Dr. Simone Glynn
Behind the Mask
May 25, 2021

GB: Good afternoon. Today is May 25, 2021. My name is Gabrielle Barr, and I'm the archivist with the Office of NIH History and Stetten Museum, and today I have the pleasure of speaking with Dr. Simone Glynn. Dr. Glynn is the Chief of the Blood Epidemiology and Clinical Therapeutic Branch at the National Heart, Lung, and Blood Institute (NHLBI), and today she is going to speak about some of the COVID work she's been doing this past year. So thank you very much for being with me.

SG: Well good afternoon , and it's a pleasure to be with you.

GB: Yes. To get started, briefly can you provide some background on NHLBI's Recipient Epidemiology and Donor Evaluation Study, also known as REDS, and then kind of explain how it's set up, and how understanding viruses like SARS-CoV-2 fits into its core functions?

SG: Sure. The REDS program, that's how we call it for short, is a large research program that currently includes four large blood collection organizations associated with 22 hospitals in the U.S. as well as participating hemo[tology] centers in Brazil participating with the University of Sao Paulo. This program which is now in its fourth phase—because actually the first REDS program started back in 1989 to study HIV and how to reduce the risk of HIV in blood products for transfusion—so this program now is in the fourth phase as of 2019. It is put together to evaluate and improve the safety and availability of the blood supply as well as the safety and effectiveness of transfusion therapies throughout the lifespan, from adults all the way down back to kids and babies. One of the major elements of this program, which conducts research, so large epidemiological studies, is that it has what we call the rapid research response capability to address emerging threats to the blood supply, and oftentimes these threats are under the form of infectious agents such as viruses.

GB: What has been your role in running the domestic REDS program?

SG: I am the program officer for this program and so I work very closely with researchers in the field of transfusion medicine and blood banking who are involved in this program to essentially put together some really key epidemiological studies to address some of the major research questions that we have to, again, make sure that the blood supply is safe for all the patients who need it.

GB: Part of the REDS program is an initiative that you lead called REDS Epidemiology Surveillance Preparedness of the Novel SARS- CoV-2 Epidemic. Quite a mouthful! That's also called the response

initiative or effort. When did you launch this initiative, and how did you go about doing that?

SG: Right, so, again, one of the roles that this large REDS program has is to be able to address potential threats to the blood supply, and the other thing the program does is that it allows us to leverage access to the blood supply and blood donors. So I'll explain a little bit more about that.

But as soon as we heard about this new virus that had emerged, we started thinking about what needed to be done to, first of all, evaluate whether SARS-CoV-2, the virus that causes COVID-19, posed a threat to the blood supply. Was it in the blood supply to begin with? And could it be transmitted by transfusion? That's an important question whenever a new viral agent occurs. And we had heard a little bit about some reports in blood donations in China that the RNA of the virus was present in a few donations. So we decided to put together a program that would evaluate whether we found evidence of the virus in the blood supply.

Also we wanted to leverage our access to the blood supply to evaluate assays to detect SARS-CoV-2, and you know it's quite important to whenever we have a new agent to make sure that we have good assays that are really going to be able to detect and be reliable about detecting the virus. We have a lot of experience doing that in the blood banking field. We also wanted to evaluate what was the proportion of blood donors who were found to have antibodies to the SARs-CoV-2 virus and be able to evaluate these proportions through time. And the reason for that is that it essentially tells you in this blood donor population, this is how many people have actually been exposed to the virus and had an immune response in the form of an antibody, and then since blood donors are giving blood throughout the U.S., you can do that. Because when they give blood, they often allow their blood to be used for research.

GB: How many participants have you gotten to date who have donated their blood for these serological studies?

SG: Well for the serological study that we did–so that's the antibody one—we were able to access 1,000 samples or more per month for six months in six different regions.

GB: Wow!

