR could partner with, support, and accelerate existing institutional mechanisms for ensuring vaccine access. Like PEPFAR, it could focus attention on data and analytics, equitable distribution, workforce development, and future pandemic preparedness, while accelerating development of additional necessary vaccines to address potential viral variants.

The success of such programs rests on immediate expansion of the supply of approved Covid-19 vaccines. India, for example, has secured substantially more vaccine than other low- and middle-income countries thanks to a partnership between AstraZeneca and the Serum Institute of India, one of the world's largest vaccine manufacturers. The agreement allowed

AstraZeneca to leverage the Serum Institute's manufacturing capacity in exchange for vaccine doses for Indian citizens. Other pharmaceutical companies have also entered into agreements to expand global production by means of horizontal cooperation. Novartis, for example, has announced an initial agreement to help manufacture the Pfizer-BioNTech vaccine.

Though pharmaceutical companies have preferred to use voluntary licensing agreements to control who can produce a patented good, pressure has mounted on the World Trade Organization to consider a Trade-Related Aspects of Intellectual Property Rights (TRIPS) waiver for Covid-19 vaccines. This proposal, put forward by India and South Africa and supported by more than 90 countries, would temporarily waive pharmaceutical patent protection, and substantially reduce the costs of manufacturing vaccines globally. Opponents of a TRIPS waiver argue that intellectual property protection is key to vaccine discovery and that without it, future innovation will be limited. While recognizing that patents provide essential incentives for companies to invest in drug and vaccine discovery, we believe the context of a pandemic, combined with the \$18 billion in public funding that has already supported the development of Covid-19 vaccines, may argue against patent protection at this time.

Even with patent waivers, we may simply lack sufficiently consistent manufacturing capacity globally to develop and produce the current generation of vaccines. Long-term investment strategies are critical if we are to withstand the current pandemic and be prepared for future ones. Beyond expanding short-term supply, foster-

ing global cooperation will better situate the global economy to rapidly supply vaccines and therapeutics in the future. Such cooperation is not only a matter of social justice, it is also a sound pragmatic response to ending a pandemic in which a virus and its variants easily cross borders. With a globally coordinated strategy, epidemiology, efficacy, and ethics can be fully aligned.

Covid-19 vaccines provide a pathway out of this pandemic, but bold, innovative policies that ensure fast and fair distribution are also critical. The United States has an unusual and urgent opportunity to ensure that Covid-19 vaccines are available to all. As Ursula von der Leyen, president of the European Commission, recently explained: “A global pandemic requires a world effort to end it — none of us will be safe

 An audio interview with Dr. Katz is available at NEJM.org

until everyone is safe.” The Biden administration is well positioned to take a leadership role in this next critical phase.

Vaccinating the world is not only a moral obligation to protect our neighbors, it also serves our self-interest by protecting our security, health, and economy. These goals will not be accomplished by making the world wait for wealthy countries to be vaccinated first. By investing in multilateral partnerships with a sense of shared commitment and employing a global allocation strategy that increases supply and manufacturing, we can meet the urgent challenge of Covid-19, while creating sustainable infrastructures and health systems for the future. Getting the world vaccinated may well be the critical test of our time.

Disclosure forms provided by the authors are available at NEJM.org.

From the Department of Medicine, Brigham and Women’s Hospital (I.T.K., R.W.), Harvard Medical School (I.T.K., R.W., A.M.B.), Massachusetts General Hospital Center for Global Health (I.T.K.), and Ariadne Labs (R.W.) — all in Boston; the Harvard Global Health Institute (I.T.K., A.M.B.), and Harvard University (A.M.B.) — both in Cambridge, MA; and the Desmond Tutu HIV Centre, University of Cape Town, Cape Town, South Africa (L.-G.B.).

This article was published on April 3, 2021, at NEJM.org.

1. Weintraub RL, Subramanian L, Karlage A, Ahmad I, Rosenberg J. COVID-19 vaccine to vaccination: why leaders must invest in delivery strategies now. *Health Aff (Millwood)* 2021;40:33-41.
2. Mullard A. How COVID vaccines are being divvied up around the world. *Nature* 2020 November 30 (Epub ahead of print).
3. Fauci AS, Eisinger RW. PEPFAR — 15 years and counting the lives saved. *N Engl J Med* 2018;378:314-6.
4. Krellenstein J, Staley P, El-Sadr WM. The world is desperate for more Covid vaccines. *New York Times*. January 12, 2021 (<https://www.nytimes.com/2021/01/12/opinion/world-covid-vaccines.html>).

DOI: 10.1056/NEJMp2103614

Copyright © 2021 Massachusetts Medical Society.

## Vancomycin Infusion Reaction — Moving beyond “Red Man Syndrome”

Santiago Alvarez-Arango, M.D., S. Michelle Ogunwale, M.D., Thomas D. Sequist, M.D., M.P.H., Caitlin M. Burk, M.D., and Kimberly G. Blumenthal, M.D.

In 1959, an article entitled “An Anaphylactoid Reaction to Vancomycin” hypothesized that vancomycin-induced histamine release from mast cells had clinical manifestations similar to those of anaphylaxis but less severe. The author named this reaction “Red Man Syndrome,” reflecting the diffuse erythema in affected patients, and the term caught on in 1985, when the *Journal* published a letter entitled “Vancomycin and the Red Man’s Syndrome.”<sup>1</sup> Although “red man” might, at first glance, be taken as a straightforward description of a white male patient with an erythematous skin

reaction, the term “Red Man” had a ready referent outside medicine, where it had long carried racist connotations.

Like “redskin,” “Red Man” calls up historical narratives that endorse and reinforce discrimination against Native American and Indigenous peoples. Such narratives were deeply embedded in popular culture: L. Frank Baum, the author of the *Wizard of Oz*, for example, wrote after the massacre at Wounded Knee, “With his fall the nobility of the Redskin is extinguished, and what few are left are a pack of whining curs who lick the hand that smites

them.” The song “What Makes the Red Man Red” in the Walt Disney movie of *Peter Pan* depicts Native Americans as animals.<sup>2</sup> Citing this history, some observers have called for replacing the trauma-invoking term,<sup>1</sup> yet “Red Man Syndrome” continues to be used by clinicians worldwide.

Current use of this term causes inequities beyond its original racist implications: by implying a white male reference, it perpetuates biases and racial norms that may undermine prompt and equitable diagnoses and treatment. Furthermore, its use as a clinical descriptor supports race-based