Dr. Jason Elinoff

Behind the Mask

January 7, 2021

GB: Good afternoon. Today is January 7th, 2021. My name is Gabrielle Barr. I am the archivist at the Office of NIH History and Stetten Museum, and I have the pleasure of speaking with Dr. Jason Elinoff. Dr. Elinoff is an investigator with the Critical Care Medicine Department at the Clinical Center, and today he's going to speak a little bit about some of his COVID-19 research. Thank you very much for being with me.

JE: Thank you for inviting me, Gabby. Appreciate it.

GB: My first question is: Can you shed a little light on the background of your study that is looking at the impact of SARS-CoV-2 to infection on the pulmonary vascular endothelial cells?

JE: The background comes from some of the initial clinical descriptions of patients, some of their complications, and symptoms and manifestations of COVID-19. It implied that there was a role or potentially involvement of the blood vessels in the body and in particular of the blood vessels in the lungs. That was an area of biology and research that we had been involved in with our studies in pulmonary arterial hypertension. Specifically, our area of interest was the cells that line those blood vessels in the lung called endothelial cells. Now endothelial cells line all our blood vessels throughout our bodies and, depending on the blood vessels, those endothelial cells have different characteristics and behave differently.

So, we had a very simple question: How did the virus which causes COVID-19, how does SARS-CoV-2 interact with those endothelial cells and what consequences does it have on endothelial cells? Our work is mainly in vitro, which just for ease of explanations is essentially in petri dishes. We create artificial systems to look at endothelial cells. But at the NIH we had the opportunity to collaborate with Jeff Taubenberger and Dan Chertow in NIAID and gain access to facilities where we could actually study live virus. And that's what we have ongoing experiments doing. We can expose these human endothelial cells to live virus and then do a number of things to look at: do the cells get infected, do they become abnormal, do they function abnormally? And try to relate that back to what we're seeing in patients.

GB: Okay, that's very interesting. You answered some of this, but can you describe how your work with pulmonary arterial hypertension prepared you for tackling COVID-19? What are the similarities and differences that you have found between COVID-19 and arterial hypertension?

JE: One of the most important things is that we were interested in lung biology before COVID-19 and specifically in the blood vessels in the lung. So, as it's becoming apparent that COVID-19 may impact the blood vessels of the lung in a unique way or it may impact it in a way that other viruses don't, we had the background or experience to start to ask questions about those effects. Now interestingly pulmonary arterial hypertension, although it's a chronic disease, is characterized by a lot of features such as inflammation, abnormal clotting of blood, and other things that have also been attributed to COVID-19, and the effects of SARS-CoV-2. And so a lot of the same biological processes that we were interested in a more chronic disease of pulmonary arterial hypertension may be manifesting in an acute way or in a short time frame in patients with this viral infection.

I guess the other overlap is that there are some hypotheses or theories about the triggering of pulmonary arterial hypertension being related to either proteins involved in the antiviral response called interferons and also potentially being related to prior exposure to maybe an undocumented viral infection that sort of triggered something. That overlap and kind of commonality—I don't know that it necessarily prepared us but it made the endeavor potentially worthwhile or have added value to whatever we learn in this kind of new direction that we've taken may actually have important implications for our work in pulmonary hypertension.

GB: That's interesting. I did have a question as I saw that you had written a little bit about your study and you had said that pulmonary embolism and shock are the most common causes of death with hypoxic respiratory failure which you said was the most predominant clinical manifestation.

JE: I should clarify, I guess. I think that pulmonary embolism or blood clots in the lung have been observed in patients with COVID-19 and they're a common cause of death—I should clarify they're probably not the most common cause of death—but those two manifestations, blood clots in the lung or shock which is associated with low blood pressure and sometimes dysfunction of the heart are causes of or complications of COVID-19, just to distinguish them from the pneumonias and the kind of abnormalities that we see in the lung tissue that is the most common severe manifestations. Even though that's the more common severe manifestation, there are these other manifestations that are clinically relevant and may be separate from pneumonia or may be related. So that description was just to bring relevance to the vascular contribution to COVID-19, the effect that the SARS-CoV-2 may be having on blood vessels throughout the body.

I should say another frequent clinical feature in patients is kidney dysfunction and kidney failure which again may be linked or tied together with blood clots and heart dysfunction and blood vessel dysfunction because of involvement or effects on blood vessels throughout the body. But those are hypotheses that we and others are testing.

GB: That was one of my other questions. What are other pulmonary and vascular complications of COVID-19 that exist that people may not even be aware of?

