

The Next Coronavirus Nightmare: There's a Drug Shortage on the Horizon



March 18, 2020 *Topic:* Security *Region:* Americas *Tags:* Coronavirus, Symptoms, Treatment, Drugs, Testing

Dr. Scott Gottlieb, the former commissioner of the Food and Drug Administration, weighs in on how to tackle the coronavirus pandemic and what the future holds for those Americans who haven't been infected by the virus.

by Jacob Heilbrunn 

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r. Scott Gottlieb, the former commissioner of the Food and Drug Administration, is a resident fellow at the American Enterprise Institute. He is a contributor to CNBC and serves on the board of a number of health technology and biotech companies.

Heilbrunn: Are there any existing drugs that you think could help address this crisis in the near term?

Gottlieb: When it comes to therapeutics, it's a three-pronged strategy. The first is to develop a vaccine. That's probably two years away. I think we have to be realistic and understand that it's probably two years until we can get a vaccine. Maybe longer. We've never developed a vaccine to a coronavirus, there are certain things we don't fully understand. There is a certain complexity involved in the kinds of vaccine platforms that we are trying to use now. It's a very novel technology.

The second strategy is looking at antivirals that can work directly against the virus. That is really going to be a game of looking at what is on the shelf, what antiviral drugs currently exist that might be able to be repurposed to this task—and that's drugs like Remdesivir, which is being developed by a company called Gilead. There are a number of other antiviral drugs that are being tested against coronavirus that have been shown to be active in vitro, meaning in test tubes, that are now being studied in vivo in animals as well as human trials.

The third leg of this strategy is to try to develop an antibody-based prophylactic. This would be an antibody that targets some feature of the virus that can be used as a prophylactic in people and, in this case, a lot of the people who are trying to develop these products are targeting what is called a spike protein. The spike protein is a part of the virus that the virus uses to gain entry into human cells. One of the companies that is pretty far ahead in developing this kind of product is Regeneron. Regeneron also was able to develop an antibody-based prophylactic that was successful in Ebola. They

also had one that they were developing against MERS (Middle-East Respiratory Syndrome) that they had studied in large primates, I believe. This is a company that has shown they can do this and they are currently developing a product against coronavirus. The virtue of this kind of a product is that it would basically be a monthly injection, that you would use it for either frontline healthcare workers or patients who are vulnerable—nursing home patients or immunocompromised patients, maybe people who are going to chemotherapy, people with significant heart disease or lung dysfunction. You give it to them monthly and it would be a prophylactic that could protect them against coronavirus.

Heilbrunn: If we aren't going to have a vaccine for the next two years, how could a therapeutic change the outcome of this pandemic?

Gottlieb: If we had the kind of prophylactic product I was describing, it would really change the contours of risk. My concern right now is that we are going to have a major epidemic now across the United States. There are different estimates of how long that is going to last, but most of the modeling shows that it is most likely to peak sometime in probably late April or early May. That is sort of the optimistic case. In seven to eight weeks the epidemic will peak. Then it will start to come down. By July, hopefully the epidemic will have coursed. There will be a sizable portion of the population who have gotten the infection so you'll have what's called herd immunity. In July and August, we'll probably have sporadic outbreaks but you shouldn't have epidemic spread. The fear is, and my concern is, that when you come back in September, you're going to have major outbreaks and the risk of another epidemic going into the winter. I think the policymakers really need to focus on that risk. That's a challenge because right now they are focused on the crisis. But they need to take steps right now to also be guarding against the risk in the fall. By September, it will be too late.

We should be investing in those therapeutics. There's no reason we can't have something like an antibody-based prophylactic. There's no reason we can't have repurposed an antiviral drug that currently exists for the purposes of targeting coronavirus. Now maybe it won't be through regulatory approval, but you should potentially have enough clinical data to prove whether one of these compounds work and that you could use it on a mass scale. There are currently trials underway with Remdesivir. We are going to turn over the card on them in April. If they show clinical benefits, by the fall you could have mass production and that product available in a treatment protocol—where you are still continuing to collect data and study it, it's not licensed, but you are providing it on a treatment basis in the context of some kind of study. You could have an antibody-based prophylactic potentially approved by the fall, that should be a relatively rapid development and scale up—if it works. And it should be fairly clear how to establish its safety profile.

Heilbrunn: Can you talk about the role of diagnostics both for patient care but also for disease surveillance?

Gottlieb: You are going to want two things. One is a point of care diagnostic. You're going to want a diagnostic that you can deploy to doctor's offices so that you can diagnose people really easily so that when you find people who have coronavirus, you can quarantine them. We're not going to wait twenty-four to forty-eight hours for a diagnostic, it really needs to be in the doctor's office. And there is no reason that is not attainable. That is something you should be able to develop within three months. We have all kinds of rapid diagnostics at doctor's offices—the flu swab, which you're probably familiar with.

The other thing you're going to want is an extremely robust surveillance system. You're going to want a system that basically looks at people who present with influenza-like illness but who test negative for the flu. And you

then test their samples to see what they have. We currently do that. We have a surveillance system distributed throughout multiple cities and we take a certain number of samples—it's a small amount—it's not tens of thousands but thousands and we test them for other things to see what is circulating in the population. We also do that to try to have an early detection in case, like, a pandemic flu stream is circulating. But we don't do it for this novel coronavirus and we don't do it on a mass scale.

