Dr. Angela Rasmussen

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Marianne O'Hare: Welcome to Conversations on Health Care with Mark Masselli and Margaret Flinter, a show where we speak to the top thought leaders in health innovation, health policy, care delivery, and the great minds who are shaping the health care of the future.

This week, Mark and Margaret speak with Dr. Angela Rasmussen, who leads the Core Virology team at the Center for Global Health Science and Security at Georgetown University Medical Center. She's an expert on emergent pathogens like Ebola, MERS and now SARS CoV-2, COVID-19. She's a leading expert on what drives the expression of viruses in humans, and talks about the importance of masking and getting vaccinated.

Lori Robertson also checks in. The Managing Editor of FactCheck.org looks at misstatements spoken about health policy in the public domain, separating the fake from the facts. And we end with a bright idea that's improving health and wellbeing in everyday lives.

If you have comments, please email us at chcradio@chc1.com, or find us on Facebook, Twitter, or wherever you listen to podcasts. And you can also hear us by asking Alexa to play the program Conversations on Health Care. Now, stay tuned for our interview with Dr. Angela Rasmussen here on Conversations on Health Care.

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Mark Masselli: We're speaking today with Dr. Angela Rasmussen, who leads the core virology team at the Center for Global Health Science and Security at Georgetown University Medical Center. Her global renowned team centers on emerging pathogens like Ebola, MERS, and now SARS CoV-2 or COVID-19, focusing on genetic and other factors that drive severe infection in humans.

Margaret Flinter: Dr. Rasmussen is a frequent contributor across the media landscape on the science behind COVID-19, from the effectiveness of mask use and vaccines and also the threat of emerging variants. She also serves on the NIH Advisory Committee on changing the culture to end sexual harassment. Her work has been published in numerous journals including [inaudible 00:02:02] and the New England Journal of Medicine. Dr. Rasmussen, we welcome you to Conversations on Health Care today.

Dr. Rasmussen: Thank you so much for having me.

Mark Masselli: Unfortunately, we have this grim milestone that the US reported this week, more than 400,000 Americans have died from COVID-19 since the pandemic began. The Novel Coronavirus, as it was first known, sent the global scientific community really into overdrive, trying to

develop a consensus on what the pathogen was and how to contain it. We've learned so much so quickly. I'm wondering if you could share with our listeners how formidable foe is COVID-19 and where do you think we are in terms of the pandemic's trajectory.

Dr. Rasmussen: Well, you know, one of the things that I think myself and a lot of my colleagues were thinking about when the news that this was a Coronavirus first came out about a year ago, was how much it was going to be like SARS classic or MERS Coronavirus. And this virus is different actually in two key ways, one good and one bad. The good part is that this certainly has a much lower case fatality rate than either SARS Coronavirus, or MERS Coronavirus. So that's excellent news. But the bad news is that it's much more transmissible. Unlike SARS classic, it can be transmitted and transmitted very effectively during the pre-symptomatic period.

Unfortunately, because we responded with really half measures such as travel bans, rather than focusing on increasing our testing and tracing capacity that would have allowed us to control this from the beginning, right now where we're at is a situation of uncontrolled community transmission throughout most of the US and in other parts of the world. And that means that people don't know when they're being exposed, they don't know that they're at risk potentially, of transmitting it to others, and that has compounded as it has spread through the population. But I think that the good news for the future of the pandemic is that now we do have vaccines that have exceeded our wildest expectations in terms of their efficacy. So really, now it's a race against the clock to see how quickly we can get as many people vaccinated as quickly as possible.

Margaret Flinter: You know, Dr. Rasmussen, one of the more confounding things about the virus is that the way it seems to just you know deal a light blow, a glancing blow to many who become infected and yet send others into what we call the cytokine storms with very rapid decline. You have long studied the drivers of Pathogenicity of viruses. When we look at the collective science that we now can agree on, as well as your own research, what do you think are the most important drivers of both infection and severe disease with COVID-19?

Dr. Rasmussen: Well, I can tell you from a molecular perspective, I think that what you just mentioned, whether a person goes into a cytokine storm or not is clearly one of the most important factors in driving COVID-19 severity, and that probably has something to do with the speed and the robustness at which a person can mount an effective innate immune response. So we've seen that people who have more severe disease outcomes tend to have diminished interferon response. An interferon is sort of like a fire alarm and a sprinkler system all in one. It will detect that there's a viral infection there, and then it will begin

secreting cytokines. When that doesn't happen at first, that results in a less effective adaptive immune response, and that also results in essentially uncontrolled inflammation. What we still don't really know is what predisposes a person to have that delayed response. It's certainly genetic. It probably also has a lot to do with epigenetics, probably also has a lot to do with other comorbidities, potentially even diet and environmental factors. So it's really complicated. We can model this and that is something that I'm working on, something many of my colleagues are working on, trying to look at that using animal models, but ultimately we still don't really have a very good idea about what predisposes a person to have those types of responses that cause severe illness.