JE: It's hard with social media out there and all the other literature and the number of articles, there's not a lot that people are unaware of right now. But I think some of the things that we're still trying to sort out is, for instance, with regard to blood clots in the lung: How much is this really happening more frequently in patients with COVID-19 versus other types of patients with similar either viral pneumonias or pneumonias caused by other conditions or other organisms? Is this something specific to COVID-19 or are we just looking into it more? We're better able to group together such large numbers of patients under the umbrella of COVID-19 that some of these manifestations look like patterns but may or may not necessarily turn out to be such unique features of COVID-19. I think that's still undetermined.

I guess the other thing that we don't know yet but I think people are wondering about are what are the potential long-term effects on lung function in patients that recover and how does that differ based on how severe their disease was at the time? That's another unknown. I'm sure a number of people are interested, including some of my colleagues at the NIH Clinical Center, Anthony Suffredini, Jeff Stritch, Dan Chertow, and Parizad Torabi-Parizi are all working on a natural history study to look at these patients over time and measure things related to their lung function, so that that'll be interesting to know.

GB: Can you please describe how your particular study is set up and the different aspects of the SARS-CoV- 2 infection that you're analyzing?

JE: As I mentioned earlier, our study currently, or a major part of it right now, is we are investigating different cells, endothelial cells, from different donors which are available commercially, and we're looking at specific types of endothelial cells in the lung and we're exposing them to virus to see if the virus enters the cell, does the virus replicate in the endothelial cells? Then also we want to study what are the consequences to things like inflammation in the endothelial cell? Do these cells become abnormal, do they get sort of activated and start producing things like cytokines which are proteins involved in inflammation, and can we correlate some of the things that we find the endothelial cells are producing with some of the samples we get from patients? There's a lot of talk about cytokines and inflammatory proteins, inflammatory mediators, that are being looked at in patients and even therapies directed at these pathways and molecules. When we expose endothelial cells in the lab to the virus, do we see similarities with what we see in blood samples from patients? We're also interested in comparing different cells from different organs to see is there any difference in susceptibility to the virus? Endothelial cells from certain parts of the lung to other parts based on the size of the blood vessels. Endothelial cells from the heart versus those from the lung. Also a question is there a difference across the donor, or for lack of a better word, for the differences in patients, so if we look at ten different sources of endothelial cells, do all ten get affected similarly or are there differences and what might account for some being more susceptible to viral infection than others? So that's a lot of questions that we're asking. Those are some of the considerations. And the one caveat being that this is an in vitro system. This is a sort of model system that we would have to see how much of it extends in terms of our observations to human and clinical either samples or lung samples, to see if we see consistency. Those are basic questions: Does the virus infect the endothelial cells? Whether or not it

infects the cells? What effects does it have on the cell? Does it change the cell behavior even without infecting it?

GB: How many donors have you gotten so far and how many are you shooting for with this phase of your study?

JE: Good question. The donors that we're getting here, these are cells isolated from commercially available sources, so these are not patients who are infected with COVID-19. These are organs that were obtained based on other conditions but generally healthy or normal circumstances prior to isolating the cells from the lung. How many we should look at is a good question. We could have probably on the order of half a dozen to a dozen different donors, but that's not known. Obviously, if we had unlimited resources in unlimited time, the more different types of samples we could get, the better. But at least as the first initial starting experiments are going to be done with around five to ten different donors just to see if we see any variability, because clearly clinically there's a lot of variability from someone getting infected with SARS-CoV-2 and having no symptoms to patients developing very severe disease.

GB: Have you noticed yet, you said one of your questions was differences in endothelial cells and like the heart versus the lungs. Have you seen that yet in your research?

JE: Yeah, that's still too early to say, so we still, unfortunately, don't have the answer to that yet.

GB: And I'm guessing the same with the patient population.

JE: Correct. That's still too early to say as well.

GB: One of my other questions was what challenges have you encountered to date and have there been anything that has surprised you yet?

JE: I think that the challenges, as many people or many different labs have been met with, are trying to get experiments done and lab work done in a safe way, keeping our colleagues safe, making sure that there's enough distance between people in the lab, making sure that we're able to do this. It's a balance between trying to get experiments done, but not having too many people in the lab for too long at a time for obvious reasons—so that's been a challenge.

I think also in this with some of our experiments we are fortunate to collaborate and have access to these fairly sophisticated laboratory environments where we can use the live virus, but that's a valuable

resource that is not accessible 24 hours a day, seven days a week. So that's another challenge, that the experiments that we want to do are not necessarily easy to do, but we're still fortunate that we have access to it.