SG: I have not done the math, but it's quite a lot of samples to be able to find out what the proportion of blood donors who have been exposed to SARS-CoV-2 would be. Now, of course, [if we are looking for the virus itself in the blood] with blood donors when they donate, they don't know [if they're infected], right, because you need to be healthy to donate so you cannot have any symptoms. So they can be either pre-symptomatic or they can be asymptomatic. You know about 20 percent of the population seems to be asymptomatic even though they get the infection, or they could be developing symptoms maybe, but later on.

So it's a really good way of finding out what the proportion in different geographies is of the blood donor population [that has SARS-CoV-2] and then doing some statistical analysis and using the demographic information that you have, you can then extrapolate that to the entire population. And the study that we put together in REDS, that serological study in response, really was a pilot study because we did that in six geographical regions, but we put together the infrastructure and the methodologies that then was used by the very large CDC national serosurvey of blood donors [that] is being conducted as we speak where they've gone to all the states. So they are covering, I think, 60 geographical regions now but using the methodology that we developed in response.

GB: Can you talk a little bit more about that, how you developed your methodology?

SG: Sure. Essentially when you're thinking about developing such a large program like the CDC wanted to do, you need to make sure it's going to work before you go to multiple regions. What you need to do is you need to assess whether, for example, you have the right testing algorithm to find out if you have antibodies against SARS-CoV-2. It sounds simple; you just do one test, but actually you want to find a very sensitive and specific test to [do] that. You want to be able to run it in many samples very quickly, so you want a high throughput assay. And then you want to double check your result, right. So if you find something you want to double check that, yes, the antibody is really there. So doing that methodology about what kind of testing algorithm should be used is a very important piece of the pilot that we did.

Another thing that we did is there was a lot of statistical, analytical methodology involved because you need to extrapolate the information that you get on a sample of blood donors—you know the 1,000 per month that I mentioned—to all blood donors and then to the general population depending on the demographic characteristics that you have. And that requires, actually, statisticians and analytical people to work on that so you need to develop the methodologies around that as well.

GB: Were you surprised by any of your initial findings?

SG: I would say no. We confirmed again in this pilot study that this kind of study could be done. We found some interesting results in the sense that when we started the testing in March of 2020, less than one percent of the blood donors that we evaluated had antibodies against the virus, and then we could see the evolution of that percentage. So in actually five of the six regions, it went up to maybe two to four percent of the blood donors by August, but in New York, for example, it went up to about 14 percent, and that was a little bit earlier than that and then went back [down]. So you can get a really good idea about the proportion of your population. And then what you can do is you can compare that to the number of cases that were reported to the CDC, and then you realize that actually there are more people who actually got the infection than were reported to have the infection, which makes sense because we know that we have some asymptomatic people or we have people who think they have

maybe a cold or something and don't report it.

GB: Oh that's really interesting. So can you talk a little bit about the longitudinal study aspect of the response effort?

SG: Sure. So this is another study that we're doing within that response project. This is a study where it's ongoing, and what we would like to do is enroll up to about 150 people with SARS-CoV-2, and it's gonna be a mixture, but primarily it's gonna be donors who donated so they were healthy, but then a few days later they developed symptoms of SARS-CoV-2, and they essentially reported that. Blood donors are great for that; they will call back the blood center and they'll say, "Now I have probably COVID-19." So what the blood center immediately does is that it puts aside the blood, hopefully before it's transfused. Some of it might have been already transfused, but again we have no evidence at all, considering the study that we did in the first aim that any potential for transfusion transmission of SARS-CoV-2 is very, very small as compared with a respiratory route of it. So this is not a concern. But what they do is that they go ahead and set aside the blood and not transfuse it, of course, and then when we know about such a report, we can go back to these blood products, and in particular the plasma which is quite a lot of fluid if you want, that was saved, and we can test that plasma for the presence of a virus. And if the virus is present then that gives you a lot of plasma that then you can save in a repository that then we can make that repository available to investigators and to industry who are doing research on the pathogenesis or the vaccines or coming up with a new assay that's better to detect the virus. So having a repository that is shareable and provided to the investigators is also one of the things that we're doing in response.

GB: Yeah, what has it taken to get that together?