What you're going to want by the fall is to really blow that out, do it at a mass scale, and obviously build out the capability to do it for coronavirus. Because this coronavirus is not really going to come and go. It's going to be with us. And unless we have those kinds of tools available to us and this kind of surveillance system in place, this is going to change daily life in perpetuity until we have a vaccine. And that's not sustainable. The kind of posture that the nation is in right now isn't sustainable. And another major epidemic won't be sustainable. So we need the tools to change the landscape for how we deal with this and people need to be really focused on that right now because I think we got caught a little flat-footed with this epidemic. We were not really anticipating that this would become an epidemic in the United States. Although there were people who felt that it would, there was not the kind of preparation, necessarily, that needed to happen two months ago to prepare for now. And you don't want to be in a situation where it's September and saying, "Gosh, I really wish we would have done some things differently in May and June so we have different tools and a different posture."

Heilbrunn: So you're saying potentially September could be even more dire than what we are experiencing now?

Gottlieb: Not necessarily, no. I actually think no because I think by September you are going to have a portion of the population which has been exposed to it. So you're going to have some herd immunity. The ability for this to rapidly propagate and become epidemic again is going to be more

limited—not impossible—but more limited. But there will still be the ability for this virus to cause sizable outbreaks. So even hundreds or thousands of cases are going to be disruptive if you have that kind of outbreak in the fall or the winter. And there is the potential for larger spread. Even though it's diminished, there's still the potential for larger spread. You don't want this being a continual threat, you want to find a way to mitigate this so that we can deal with it. There are lots of viruses and bacteria that circulate, that are very dangerous, but we have developed tools for dealing with them, and they've become part of daily life. We know how to deal with them. Some people succumb to them but for the vast majority of the population, we are able to use effective therapeutics and effective diagnostics tools so we can mitigate the threat and life goes on. What I am saying is that we cannot keep the economy shut forever and we probably can't sustain another epidemic or sizable outbreak of this.

And the other side of the equation here is that the immunity you get after you get infected—there is now good evidence that people who even become mildly infected to coronavirus develop a sustainable immunity (and there's now evidence, in monkeys, in a study that just came out recently, that monkeys who develop the infection and were rechallenged with this virus could not become reinfected). So there is some pretty good evidence and there is also some evidence for humans that suggest that. So there is pretty good evidence to suggest that you develop immunity and you can't be reinfected, but I think most people believe that that immunity is not a life-long immunity and that it will last for a period of time and then it will wane. And maybe the second time you get the infection it won't be as severe, but you don't have enduring immunity. Even if 10–20 percent of the population gets coronavirus—and I hope it's not that many and that we can keep it down to much less than that—but even if a sizable portion of the population gets coronavirus, and you have a portion that is immune to it after it courses its way through society and around the world, even those people could probably be susceptible to it at some point in the future.

Heilbrunn: Do you think we are taking drastic enough steps right now to prevent the spread, or would you recommend even more sweeping measures as far as the isolation of the U.S. population?

Gottlieb: I feel more confident now than I felt a week ago because of the aggressive steps that governors and mayors have been taking. If you look at what Andrew Cuomo has done in New York, he's been very aggressive right from the outset. So I think we're seeing very aggressive actions on the part of governors and mayors to mitigate the spread of the virus. My only concern is that it's not uniform across the nation. There are still some cities and some states that probably have a bigger risk, or a bigger threat from major outbreaks, that haven't been as aggressive, so the weakest link is always the weakest link. So if everyone else is taking aggressive steps and one city doesn't, and that city becomes the focal point of the epidemic, and continues

to seed other parts of America, that puts everyone in a difficult spot, even the cities which have taken aggressive steps. So I think it needs to be consistent across the country.

And it's not that every part of the nation needs to have schools closed and curfews and bars closed, restaurants closed. There is a component of this where you're going to be reactive, not just preemptive—there are certain things you want to do that are preemptive—but there are certain things you are going to do that are going to be reactive. You're going to wait until you have some cases identified or evidence of some community spread before you take certain actions—and that's appropriate. But certainly for the cities where there is evidence of the same community transmission, where you know you have community spread, you should have a consistent approach to the kinds of mitigation steps that we are taking.

But the fact that San Francisco and New York have taken such aggressive actions, and that we've seen such aggressive action in Ohio and Illinois, Boston and Massachusetts, I think that that's going to bode well for trying to get a handle on this epidemic. And I think in some respects that we're further ahead of where China was at a relative point in their epidemic, in terms of our ability to identify the spread and the community, or at least acknowledge the spread in their community. I think China identified the spread in their community earlier, but just didn't acknowledge it and were unwilling to take tough mitigation steps. The point at which China acknowledged there was sustained community transmission, which was long after the fact, and the lockdown in Wuhan was about six weeks. They took a long time to take their mitigation steps.