Mark Masselli: Dr. Rasmussen, you know, we've had a number of guests on over the years. Over this last year, Dr. Fauci has been on a couple of times. People are focused in on this mutation or this new strain, the UK variant that's come up. I think we've heard from him and maybe others that Coronaviruses, they're going to mutate, they're going to do things, and I'm wondering what's your sense of this variant.

Dr. Rasmussen: So this is still very much an ongoing area of research, but the epidemiological evidence does suggest that both the B117 UK variant, as well as the 501Y.V2 variant from South Africa, and the P1 variant from Brazil, are all more transmissible. And that's largely based on epidemiological evidence that those variants rapidly became dominant, suggesting that they had some sort of advantage to outcompete other variants. We do expect variants to emerge, and it's not unreasonable to expect that variants would emerge that are more efficient at infecting a human host, because that's really what a virus is driven to do evolutionarily. In terms of immunity, I mean, that's really the million dollar question right now, we really do need to know how well vaccines are going to work against these, and new preprints came out suggesting that while the B117 variant doesn't appear to be a problem in terms of the vaccine, the mutations in the 501Y.V2 variant from South Africa, are another story, and we should be concerned because several of these mutations have been shown to reduce antibody neutralization. So antibodies do not neutralize it as well.

But the good news here is that when you have serum from somebody who's been vaccinated, they're making antibodies for the entire spike protein. And the same study that showed that those particular mutations resulted in a loss of neutralization, were still effectively neutralized by vaccinated sera. So, the serum from people, the totality of the antibodies that they made against the spike protein in the vaccine, were still capable of neutralizing at least pseudoviruses that contained that spike protein. So that suggests that overall, the antibodies are generating a response that's still protective. The

bottom line here is that vaccines should probably still work against these new variants, but we do need to do more genomic surveillance to see other variants that might emerge in the future, especially as more people get vaccinated, and there's going to be increased selection pressure on the virus to mutate further. Again, we need to vaccinate as many people as possible and keep looking at the virus to make sure we don't need to adjust the vaccines in the future.

Margaret Flinter: Well, we have seen the arrival of the vaccines. The speed at which they were developed, the safety testing with which they were developed is really one of the few bright spots in this pandemic. There is still a lot of vaccine hesitancy. Give us what you use as your best both scientific and layperson argument for why the vaccine really is both safe and effective as we're trying to communicate this message out to people and get them to take advantage of the fact that the vaccines are here today.

Dr. Rasmussen: There are a lot of different reasons, many of them justified for being hesitant to take these vaccines. I start usually by reminding people that these vaccines, and the speed at which they were developed, and their efficacy is really one of the greatest scientific achievements of my lifetime, and we should really regard it as that. I think it's really important that we engage with people with what their actual concerns are, and we should do so seriously. Vaccine hesitancy can be associated with these more extreme views, and often with people who are not going to be convinced that vaccines are safe or effective no matter what you say to them. I think we need to stop approaching vaccine hesitancy as if all people are coming from that space, because I think many people who are concerned about the vaccines really do have legitimate concerns. And for example, people want to know if these vaccines were developed so quickly, and this pipeline normally takes years and years or even decades, then how do we know that these vaccines actually do work and are safe.

And we normally develop vaccines as a sequential process. We start by spending a couple years designing the vaccine, then we spend a couple more years testing it on animals, then we spend a couple more years doing Phase I, II trials, then we finally spend a couple more years after that doing phase III trials that usually go for a lot longer, because we're also looking at vaccine durability. In this case, we did many of those things at the same time. So the vaccines that are ahead in the race, the ones that already have authorization, are vaccines that can be designed using computers. We already had some data suggesting that mRNA vaccines are safe from other phase I trials that had been done before the pandemic, so we were able to move right into phase I clinical trials while doing the preclinical animal studies at the same time. Now, the phase III part of the process was done in a more rapid period of time because we decided not to look at

durability, and that's really the one thing that's been sacrificed. So we still used tens of thousands of patients, the trial sizes for the phase III trials were the same, we just didn't look at durability, but that's still going to be looked at long term.