As far as surprises, I don't know, I'm not sure if they would call them surprises, but recently there are studies already coming out about whether or not the endothelial cells are infected and there's still not yet consistency, I don't think, across the different studies and so maybe that's interesting to see. I mean part of that is probably because people are trying to get the information out that they find as quickly as possible to make it widely known, but that may not lend itself to careful double-checking and making sure that experiments are done rigorously. That sometimes can lead to kind of inconsistent results. I think that probably the main thing would be some of the still unsolved questions that are out there and some inconsistencies. But that makes it more appealing to continue our studies.

GB: Can you speak a little bit about the tools, technologies, and programs that you're using to conduct your study.

JE: I'd say one of the biggest, I guess for lack of a better word, tools or resources, is really the live virus. Within the NIH community pretty soon we're going to have access to different strains of virus potentially. We're very fortunate to have access to that resource. But in addition we are using, or plan to use once we set up our model system, some fairly sophisticated techniques for looking at changes in the endothelial cells in their gene expression in a genome-wide way. Not just be looking at a very few genes, but also using other technologies to examine changes in protein expression and production by the cells again, in a very broad unbiased way, to cast a wide net to find out what are the differences and what is the impact of the virus on endothelial cells. Then down the line the other thing we hope to utilize is some imaging capabilities to not only measure gene changes and protein changes but actually to look at possible structural changes in the endothelial cells and visualize what's going on in the cell in a very high-resolution way.

GB: What has been your role in this project?

JE: My primary role has been to try to organize and to coordinate our collaborations and our relationships with the different labs. I have some great colleagues that work in our lab, namely, Dr. Li Yuan Chen, Dr. Ed Dougherty, and a postbac, Alyssa Long, who's doing a lot of the work with cell culture. Then working with Jeff Taubenberger in his lab. A lot of it’s coordination and overseeing and then analyzing and interpreting results, discussing results. So, a little less hands-on with the day-to-day pipetting and stuff. Its more on a supervisory or advisory role, but there's fortunately a lot of input, a lot of discussion amongst our groups, and we try to get people's different viewpoints and the different perspectives and way of looking at things, they're approaching an obstacle or a problem as well as the way of interpreting results. I think it's important to try to include all those different opinions and things.

GB: Definitely. What has it been like to work at home or on campus? I imagine you're doing a combination.

JE: Right. I do still have to go back to campus both for lab work but also some clinical work in the ICU. Then actually some of our pulmonary arterial hypertension studies, we still have some ongoing, we have patients who come into the Clinical Center as part of maintaining those studies. I guess the balance of trying to make sure when you come into work that people are distanced. I currently share an office now which was very small pre-pandemic, and is now prohibitively small during the pandemic, so that we both really can't be there at the same time. That takes a lot of coordination. I would say when you're in the hospital taking care of patients, it doesn't seem all that different than previously. You know the hospital has maintained its activities as needed. Then working at home is challenging because of various interruptions but it's feasible, I guess, and I'm not the only one dealing with that. A lot of us are having to deal with that.

GB: Have there been opportunities now working from home?

JE: The one benefit has been definitely the ability to exercise on a more regular basis working from home; it's easier to fit that in than commuting back and forth to work.

GB: This is one of my last questions. Have you received your vaccination yet and, if so, what was that experience like?

JE: I got my first dose on December 28th. It went fine. Actually, just this week I had a little bit of itching and redness at the vaccine site but otherwise it's been fine. My wife is also in healthcare and she received her vaccine that day too. At the NIH we've been receiving the Moderna one. Through her work she received the Pfizer one, so we're our own comparative effectiveness study.

GB: Is there anything else that you would want to share as an NIH scientist but also as a person living through the pandemic?

JE: I think that the pandemic has brought a sense of unity among people at the NIH. I mean, we always had a shared purpose but this one has really crystallized into a unifying, shared purpose on a single entity in some ways and that's been neat to see. It's definitely been neat to see some of the patients that have been willing to participate in studies related to COVID-19 and their willingness to contribute to the knowledge going forward. That's been very impressive to see patients, and then all the workers in the ICU and the Clinical Center and their dedication. It has been really impressive, particularly the

nursing staff and respiratory therapists who have patient contact on a nearly continual basis of their 12-hour shifts, it's just been neat to see. They've performed exceptionally, I think is a good word for it.

GB: Thank you very much for your research and for speaking with me. I wish you and your family and those working with you all the best.

JE: Thank you very much.