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GUEST ESSAY

The Vaccines We Have Are Good. But They Could Be So Much Better.

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Soon after the novel coronavirus emerged, its genome was sequenced and vaccines were developed at, yes, warp speed. These are all herculean tasks that deserve praise. But America's achievement stops there. The initial vaccine strategy was reactive and tactical, not decisive and strategic. While it prioritized getting safe, effective vaccines into bodies as quickly as possible, it did not consider how to prevent variants or subsequent waves of the virus.

All coronaviruses produce variants, and as with prior coronavirus outbreaks, variants of SARS-CoV-2 emerged as the virus spread from Wuhan, China, across the planet. The next danger is the further evolution of variants that can overcome the immunity provided by existing Covid-19 vaccines and prior infections.

The second generation of Covid-19 vaccines, which are now in development as booster shots, is aimed at known variants, but they are not designed with future variants in mind. This is "whack-a-mole" vaccine development, an inefficient and costly approach that chases yesterday's virus. What we need is "kill shot" immunity, which would protect people against all current and future variants and bring an end to the pandemic.

It is possible to make a vaccine like this — if scientists closely study the patterns of how viruses mutate, and design vaccines for the viruses that we're about to face, not just the ones we have now. This approach is especially important considering the number of ways viruses can emerge in humans, including from natural spillover (when a virus spreads from one species to another) or an accident in a virus research laboratory ("lab leak") — both scenarios that are, appropriately, the subject of serious investigation.

Whatever the results of those inquiries, the United States must use this pandemic to ensure that emergency vaccine development can address all possibilities.

OPINION CONVERSATION

Questions surrounding the Covid-19 vaccine and its rollout.

- **When is it still important to wear a face mask?**
  Three health experts address readers' questions about mask guidelines.
- **Who isn't getting vaccinated, and why?**
  Sema K. Sgaier, a researcher who uses data to address health problems, looks at the motivations of the unvaccinated.
- **What can I do while my children are still unvaccinated?**
  David Leonhardt writes about the difficult safety calculations families will face.
- **When can we declare the pandemic over?**
  Aaron E. Carroll, a professor of pediatrics, writes that some danger will still exist when things return to "normal."

One approach is to predict which variants are most likely to occur in a circulating virus and prepare to defeat them in advance using pre-designed vaccines. This might seem futuristic, but the capability already exists.

The ability to predict and counter pathogens emerging naturally, as well as genetically altered ones released from unregulated laboratories, was first developed by the U.S. government over a decade ago. In 2008, while working at the Defense Advanced Research Projects Agency, also known as Darpa, our team, led by Dr. Callahan, became alarmed by a series of bird flu outbreaks in humans associated with several foreign poultry vaccine companies.

We were particularly concerned that well-intentioned but unregulated virus research in foreign laboratories could produce viruses that were highly infectious and capable of spreading rapidly in human populations. Between 2008 and 2016, Darpa developed a program called Prophecy to study the evolution of viruses to predict mutations and develop vaccines. The agency combined it with an alert network run by doctors working in at least seven hospitals around the world, including in places such as Singapore; Jakarta, Indonesia; and Hong Kong.

Here's how Prophecy worked: First, researchers studied the genome of a dangerous virus to identify areas where the virus can mutate without destroying its ability to reproduce. An overwhelming majority of mutations make a virus weaker, so most mutations can be ignored. Second, scientists used computer models to test the remaining mutated viruses and simulate all possible changes in surface proteins, which are important for a virus's ability to infect. Scientists then designed antibodies on the computer to target these proteins and help the body recognize the virus and fight it off. By working with our research partners, we could confirm our predictions by sequencing the newest variants obtained from patients around the world. Scientists can further adjust the designer vaccine or antibody based on immunity observed among people who survived the infection.

In addition to strengthening global health and health security, technologies and processes developed under Prophecy were instrumental in helping pharmaceutical companies make experimental vaccines and antibodies more rapidly to treat cancers that evaded the patient's immune system, and drugs that would prevent emergence of antibiotic-resistant microbes.

Unfortunately, the changes in U.S. political leadership in 2016 as well as budget changes led to the demise of research collaborations in nine countries, including China, Russia, Indonesia and Nigeria.

The Biden administration's re-engagement in global health signals an opportunity to restart Prophecy or a similar program.

As the United States begins month 18 of the pandemic, the nation should carefully reconsider the next steps in vaccine development. We need to restore foreign research collaborations and re-establish surveillance at international hot spots where animal-to-human infections commonly occur, in China and other countries. Second, the United States must resume relationships with foreign laboratories that work with dangerous pathogens to ensure safe, secure and ethical best practices. These collaborations can be incentivized by sharing technologies such as mRNA vaccines. Third, Prophecy and similar tools need to be updated to better assess whether a virus is natural or engineered. Determining the origin of a virus allows those in charge to put in place controls to reduce the frequency and severity of future pandemics.

While Prophecy's first act was accurate prediction of pathogen evolution, it was the program's second act that best serves us now: the ability to anticipate viral mutations before they occur and to counter the mutations using vaccines. These kinds of vaccines are already being studied in advanced clinical trials to prevent recurrence of drug-resistant cancers and to produce a universal influenza vaccine. Bringing these technologies to the fight against coronavirus variants could help end the current pandemic and prevent the next one. The nation should move quickly.

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