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.

In the last few weeks, it feels as though there has been shift in our thinking - from the short-term to the long-term. It seems like we want to move beyond surviving for the day, to thinking about what’s in store over the next month or year. As we imagine our futures, we look for updates, knowledge, and maybe even that glimmer of hope in a never-ending array of news articles, blogs—and even podcasts. But if there’s one thing we’ve learned in our brief relationship with COVID-19 is that there still seems to be an awful lot of uncertainty about this virus. With the push for states to relax social distancing measures—we risk framing our futures around incomplete information or inaccurate assumptions. So, like any good podcast, we hope this episode offers a little clarity around what we know and don’t know about COVID-19.

Dr. Micaela Martinez, An assistant professor of environmental health sciences at Columbia’s Mailman School of Public Health, is an infectious disease ecologist who uses evolutionary and ecological principles to study pathogens like polio, the measles—and COVID-19.

Her work around COVID-19 helps us to better understand how the disease has spread, how many people may have been infected and what immunity may or may not mean for the survivors. Dr. Martinez, I wanted to start with a question about the area you work in. You’re an infectious disease ecologist. Can you explain this area of work a little bit for our audience?

DR. MICHAELA MARTINEZ

Yes, so I did my PhD in ecology and evolutionary biology, and infectious disease ecology essentially encompasses two types of scientists: those of us that focus on using ecological principles—things like predator/prey interactions and then applying those to infectious diseases. Thinking about infections, essentially, as being predators that have smaller body sizes than their prey, so we’re actually able to leverage the same types of mathematics and principles from ecology that were developed for predators and prey and apply those to infectious diseases. And then the other group of disease ecologists—which I kind of, span both of these—are individuals who really focus on evolutionary biology and taking evolutionary principles, thinking about things such as natural selection and populations and how those apply to human medicine and the evolution of not only our species, but the pathogens that infect us.
Moving to some of the work that you’ve been doing more recently, as COVID-19 has spread across New York, you’ve been creating graphics to map that progression across the city and state. What stories are you seeing in those images as time goes on?

Dr. Michaela Martinez

One that’s very clear, state-wise, since I started tracking this back in mid-March, is that this disease progression, in terms of spatially, across our state has followed what we call “meta-population dynamics.” So, this idea that you can have some populations where the disease pops-up and you have an epidemic taking off, such as here in New York and the counties surrounding it, and then what you end up seeing is that in neighboring populations and in other populations in the state that are also big, such as Rochester and Buffalo, that you start to see these sparks. So, cases popping up there and then once you have the seeding of an outbreak in these other spatial locations, that then you start to see across a whole landscape, across a whole state, the infections starting to emerge. This is something that is very commonly seen in infectious disease systems, where if you look landscape-wise, you can see this kind of source-sink type of dynamic, where you have a source of infection such as New York City and then the “sink” populations, which are all of the other smaller counties that get sparks from the bigger city.

Maria Andriella O’Brien

What do we know about the climate conditions that this virus thrives in?

Dr. Michaela Martinez

Well, right now, we really don’t know much of anything because this is a newly emerged pathogen and this is something that has been of a lot of interest to news media. The thing is, this infection emerged just months ago, so we haven’t even experienced a full calendar year of this infection being in human populations so anyone that claims to know what the climate effects are going to be on its transmission, they’re not being completely honest. The best that we can do, is we can look to other coronaviruses to give us some information. So, we have four endemic coronaviruses here in the United States, which are common causes of the cold—those are winter-time infections, their transmission is associated with low temperature and humidity. Now, we don’t know if SARS-CoV-2 is going to behave like its sister viruses and if it will also be a winter-time infection. SARS emerged but it ended up kind of sputtering out before it took hold as a seasonal, recurring disease and so we can’t really look to SARS for much information about the seasonality. But, one of the things that we do know in terms of recurring epidemics—
so these are outbreaks that happen year after year after year—so you can think of things like polio outbreaks in the summer, measles outbreaks in the spring, chickenpox outbreaks in the spring, flu outbreaks in the winter. These recurrent epidemic dynamics, or the re-occurrence of these, is tied to two things: it’s tied to seasonal changes in transmission, but also these epidemics are very much dictated by the availability of susceptible people in the population to get infected. You can think of disease outbreaks like forest fires. If there’s enough kindling, then you can have a forest fire. But as soon as that kindling starts to be burned through, that fire stops, or it starts to die away. And so what happens with recurrent outbreaks is that the transmission rate can go up in the high transmission season for that disease, and so you have cases climbing, climbing, climbing, and then at some point it starts to burn out of susceptibles, so that epidemic starts to turn around and decline because not only has it burned through susceptibles, but also there could be seasonal declines in the transmission. It’s not a simple on and off switch in terms of the weather that dictates the seasonality of infections. It also is this process of susceptible burnout.