SG: Well, we're still in the midst of doing that because between the longitudinal study, which I should mention; we are enrolling about 150 mostly blood donors who were found later on to have COVID into this longitudinal study over a nine month-period. We're gonna be getting blood samples and also nasal swabs and saliva samples from these SARS-CoV-2 positive people, and what we're gonna do is study some of them [and] save most of those in that repository in addition to the plasma that I mentioned before. It's ongoing. It takes actually quite a lot of work, as you can imagine, from the researchers because you need to have a whole process to collect things, process the samples, correctly ship them, store them correctly—so there are a lot of procedures that have to be put in place to do that well. But the REDS investigators are highly qualified to do that, and they've done that in the past.

GB: From what you've done so far, what have you all learned about the trajectory of COVID as well as how to prevent blood clots, which is one effect of SARS-CoV-2 on some patients?

SG: So what we've done in terms of the blood clots… as you know NHLBI is supporting several clinical trials to evaluate some anti-coagulation therapies in different patient populations with SARS-CoV-2 and COVID-19 to try to evaluate which one of those therapies or combination of therapies might be best to use, again in different settings: outpatients, inpatients, moderately sick patients in the hospital, to all the way to very severely sick patients in the hospital. So those clinical trials are on their way right now, and they are part of what's called the ACTIV-4 master protocols.

GB: Is REDS's response initiative still looking at convalescent plasma as a potential treatment?

SG: The convalescent plasma trial that was supported by NHLBI was called the C3PO trial, and it was conducted by the investigators that are part of a large network comprised of emergency room doctors which is called SIREN. So this is a different program than REDS, but that study was completed and stopped after a little bit more than 500 participants were included. This was a study looking at patients who came to the emergency room and also with evidence of COVID-19. They were tested for it and were found to have the disease, but also they had some risk factors that made them potentially more prone to have a severe symptomatic COVID-19, and so the clinical trial was done to evaluate whether a transfusion with convalescent plasma against COVID-19 as compared to just a placebo saline infusion would help them. So the reports of that study, we hope, will be published soon.

GB: Definitely. What has your experience been like so far in coordinating all this data collection and analysis amongst all the different collaborators because it sounds like you work with a lot of different centers and investigators?

SG: The experience that I've had is that, really, this pandemic, I guess you could say that's one of the good things about it. There is not much good about it, but this pandemic has definitely shown that researchers, in whatever field you are in, you want to work together and try to help people and try to put together studies to try to reduce the number of people who get sick with the disease and help them so the collaboration has been tremendous among investigators.

GB: That's really wonderful. Personally, what have been some challenges and opportunities for you as an individual who's living through this pandemic but also a scientist?

SG: Well, I think you put your mind to identify how you can help and what kind of research programs can be put together through collaborations, and it's not only collaborations among researchers outside of NIH, but it's also collaborations with your colleagues in other agencies. That's what I did, try to put my mind to, okay, so this is my area of expertise, and where can we help out in terms of responding to this pandemic? It's only a small part of everything else, but it's hopefully something.

GB: Definitely. So this is a thought-provoking question: It's been said that blood is the unsung hero in cracking a lot of the mysteries around COVID-19. What mystery do you hope to still solve about this disease, and how do you think analyzing blood can be part of the process?

SG: Well, I certainly think that there is a lot of inflammation, and as you mentioned before, some definitive issues with coagulation going on as a response to the virus, so trying to understand what is happening. So [researching] more of the pathogenesis, which often is reflected in what happens in the blood, because you can measure inflammatory elements and then evaluate what is important, what may be some of the factors that might make someone more likely to have severe disease, for example? And also it may reveal some elements that you can target potential therapies against and then you can put together a clinical trial around that question. There's still a lot of unsolved questions on this virus. I think the other thing to me that comes to mind is that this is one virus that's caused havoc, but there are many potential other viruses out there, and we need to prepare and think proactively about what could we do if another pandemic came our way, because chances are it will. And if we can be ready, or more ready if you want, to address such a challenging situation, I think we'll all be better off with that.

GB: Definitely. Thank you very much for your service, and I wish you and your team continued success and also continued safety.

SG: Thank you.