

EYE ON THE NEWS

Ending Covid

It will take some time, but rest assured: a coronavirus vaccine is coming, and it will work. **Peter Kolchinsky** March 31, 2020

The biopharmaceutical industry will be able to make a Covid-19 vaccine—probably a few of them—using various existing vaccine technologies. But many people worry that Covid-19 will mutate and evade our vaccines, as the flu virus does each season. Covid-19 is fundamentally different from flu viruses, though, in ways that will allow our first-generation vaccines to hold up well. To the extent that Covid does mutate, it's likely to do so much more slowly than the flu virus does, buying us time to create new and improved vaccines.

Every virus has a genome composed of genetic material (either RNA or DNA) that encodes instructions for replicating the virus. When a virus infects a cell, it accesses machinery for making copies of its genomic instructions and follows those instructions to make viral proteins that assemble, with copies of the instructions, to form more viruses (which then pop out of the cell to infect new cells, either in the same host or in someone new).

There is a critical difference between coronaviruses and flu. The novel coronavirus genome is made of one long strand of genetic code. This makes it an "unsegmented" virus—like a set of instructions that fit on a single page. The flu virus has eight genomic segments, so its code fits on eight "pages." That's not common for viruses, and it gives the flu a special ability. Because the major parts of the flu virus are described on separate pages (segments) of its genome, when two different flu viruses infect the same cell, they can swap pages.

Imagine two people with eight-page reports fighting over a copy machine. In the tussle, some copies might turn out to have a mix of pages from two different reports. This page-swapping process, where viruses exchange parts of their genome, is called reassortment. The flu can change rapidly when multiple strains pass through the same host. But coronavirus, as a one-page report, tends to stay together, and while coronaviruses can swap sections—in a process known as recombination—it is difficult to achieve and thus rare. (Imagine two pages ripping in the same way and swapping pieces that get glued together again.)

Coronavirus does mutate. All viruses mutate, in a way that can be likened to typos introduced by the copying process. Instead of a copy machine, imagine that a page of text is read by a scanner that then attempts to transcribe the words into a text file. The scanner may transcribe a page of text imperfectly, introducing an "I" for an "I," and when that's printed out and then scanned again, the scanner makes more transcription mistakes on top of the old ones. After many cycles, the accumulating mutations in the code cause features of the virus to change gradually, a process called "drift." When flu virus swaps entire pages with a different flu virus in a reassortment, we call that "shift." Drift through typos tends to cause small changes. Shift through reassortment causes bigger ones.

A vaccine is like a description of a wanted criminal: it tells your immune cells whom to look out for. So long as the suspect's appearance doesn't change too much, then the vaccine works. To the extent that the flu virus we see one year is only slightly different than the ones we've seen in recent years, our immune systems are at least partially prepared, and so we are partly protected. Even if we do get infected, it might be a milder illness because our immune system can react more quickly to fight it off.

Laboratories around the world are constantly surveilling today's flu strains and giving flu-vaccine manufacturers a heads-up as to what the viruses look like. So if we see a new strain of flu in Asia, it's probably a good idea to start making a vaccine against it for the U.S. before that strain comes to our shores. Because large-scale manufacturing of current flu vaccines takes about six

months from the time when we spot a new flu strain, the vaccines are six months out of date by the time we get them. Some years, the flu swaps out a genomic page with a less familiar strain—maybe one we haven't seen for a decade or so—and we get the vaccine wrong. When that happens, we suffer through a bad flu season, since our immune systems are less ready to fight it off.

In the worst case, the flu can suddenly pick up a page from a bird- or pig-flu strain to which most humans have had zero exposure. This can be far more deadly, because the new virus can evade our herd immunity entirely, cutting through the population unopposed. That's a flu pandemic.

Today's novel coronavirus was brewing within bats for a long time, mutating into its current form through various typos and, to a lesser extent, rare recombination events among coronaviruses. Now that it's here, it's as new to us as a shifted flu strain that we've never seen before, and it's causing a pandemic. But once we've developed a vaccine for this strain—and once we've all taken it—we'll have herd immunity to it.

That immunity may fade as our immune system forgets the picture that the vaccine showed it, but we can solve that by getting booster shots of the same Covid-19 vaccine periodically. What we don't have to worry about is the virus rapidly mutating away from our vaccines as fast as flu can, because owing to its simplicity, it can't pull off the flu's face-swapping tricks.

We hear reports that the novel coronavirus is already mutating into new strains, but these mutations are minor, and they're unlikely to add up to anything significant. Even identical human twins have many genetic differences between them, but we still think of them as identical. In the case of Covid-19, very few of the changes we've seen so far would affect a vaccine. But if such changes do accumulate over time, our vaccine programs will be able to keep up.

Think of it this way: if flu evolves with the speed of a growing vine, then coronavirus is like a cactus. If you look very closely, a cactus can appear to be changing from day to day, but it's nothing like a vine.

We're now inventing new vaccines from scratch and could plausibly go from nothing to a marketed vaccine in about a year. If laboratories around the world detect that this coronavirus is changing gradually, we'll most likely have time to match new strains before they change enough to cause a new outbreak. Rest assured: a vaccine is coming, it will work, and it will continue to work for as long as humanity must contend with Covid-19. Until then, we must maintain our social distancing so that our strained health-care system can keep up with the infections that we can't seem to prevent.

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