MARIA ANDRIELLA O’BRIEN

In what I’ve read about the 1918 flu, it sounded as though the second wave of the flu was much worse than the first wave due to mutations in the underlying virus. As people are thinking about a potential second wave of COVID-19, what do you think are the things we really need to take into account to prepare for it? Because, on the one hand, there’s the hope that all those people who already had it would now be immune to it, but then there’s the potential that the virus itself might mutate or there are questions about how long people would remain immune to it after having had it.

DR. MICHAELA MARTINEZ

So, a couple things there. With regards to using flu as kind of a benchmark or reference point to understand what will happen for SARS-CoV-2, one thing to be reminded of is that the biology of different viruses is very different from virus to virus, right? So, us as humans, our perspective is like, “Oh, they’re all viruses, we might take from one to learn about another,” but really when you’re comparing something like flu and SARS-CoV-2, that’s like taking—I don’t know—a humpback whale and a mouse, or you know. So, we always have to be very careful that our human perspective on these things is very skewed when it comes to viruses. Now, in terms of the evolvability, I’m not sure—I’m not too familiar with the phylogenetics of the coronaviruses in terms of their mutation rates and how rapidly they evolve. Flu is notorious; a very, very rapidly evolving virus—flu and HIV. And those are the viruses that, they’re so quickly evolving, that’s why we don’t have good vaccines for them, or vaccines that last very long. That’s not the case with a lot of other viruses. We have viruses like measles, which hasn’t really evolved since—forever—which is why we can use the same vaccine that we made in the 1950’s. Right now, we
really have to look towards the data and do a lot of work on sequencing and measure mutation rates, measure the amount of evolution that’s happening in the virus to get a handle on that. Secondly, when it comes to the immunity work, the narrative, which is a pretty kind of a naive one, frankly in the news media, is that if a person is infected previously, and then they have antibodies, and we do serology tests, then maybe they’re going to have some protection for either a long time or some short time. There is really no data to justify that whatsoever at this point.

With any infection, if it is your first time getting infected, what happens is after a couple weeks, your adaptive immune system kicks in. This is the part of your immune system that its job is to remember pathogens you’ve been infected with and generate antibodies in cells that are specific to that pathogen so that if you get infected again, you’ll be able to deal with it. Now, the thing with antibodies, is antibodies are not always enough to protect you from infection. And there is a whole spectrum of the amount of immunological memory that our bodies generate. So, for some things, we’re really good at remembering a pathogen, and antibodies themselves will be enough to protect you. And these are things usually, we have vaccines for—so things like measles, polio, chickenpox—we can launch very strong memory to those things. But then, there are other pathogens which we’re just not good at doing that, and those include some pathogens that they’re just highly evolvable like HIV, flu, and also just some pathogens where really antibodies aren’t doing all of that much of the work, it’s mostly cells of your immune system that are responsible for taking out those pathogens. We really don’t know at this point, and the other thing to be very cautioned with, is that we know from SARS that actually SARS antibodies, the presence of them, could actually cause antibody-dependent enhancement, meaning that they could make you worse off from the infection. And we know that from SARS-CoV-2 that there’s a lot of immunopathology. What people are dying of is not the virus itself destroying their bodies, what people are dying of is their immune system overreacting to the virus and destroying their bodies. With that information, it’s not only premature but also, potentially dangerous to have this narrative that our antibodies are going to rescue us in the long-term or in the short-term because right now we really don’t know if they will be protective. There’s also this potential for them to be detrimental. This is not the only infection for which that phenomenon occurs. For dengue viruses that happens where, if you’ve been infected once, and then you get infected again, you’re much more likely to get hemorrhagic fever. If SARS is any indication, and what we’re seeing so far for COVID-19, we need to be a lot more cautious when it comes to talking about immunity.