But the number of people that we looked at in the phase III trials is comparable and that allows us to look at safety, at least short term safety very effectively. We didn't really sacrifice anything. And using symptomatic COVID-19 as an endpoint for the trial rather than looking at something like infection, that maybe harder to measure in asymptomatic people, allowed us to get efficacy data very quickly. Now, that's not the only form of vaccine hesitancy. Others are concerned about whether the vaccine is going to be safe for certain subgroups of people, and in particular communities of color, because historically, those communities have been terribly exploited by biomedical researchers, and in addition to that, actually I think that those communities are disproportionately affected by the pandemic because of disparities that exist due to racism.

So I think that it's really important also to engage very seriously with those concerns, and in many cases, to have trusted messengers. So, people from their own communities, as well as physicians from within those communities communicating exactly why those vaccines are more important for the higher risk communities to be taking than not, and that ultimately these vaccines save lives. And some people are just saying, well, I'd rather wait and see. And sort of by necessity, most people are going to have to wait and see because we don't have a sufficient supply to vaccinate everybody on demand right now. What we really need to be thinking about right now at this moment, is how we're going to improve distribution. To give the vaccine to everybody who wants it and everybody who needs it we need to be thinking about all of these things, but we also need to be thinking about what is the most urgent problem facing us right now, and that is vaccine distribution and supply.

Mark Masselli: We're speaking today with Dr. Angela Rasmussen, who leads the virology team at the Center for Global Health Science and Security at Georgetown University. Well, we have the 46th President who has been inaugurated, and really he's called for a huge public health intervention. But we also have wearing mask, for those who are hesitant, we remind them wearing masks, social distancing, and avoiding large crowds is very important. But I want to get back to the virus itself. It seems to me that it's finding ways to survive, and that we've got to have more clinical trials that are going on. Talk about what other things are happening in the background, because I would assume that we want to do other types of trials, not only on vaccines, but we also want to look at all these others. Who's leading that? Where in the scientific community they're saying, hey wait, we need

to start running some parallel studies to look at opportunities that might be in front of us?

Dr. Rasmussen: Well, ultimately, when it comes down to testing products, whether they be vaccines or therapeutics, academic institutions are not capable of making a product that will be sold on the market. They don't have the manufacturing capacity, they don't have the regulatory resources, things like that. So ultimately, if you're talking about something that's going to be used for the public, unless it's something like convalescent plasma, that's not really a pharmaceutical product, you're really talking about making sure that you are partnering with a pharmaceutical company. But you know, there are plenty of academic institutions that are running trials with existing drugs, using things like back when we were all talking about Hydroxychloroquine, a number of different academic institutions were running clinical trials with that, because it's an already available existing generic drug, and in that context, you're just using something that's already there and so you can test it out in your own medical center.

For new vaccines, all of them have a pharmaceutical partner, because they will certainly need somebody to manufacture and distribute that vaccine, as well as to seek FDA approval, which is a very expensive and cumbersome process. Around the world though, there are numerous trials going on for both novel therapeutics and making new vaccines, you know, many vaccines that are at different places in the development pipeline. I think the last time I checked the tracker there were over 300 different vaccine candidates. Some will only be available in certain countries, and so this is where organizations like the World Health Organization come into this. That is something that hasn't gotten as much coverage here in the US, just because our prior President expressed intentions to withdraw from the World Health Organization and did not participate in the Covax Group, which is a consortium of countries led by the WHO, by CEPI, and GAVI which are two vaccine organizations to develop vaccines and manufacture and supply them to the entire world. And this is something we need to be thinking about long term.

It's not necessarily developing new vaccines, but it's figuring out how we can take the vaccine supply that we have, get it from countries, wealthy countries like the United States, and make sure that they're being equitably distributed worldwide. Because especially in places that don't have as much health care infrastructure, low and middle income countries that may not be able to purchase millions and millions of vaccine doses, it's going to be absolutely critical that we still find a way to get vaccines to all the people in those countries. Because this is a pandemic and by definition, it's affecting the entire world, this isn't going to be over once we reach the herd immunity threshold in the United States. This will only be over when we reach

the herd immunity threshold globally. So that I think is something that I'm hopeful that the new Biden administration will be more involved in, is really working with international partners collaboratively to make sure that everybody in the world can have access to these vaccines, because until all of us are safe, none of us are safe**.**

Margaret Flinter: You know, Dr. Rasmussen, I'd be curious for your thoughts on what we've learned, right? I think back to the days in New York last spring, and your heart just goes out to all of our clinical colleagues who had so little tools to work with. You know, aside from all the worries about PPE and so forth, we just didn't know a lot about how to treat this. And my guess is that we have learned some very important things about how to treat cytokine storm and how to treat other overwhelming viral infections like that. And I wonder if you could, it's kind of a complicated question again, but both comment on what we've learned about the care of the individual, and what we've learned about what we need to do as a public health community whenever a new threat like this arises down the road. Can you try and talk about at least one of the two?

