EPISODE 3: NEXT MOVES, ACCORDING TO SCIENCE

MARIA ANDRIELLA O'BRIEN

Hello and welcome to Columbia Public Health Now, a podcast devoted to exploring the local and global implications of public health challenges in our communities. This Spring, we are focusing the series on the novel coronavirus, otherwise known as COVID-19, and its impact on our world and our health. I am your host Maria Andriella O'Brien and I thank you for listening.

Day by day, the world keeps shifting for everyone thanks to COVID-19. Some quick stats as of March 18th – WHO reports nearly 208,000 cases of infection, with more than 8,200 deaths. In the United States, confirmed cases tops 7,000, a dramatic increase fueled by, in part, by increased access to testing. Even so, experts believe that the true number of people infected with the disease is much higher. Having declared a state of national emergency, President Donald Trump has asked Americans to work from home if possible, and avoid unnecessary travel and gatherings of more than 10 people. While the restrictions apply for the next 15 days, the President said additional measures may become necessary and could last into the summer months. In addition, a number of states and localities have added their own mandates. New York City – the city that never sleeps – has closed schools, bars, restaurants, and gyms and is considering implementing a curfew. Just over the George Washington Bridge, in Bergen County NJ, strict curfews mean that after 8pm, an unusual quiet settles over the suburbs where you no longer hear the background hum of cars, voices and kids playing outside. Most of the time, it feels pretty surreal. But this is our new normal for the near future.

Last week I interviewed Dr. Stephen Morse in an empty auditorium. This week, I’m interviewing Dr. W. Ian Lipkin in a building that’s nearly empty as staff, faculty and students have all mostly cleared out to work and study remotely. Dr. Lipkin is Director for Columbia’s Center for Infection and Immunity, and the John Snow Professor of Epidemiology at Columbia’s Mailman School of Public Health. If you’ve seen the movie Contagion, you have an idea of the work Dr. Lipkin does – he was a science advisor to the movie. Right now, Dr. Lipkin is pushing himself to extremes – splitting his time between working in the lab to develop new tests and potential treatments for the coronavirus, while also talking to reporters, policymakers, fellow scientists – anyone he can reach – to share the facts about the virus and what actions are needed to save lives.

Dr. Lipkin, thank you for joining us.

DR. IAN LIPKIN

Happy to be here.
MARIA ANDRIELLA O’BRIEN
You were in China during the first weeks of the epidemic—what did you see and how did it compare to your experiences in China during the SARS epidemic in 2003?

DR. IAN LIPKIN
My experience in 2003 was fairly similar, in Beijing, to what I saw in Guangzhou in 2020. Deserted streets, people wearing personal protective equipment, gloves, masks, closed stores, restaurants, enormous impact on the social structure, and very difficult for people to make a living, to take care of activities of daily living. And, of course in Wuhan, Hubei Province—where I didn’t go at this time—enormous amount of morbidity and mortality.

MARIA ANDRIELLA O’BRIEN
There have been reports that it is the hyperimmune system response that causes the worst symptoms for some people. Can you explain that?

DR. IAN LIPKIN
Yes, when you have infections as the virus grows inside of a cell, it reproduces itself, it triggers certain immune mechanisms inside the cell that result in damage and cell death, and also the recruitment of molecules known as cytokines and chemokines. What these do is they bring in all sorts of inflammatory cells that release toxic substances that are designed, through evolution, to clear the infected cells but there are bystander effects that are quite damaging. So, you can wind up with organ system damage, your liver may fail, your kidneys may fail, you lose blood volume which results in shock, and you can have central nervous system damage as well. Some of these cytokine responses can be blocked by using antibodies that actually bind to the cytokines—the proteins that are responsible for this damage—and you can alleviate, or mitigate, some of the symptoms by this sort of an effort. One of them is an antibody directed against IL-6 [cytokine] that has already been used in China and appears to have some efficacy and there’s some clinical trials that are proceeding here now that address the same sorts of mechanisms.
MARIA ANDRIELLA O’BRIEN

In our previous episode, Dr. Morse discussed the geographic origin of the virus in China and how it spread across the globe. It shouldn’t surprise us that there’s been a lot of speculation about the biological origin of this disease. Dr. Lipkin, can you tell us a bit more about what is now known about COVID-19 and how you think it was initially transmitted to humans?

DR. IAN LIPKIN

We’ve learned a great deal about the origins of the virus; it looks most similar to a virus that was identified in bats in Yunnan, which is another region in China not far from Hubei. We don’t fully understand how it changed and became more capable of transmission in humans because there are some genetic differences, but nonetheless we’re confident in saying the origin of the virus was in fact a bat. We know that it’s highly transmissible from person to person, and although it was thought initially that some people were primarily infected by exposures to animals, the vast majority of cases are clearly human-to-human.