MARIA ANDRIELLA O’BRIEN

There’s been talk about whether or not COVID-19 will become endemic—you know, regularly found among people living in certain parts of the globe. Any thoughts on where we might see that happening?
In order for an infection to establish, it’s pretty basic ingredients. You have to have the maintenance of susceptible individuals in the population for that virus to be able to stick around and maintain infections in the population, and the virus has to be able to continue propagating. You always have to have at least one person infected at all times for the virus to not go extinct. There are only a couple ways that viruses ever drive themselves to extinction and that typically only happens if they’re so infectious and so lethal that they kind of burn through susceptibles very fast, they kill people that they infect, and so they kind of burn themselves out, and can go extinct. The second way that viruses are driven to extinction is usually by the hand of humans, where we try to drive them to extinction. And that’s either by doing things like quarantine, contact tracing, vaccination, where we literally try to get rid of every single infection in the population—every single infection in every population in the world, simultaneously so it’s driven extinct. To date, there’s only been one human infectious disease which we’ve ever driven to extinction, that’s smallpox. Polio has been a very long, long fight to drive polio to extinction, which still has not happened. Guinea worm is another example, that’s very hopeful right now. And so, as far as I see it, if we were to be able to have a vaccine that induces sterilizing immunity, which is immunity that protects from infection rather than just protects from symptoms or disease—that’s a very important thing. Then, and we were able to vaccinate a sufficient number of people, which given how transmissible this virus is, is you know, going to be a very high percent of the population. If we’re able to vaccinate enough people, fast enough, we could potentially this thing to extinction. But that would require, again, a vaccine that induces sterilizing immunity and there is a chance that we could stamp it out by tracing every single infection, and that’s going to be people who aren’t even showing symptoms and that is very, very difficult. It’s one of those things, it’s possible it won’t become a recurrent disease, but it’s going to take a lot of effort for it not to—or it would have to burn itself out, which I don’t think that that’s super likely given the biology we know at this point.

Are there any policies or steps that you think could be game-changers, aside from vaccines, which I think are the obvious items that come to mind?

Vaccines are going to be very important when it comes to the long-term maintenance of this public health crisis; getting the public health crisis under control and preventing this from being a high-death toll recurrent epidemic disease—vaccines are going to be what we have to lean on. But the other thing that we can lean on, both going forward and sooner than we have a vaccine, is coming up with therapeutics that are meant to deal with the hyperinflammatory responses and
cytokine storms that are actually killing people. Because right now, there’s a very high portion of infections that are undocumented; they’re undocumented either because those individuals are not showing symptoms, they don’t know that they’re sick or they’re not in touch with the healthcare system—there are many reasons for that. But the thing is, is that given that a large majority of these infections are likely not so severe, the big problem, is people dying of the infection and people being hospitalized, people having ARDS (acute respiratory distress syndrome). If we can understand the biology that’s triggering that, and we know that at this point, it’s the immune system. So, if we can have anti-inflammatory treatments that are meant to manage the damage that is done by our immune system, then potentially, the infection could still be around but we would still be protecting people from the severe disease. And this is not the first infection for which we’ve had this type of phenomenon. I did my PhD on polio, and for polio, the large majority of people—over 99% of people infected—didn’t show symptoms, or they would have very, very mild symptoms. But it was that one percent that would be paralyzed for the rest of their lives by the virus. And so, with the two polio vaccines, one the vaccines is actually not so great at protecting you from infection, but it’s really, really good at protecting you from being paralyzed. That’s a vaccine that we use here in the states. That vaccine is similar to what a therapeutic would be—a therapeutic that targets the immune system in this case for COVID-19, where you can have something that it’s not going to protect you from the infection, but that’s okay—as long as it’s keeping you from ending up on a ventilator or succumbing to the disease completely. And so, that’s what I think is actually quite hopeful and am looking to being able to contribute to.

MARIA ANDRIELLA O’BRIEN

Speaking about how our immune system reacts, some of your work has focused on how the human immune system seems to change throughout the year. Can you maybe talk to how some of that variation might impact the way our bodies respond to COVID-19?