Dr. Rasmussen: Yeah, I can try to tackle that in general. And it's probably going to have to be the latter question about preparedness, because I'm not a physician, I don't treat patients, and the only thing I can say about that is that it's clear from talking to my colleagues who are physicians, respiratory therapists, nurses, who are treating patients that we have come far in how we treat people who have severe COVID at least, but really, we don't have a lot of really good targeted strategies. Our antiviral drugs are only really effective. They're kind of effective, but they have to be given as early as possible, and given that they're all delivered by IV infusion it can be very difficult to do that at the time of diagnosis. We also don't have a sufficient supply to be treating everybody who tests positive for SARS Coronavirus-2 with therapeutic monoclonal antibodies, for example. So, you know, that has been sort of -- it's been a disappointment that we don't have better antiviral therapeutics.

In terms of treating the cytokine storm, a lot of the clinical trials for existing drugs that target specific cytokines, such as Tocilizumab, which targets IL-6, which is a major pro-inflammatory cytokine, have really been also disappointing. They've really showed no effect or therapeutic benefit. The only thing that has, is a really old drug, but that's also a very, very potent broad spectrum anti-inflammatory steroid and that's Dexamethasone treatment, which does have a significant mortality benefit, at least for patients receiving supplemental oxygen. So we've come a little ways, but we still have a long way to go, I think, in terms of translating what we know about the pathogenesis of COVID-19 into treatments that will be useful in the clinic and will be available to a lot of people who need them. I

think though, that in general, for public health and being prepared for other pandemics, that that will happen, because it's not a question of if, but a question of when. There are thousands of other circulating Coronaviruses alone. Plus, there are 24 other families of viruses that can also have the potential to be human pathogens. And in a sense, we should count ourselves lucky that something like this emerged instead of something like a more transmissible Nipah virus, for example, that has a much higher fatality rate.

So, we need to be prepared though, for that disease X to emerge in the future, and that means basically increasing our investment in research across the board. And that's everything from basic research, surveillance, basic virology to understand better how these viruses work so we can try to find some of their weak spots, all the way up to translational things, looking at new vaccine platforms that could be used to generate new vaccines against a novel pathogen very rapidly. Things like, you know, how would we potentially take mRNA vaccines for example, and be able to start manufacturing them right away without necessarily needing to do a phase III clinical trial. How would we be able to speed up the process?

And I think the vaccine operation warp speed, the expedited vaccine review process, does give us a starting point at least for removing some of the regulatory roadblocks and red tape that sometimes get in the way of this. But ultimately, I mean, I think you can’t always fix problems by throwing money at them, but you also can't do meaningful research if you don't have funding to support it. And historically, with Coronaviruses anyways, but many other emerging viruses, when there is an epidemic of a novel emerging virus, and this is true for SARS, for MERS and I hope it won't be the case for SARS-2, there's an immediate influx of funding as people are paying attention to the crisis. And so people drop everything and start working on these viruses, and then that money goes away, so they can't renew their grants. Any research they were conducting on the virus will stop because they can't afford to keep doing it.

We really need to stop funding scientific research, especially that has important pandemic preparedness implications with this boom and bust cycle of funding. If we really want to be prepared for the next pandemic, we need to make sure that we're doing the research before that virus emerges and not scrambling to find out about it afterwards. And that means that we're going to have to make a significant investment without an expectation of a payoff because that's the irony of pandemic preparedness research. If you're actually succeeding at it, then it looks like you're not doing anything because there's no new pandemic. So I would hope that people, as they're more interested in science and viruses in general, which is a wonderful silver lining anyways of this pandemic for me, I hope that

people will also remember this for some time to come and understand why we need to put more effort into preparedness measures like this.