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Before we dive into our next question, we thought it would be helpful for our audience if we ran through some of the basic science terms involved in Dr. Lipkin’s research. An assay is a laboratory test that can measure the presence and characteristics of a specific substance. An antibody is a protein the body produces as part of the immune response. Antibodies identify and neutralize foreign objects such as bacteria or viruses. Even after the pathogen clears from the body there will be antibodies left behind. That’s why an antibody test is useful – you can see who had an infection even if they didn’t have symptoms. Plasma is a component of blood used in medical tests. Now, back to our interview. Dr. Lipkin, can you please share with us what the Center for Infection and Immunity is working on to address the coronavirus outbreak?

DR. IAN LIPKIN

We are trying to build antibody assays that will allow us to detect everyone who’s infected, not just those who are currently infected. What happens typically in the early phases of a disease is that you use a method called “polymerase chain reaction” that allows you to find molecular
epidemiology that something has gone awry; you find the genes of the virus. As that particular acute phase of the illness recedes, you still have an immune response to the virus, and that you can detect with these antibody assays. We have been working on building PCR assays as well as antibody assays in the Center for Infection and Immunity. The other things we’re doing, is trying to find ways in which we can collaborate with others in looking at people who have high titers of antibodies that neutralize the virus and use those plasma samples from individuals who have recovered to treat and prevent disease in people who have just been exposed. We’re also looking at the potential for ultraviolet light, that’s adjusted so it doesn’t cause skin cancer or cataract formation, to sterilize surfaces and we’re also beginning to look at a number of other potential drug interventions that might be helpful. There are some small studies that suggest that there are particular drugs that may be useful in controlling infection. One of them is a drug called Plaquenil, which is a drug that’s used for treatment of malaria, which can be repurposed and used to perhaps prevent disease. There’s some evidence from a paper soon to be published out of China that suggests that antibodies present in the blood of people who have recovered, can be taken out of the body of the person who’s recovered and infused into the individual who’s been exposed to prevent disease. The earlier the intervention, the better the probability that you’re going to have an impact.

MARIA ANDRIELLA O’BRIEN

You mentioned two potential interventions. How long does it take for those to become publicly available?

DR. IAN LIPKIN

So, drugs and diagnostics are both regulated by the Food and Drug Administration. With the Food and Drug Administration, there are a series of obligatory bars that you have to hit before you’re permitted to license and sell something—that means charge an insurance company, for example, or even use it to guide clinical medicine. You have to demonstrate the limits of detection that your assay, your test, is reproducible and you have to show that it really meets some indication. To some extent, these criteria have been relaxed because of the need that is quite urgent to have assays that can be used for this new infectious disease. Nonetheless, it does take a certain amount of work to get through this and we’re not quite there yet. We’re focusing on that. The importance of tests is it allows you to identify people who have been exposed, who have become infected, who may not even know that they have this virus—they could have some other kind of respiratory tract infection. So, our tests are typically multiplexed, they’re designed to address multiple potential causes of infection—not just the coronavirus.
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Though in fact our first tests may only be coronavirus-focused because that’s where the greatest need is at present. Drugs are even more challenging than diagnostic tests because you need to prove that giving the medication is safe. The easiest way to do this is to select some sort of a drug that is already proof for another condition so that you can just repurpose it; if you can repurpose it then the safety testing is much simplified. You just need to make sure that nothing is different as a result of the underlying condition which may differ. So, one of the drugs that one would try to use now, for example, is a drug that's been useful for treatment of another infectious disease, and if in fact we can demonstrate this, because it’s an oral drug, you might be able to give this to people who are working on the front lines in a hospital or a first responder of any sort—a fireman, policeman, somebody working at the border, a TSA officer—so that you would minimize their risk. It’s always easier to deliver a drug that is prophylactic, that prevents infection, than to treat infection once it’s taken hold. Once the virus is inside of cells it can become very difficult to dislodge it.

The plasma therapy option, which is something that people have been using now for well over a hundred years, is something we are very eager to explore, and we’re in the process of trying to pursue Institutional Review Boards’ approval so that we can identify people in the New York area that have been infected, see whether or not they have antibodies that will kill the virus, and if they do, then get those people to agree to participate and be heroes and save other people in this area.

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My last question, there’s been a lot of talk about “bending the curve,” is it possible for the United States to still bend the curve or have we missed a bit of that opportunity?

DR. IAN LIPKIN

Well the answer is yes on both parts of the question. We can still bend the curve, we’re also late in trying to do so. We should have been much more vigorous about isolation and the Chinese were successful in doing this as I saw while I was there by insisting on, not only people that isolate themselves, but they went so far as to insist that when people were outside, they wear masks and they wear gloves. If they want to go outside, to venture outside, it would be one person per household, one or two days a week would go out and get provisions for everyone else. If we went that far, if we really pushed, we could further flatten the curve and save many, many people. I just don’t know that this culture is going to be willing to do what it takes. So, I’m cautiously optimistic that people will step up. Nonetheless it took a very long time, longer than it should have done, for us to get to where we are at present.