DR. MICHAELA MARTINEZ

Some of the work that my lab does focuses on circadian rhythms and seasonal changes in the human body. Circadian rhythms are 24-hour cycles in our body that are driven by our body clocks. And seasonal biological rhythms, which we call annual rhythms are similar, but they happen on the calendar year. I got into this area as an ecologist; humans, we’re mammals, and we’re not all that different from other animals—there’s a reason why mice are used as model systems in immunology—it’s because we have similar immune systems. On this principle of biological clocks are very evolutionarily old, we see it’s very common among vertebrates so like, mammals, birds, that they have these seasonal rhythms, including in their immune system that we started to look at this for humans as well. And so, what we found to date is that the immune system has its own biological clock. So, cells of our immune system are ticking away around a
24-hour cycle and our immune system gets restructured and right now the hypothesis we’re trying to test is that, these 24-hour clocks in the cells our immune system, if they actually change with the seasons as the day-length changes. Because our body clock is actually trained by light and at this point, we’re actually waiting after the shut-down, to be able to analyze all of our seasonal samples. But the main reason we’re looking at seasonality is to be able to understand how we can potentially use this restructuring that happens not only in our immune system but also our hormones, our metabolism, to improve the efficacy of things like vaccines or treatments. If we have a full understanding of how our bodies are changing with the day and night, and with the seasons, then we may be able to find windows of opportunity when we can administer therapeutics where we just give them that extra edge to have them be more effective. And so, this is something potentially down the line could play a role when it comes to the timing of vaccination but right now we’re still in early days of it.

MARIA ANDRIELLA O’BRIEN

One last question before we wrap up, on the topic of immune systems. Kids don’t seem to be getting COVID-19, or at least we’re not sure if they’re getting them, they’re not showing the symptoms and we haven’t done mass testing of kids to really understand what’s going on with them. So, I’m going to ask you: what do you think is going on with them?

DR. MICHAELA MARTINEZ

So, this is something that we’re actively trying to kind of pull together the state of the science on it. I have to give credit to our full group, myself and then Andrew Yates who’s over in pathology, Andrea Graham who’s at Princeton University, and then Natalie Riddell who’s at the University of Surrey which is outside of London; we have all of our labs working on the immunopathology of COVID and this is something that we have discussed very actively and right now kind of our working hypothesis on this is, the older an individual is, the more vulnerable they are to severe outcomes. And for young children, we are seeing very, very little severe outcomes. Now, when we combine that observation that we’re seeing at the population level with the immunology data that we have so far, which is literally by scouring the literature for SARS-CoV-2 and for SARS, what we found is that, as I mentioned before, what is making people very sick, so what drives ARDS is a hyper-inflammatory response. It is cells of your immune system that start doing damage to the lungs, and they start releasing all these chemicals that are inflammatory molecules, and it is that damage to the lung, which is making it so people are ending up on ventilators, and then if this continues, that all of these what we call “a cytokine storm,” our immune system starts making so many of these inflammatory molecules that it literally makes your organs start shutting down, and that’s what’s killing people. And so, all of that process, that part of your immune system that is doing all of that damage, is the memory part of our immune system and that’s the part of our immune system that learns through time, as we’re exposed to
lots of things throughout our life. Now, if we look at this memory side of our immune system, our “adaptive immunity,” as we call it, it’s very, very different in older individuals versus children because their immune systems are still in early phases of learning—just like their minds are, right. We actually think it is the state of our immunological memory, like how many cells we have that are memory cells, that are prone to inflammation because they’ve been dealing with pathogens for so long that they’re literally in a different state in older adults than in children. In the context of COVID-19, but other work that I’ve been involved with in the same group, we’ve discussed a lot—you can think about time, instead of chronological time, we think about people’s age in chronology, like “Are you 10 years old? Are you 50 years old?” You can think about “immunological time,” the state of people’s immune system being reflective of their age and their response to environmental challenges like pathogens. We actually think, this is a newer idea, within immunology and biology in general, there’s more and more evidence that the aging process is tied to the immune system and it’s immunosenescent; so, these changes in our immune system that actually drive our bodies to senescence, and eventually death. Most death is actually caused by our immune systems, ultimately. We think that the difference between older individuals and younger individuals is probably hidden there in this immunological memory side of it because it’s that part of our immune system that eventually leads to very severe outcomes for COVID.

MARIA ANDRIELLA O’BRIEN

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