Mark Masselli: We've been speaking today with renowned virologist Dr. Angela Rasmussen at the Center for Global Health Science and Security at Georgetown University. You can access her many published papers and articles by going to www.angelarasmussen.org, or you can follow her on Twitter at @angie_rasmussen. Dr. Rasmussen, thank you so much for your tenacious efforts of your own and of your colleagues in uncovering the secrets of all these deadly global pathogens, your innate gift to making it understandable, and also for joining us today on Conversations on Health Care.

Dr. Rasmussen: Thank you.

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Mark Masselli: At Conversations on Health Care, we want our audience to be truly in the know when it comes to the facts about health care reform and policy. Lori Robertson is an award-winning journalist and Managing Editor of FactCheck.org, a nonpartisan, nonprofit consumer advocate for voters that aim to reduce the level of deception in U.S. politics. Lori, what have you got for us this week?

Lori Robertson: Two COVID-19 vaccines are now authorized in the US by the Food and Drug Administration, one vaccine from Pfizer and BioNTech, and another from Moderna. We'll take a look at how these vaccines work. Both the Pfizer BioNTech and Moderna vaccines are mRNA vaccines that require two doses. The vaccines work by triggering an immune response against the spike protein of the SARS CoV-2 virus. That spike protein sits on the surface of the Coronavirus and is what the virus uses to enter cells. The vaccines are made of modified messenger RNA, or mRNA, wrapped in a special blend of fatty molecules known as lipid nanoparticles. The mRNA provides instructions for cells to make their own spike proteins, prompting the body to generate protective antibodies and activate T cells. The lipids help deliver the RNA into cells and prevent it from being degraded too quickly. As the Centers for Disease Control and Prevention has explained, there is no way to catch COVID-19 from this type of vaccine because the vaccine is not made of a virus. And because the mRNA from the vaccine doesn't enter the nucleus, the part of the cell that houses DNA, it ‘does not affect or interact with a person's DNA.’ contrary to some online rumors. And that's my fact check for this week. I'm Lori Robertson, Managing Editor of FactCheck.org.

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Margaret Flinter: FactCheck.org is committed to factual accuracy from the country’s

major political players and is a project of the Annenberg Public Policy Center at the University of Pennsylvania. If you have a fact that you'd like checked, email us at www.chcradio.com. We'll have FactCheck.org's Lori Robertson check it out for you here on Conversations on Health Care.

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Mark Masselli: Each week, Conversation highlights a bright idea about how to make wellness a part of our communities and everyday lives.

Over the past few decades, kids have been getting less and less physical activity throughout the school day. The University of Michigan researchers wanted to find a creative and effective solution that would increase kids' movement without disrupting the school day.

Dr. Rebecca Hasson: We looked at the scientific literature in terms of prolonged sitting, and they have demonstrated that if you just do two minutes of activity, a small burst, get up, do some movement, sit back down, activity in that small of a dose can have dramatic improvements on health, on cognition, on learning. So we decided to develop an intervention, a program that would allow children to get these small bursts of activity throughout the day.

Mark Masselli: Dr. Rebecca Hasson is principal investigator for InPACT - Interruption of Prolonged Sitting with Activity. She wanted to find out if just two to three minute short bursts of physical activity five times a day would impact the kids' cumulative movement.

Dr. Rebecca Hasson: We typically see in PE or recess lower participation in girls compared to boys, but in classroom activity breaks you actually see similar rates of participation. We also saw that for children who are carrying a few extra pounds, that those children also were exercising at a high intensity.

Mark Masselli: Dr. Hasson said they wanted to design the intervention that would be easy for teachers to adopt and manage. So they created videos designed to get kids moving quickly.

Dr. Rebecca Hasson: We created a compendium of 200 activity breaks that are just three minutes long. So the teachers had a variety of different types of activities, whether it was jumping jacks, something that will get their heart rate in a target heart zone.

Mark Masselli: Kids burned on average about 150 more calories per day, had accrued a significant amount of physical activity. A low cost, easily adoptable fitness intervention for kids, allowing short bursts of physical activity throughout the school day, empowering kids to move more positively impacting the learning experience, now that's a bright idea.

Dr. Angela Rasmussen

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Mark Masselli: You've been listening to Conversations on Health Care. I'm Mark Masselli.

Margaret Flinter: And I'm Margaret Flinter.

Mark Masselli: Peace and Health.

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Marianne O'Hare: Conversations on Health Care is recorded at WESU at Wesleyan University, streaming live at www.chcradio.com, iTunes, or wherever you listen to podcasts. If you have comments, please email us at www.chcradio@chc1.com, or find us on Facebook or Twitter. We love hearing from you. This show is brought to you by the Community Health Center.

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