There are some places that I don't think we have taken strong enough action relative to the threat. I've been very concerned that Seattle didn't take mitigation steps early enough and still hasn't taken mitigation steps that are as strenuous as what I think meet the risks they are facing. I think Seattle and

New York City look like the biggest hot spots in the country in terms of having sustained community transmission and we are going to start turning over the card on that. We didn't really have the diagnostics in place to really identify the scope of the spread that was going on in these states, but we are going to have that screening in place by the end of this week. And with increased screening we are going to start seeing a rapid acceleration, I fear, of the number of cases.

Heilbrunn: Given how reliant we are on overseas drug manufacturing, at a time of crisis like we are now, what about the safety of the drug supply? Should Americans be worried about accessing medicines in the coming months or is that not a huge concern?

Gottlieb: I think that is a point of concern. I think there is a real risk that we see a series of drug shortages out of what is going on globally. The FDA has talked about twenty sole source drugs from China that are at risk because they are only produced in China. I think the list of drugs that could be at risk is much larger than that. It's not just drugs that are exclusively manufactured in one location, but drugs where a partial proportion of the total supply is manufactured in one location. If 20 or 30 percent of all the available drug is manufactured in a location offsite, that is enough to sustain a pretty significant shortage of that drug. Because you don't have a lot of excess capacity in that system where other manufacturers can just easily make it up. But it's a complicated supply chain and there are disruptions throughout the supply chain because this is a global crisis. In China, a lot of what's manufactured are the chemicals and inputs that go into drugs, so it gets shipped to India, and the active pharmaceutical ingredients, the actual chemical that is the drug gets manufactured in India, and that API (active pharmaceutical ingredient) get shipped to parts of Europe or other parts of the world and gets tableted, turned into drugs. That's a complicated supply chain. And at every point in that supply chain, you have had epidemic spread

or you're probably going to have epidemic spread. India looks very suspect right now and there is the potential for disruptions.

The other thing to think about when we are talking about diagnostic screening and rolling that out on a mass scale is that there are shortages of reagents used to extract the RNA from the samples, the actual viral RNA that is in the sample, such as a nose swab. There are reportedly shortages of the reagents needed to extract that RNA and test that sample. There are also reports of the potential for shortages of the actual swabs used to swab people's noses to get the same itself.

What it demonstrates is that the weakest point in this complicated supply chain for critical products is often the lowest margin product. Because the high margin products, the [machine that actually performs the diagnostic screening—that's a machine that costs hundreds of thousands of dollars. That's going to have a very secure supply chain so they can be sure that they can continue producing those machines. They've invested heavily into manufacturing, they have redundant capacity, they have a continuity of business plans. It's always the lowest-margin product in a supply chain, that's still a critical product, that ends up being the weak link. In those cases, it's a consolidated manufacturer who hasn't invested as much in redundant capacity, who hasn't invested in manufacturing itself so the manufacturing could be more vulnerable. So in this case, what is the lowest margin product involved in screening a patient for coronavirus? It's the Q-Tip. So you need to think about what the weakest point in the supply chain is for when you have any critical activity. You can use economics to figure it out because it's usually the lowest-margin product.

Heilbrunn: Clearly relying on overseas supply chains can pose risks to domestic drug supply. Given how much money we are investing in the development of these new products, and the urgent need to have them available to patients in the U.S., how confident do you feel that we will have

domestic capacity to manufacture the drugs and vaccines to combat this disease?

Gottlieb: The kinds of products that I'm talking about would be branded products made by branded companies. Typically, some of that manufacturing is domestic. Some of the branded companies have business plans in place that allow them to have supplies on hand to continue seamless manufacturing for very extended periods of time—up to a year—Regeneron, for example, the company that I talked about that is developing the antibody, their manufacturing is domestic. Whatever is done outside the United States, I would believe that they would have tight control over their supply chain and the ability to continue manufacturing because you are dealing with higher-margin products and businesses that have invested substantial resources into their manufacturing.

After the devastation in Puerto Rico following the hurricane there, and I was at FDA when we grappled with that crisis, fully 10 percent of all the manufacturing capacity for drugs destined for the United States were taken offline. So 10 percent of all the drugs that Americans consume, the manufacturing was offline. I called around to every CEO who had a plant down there to get an assessment of it and we worked very closely with the companies. Almost consistently, the companies that had the biggest challenges that were manufacturing the lowest-margin products. So it was the companies manufacturing medical devices that were lower margin or the drugs. The branded companies that were manufacturing drugs there had very hardened facilities. They had redundant generators, they had months and months of fuel on hand, they had no disruptions in their manufacturing because their facilities were so well equipped. They were manufacturing products that were very high margin. If you are making a pill that costs \$100,000, you are going to invest in the things you need to make sure that you can keep manufacturing that pill. And the amount of money that it takes to ensure that there will absolutely not be a disruption in manufacturing that pill is going to be a small percentage of the total margin on that product. So you will want to make sure that there are no disruptions.

So, what I would be worried about coming out of this are those products—generic drugs and things that are lower-margin products—where there hasn't been as much investment in redundant capacity and hardening supply chains.

Jacob Heilbrunn is the editor of the National Interest.