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Oral History
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Interviewed by Gabrielle Barr, Archivist, Office of NIH History and Stetten Museum, NIH

Barr: Good afternoon. Today is August 4, 2021. My name is Gabrielle Barr, and I'm the Archivist at the Office of NIH History and Stetten Museum. Today, I have the pleasure of speaking with Dr. Barbara Karp. Dr. Karp is a Program Director for the Division of Clinical Research at the National Institute of Neurological Disorders and Stroke (NINDS). Today, she's going to speak about in particular the COVID-19 Neuro Databank/Biobank called "NeuroCOVID" that's about COVID-19 neurological disorders. Thank you very much for being with me.

Karp: Thank you.

Barr: To begin, can you talk about some of the neurological symptoms people experience who have an active case of COVID-19 and the types of symptoms that persist sometimes when a person has presumably recovered from the disease?

Karp: Okay. First, I want to clarify that I'm the program director for a particular program in the Division of Clinical Research, which is called EPPIC-Net [Early Phase Pain Investigation Clinical Network]. The NeuroCOVID project is part of that. Also, it is not just a biobank. It's largely a databank to collect data, rather than samples, although samples are part of it as well.

To get to your question about neurologic symptoms: With the first reports of COVID back in early 2020, it was noticed that there was a very high risk of stroke, even in those without clear risk factors for stroke, especially in ICU [intensive care unit] and hospitalized patients. In people in the ICU, there were reports of seizures and mental-status changes, confusion, delirium, and these all raised concerns for us. So, during acute COVID in people who were hospitalized, especially in the ICU, there were very serious neurologic complications. In people who were not hospitalized, some of the major neurologic symptoms that they reported were fatigue. Some people also developed a neurologic condition called Guillain-Barré syndrome. There were a number of neurologic complications that people had during acute COVID.

Of more concern now is that we have patients coming through acute COVID with what's been called the long-haul symptoms or persistent symptoms. The major symptoms reported among the people who have persistent symptoms in terms of neurologic dysfunction, are extreme fatigue and fatiguability—getting tired very quickly with very little activity—and what they commonly call brain fog, just feeling like you're not thinking as clearly as you normally do. It's at the level that interferes with work and quality of life. There are also a lot of reports of blood pressure changes and effects on the autonomic nervous system that controls heart rate and blood pressure. People report feeling faint when they stand up or that they have palpitations and a racing heartbeat, insomnia and sleep problems. Those are probably the more common neurological symptoms that we're seeing in the long-term patients.

Barr: I read somewhere that a percentage of patients have reported psychological issues as well as occasionally there have been strokes linked to COVID-19. Can you comment on that?

Karp: The strokes are common and there seems to be, especially in the sickest patients, a hypercoagulable state, which means that people clot very easily and some of those clots get up to the circulation in the brain and cause strokes or clotting in the blood vessels directly themselves. Stroke is clearly a problem in acute COVID patients.

In terms of psychological issues, part of that is the brain fog and cognitive dysfunction, but in ICU patients, there were also concerns about delirium and psychosis emerging in COVID patients who had no psychiatric history previously. As we get more experience with the people coming through COVID, there are reports of mood disorders as well as the kind of cognitive clouding that goes along with it. So, we put these together into neuropsychiatric symptoms. They're probably all part of what COVID does to the brain.

Barr: Were specialists in your field surprised at the extent of the neurological issues presented by patients who've had COVID or who are having COVID right now.?

Karp: We were surprised. The reason is that we have some experience with other coronaviruses and these sorts of neurologic involvement were not as common with those.

Barr: When did the National Institute of Neurological Disorders and Stroke begin planning the COVID-19 Neuro Databank and Biobank called NeuroCOVID? And what were some of the ideas suggested for creating this resource?

Karp: Okay. We started thinking about it early in the pandemic when the first reports of stroke, mental-status changes, and loss of smell in COVID patients started appearing. We started thinking along two pathways. One is what is COVID doing to the brain? How does it cause these symptoms? And what symptoms does it actually cause apart from those that you would normally see in the ICU setting? Some people have mental-status changes when they're in the ICU, regardless of the cause. They're very sick, their whole pattern of life is disrupted. We needed to define what was different about the neurologic complications of this particular illness.

Then we were also concerned about the effects COVID might have on people with pre-existing neurologic illnesses. Especially since COVID has some inflammatory and immune aspects to it, we were concerned about it having unusual effects or maybe worsening diseases like epilepsy or multiple sclerosis or other sorts of neurologic conditions.

We wanted to focus on two aspects—the neurologic complications of COVID itself and then the COVID effects on pre-existing neurologic conditions. We started thinking about how best to do that. We already have within NINDS research networks that include databanks and biobanks. So we utilized those resources. And we issued a request for applications from existing centers to see if they would take this on. Those applications were reviewed and the award to set up the databank and biobank went to New York University [NYU]. They actively started talking to us about what data we wanted to collect and how we would collect it. So that's how it started.

Barr: Can you talk a little bit about what types of data are being collected and what kinds of samples that you are acquiring?

Karp: We're asking for patients and their doctors to fill out a number of questionnaires that focus initially on COVID symptoms. Then if somebody were to report headaches, they would answer more questions about headaches. If they report seizures, then they get more questions about seizures. It's a logical series of questions that asks them about their symptoms. We try to use what are called common data elements to the extent possible. These are tools that NIH and others have developed that lets us collect data in a way that's in common with a lot of other centers. The data can be combined easily so that we can add it into other databanks, or we can take in data from other databanks, and the data meshes well.

We don't collect any samples directly for our repository. We ask them if they've had samples stored. If somebody has had a spinal tap, or somebody has blood already available, we can either take that in and store it in our biobank, or we can track in our database that the samples are available. If a researcher wanted to access them, they would know where to apply and where to find them and what samples were available.

Barr: Are there certain criteria for being accepted into this databank or biobank? There are patients who think that they have had COVID when maybe they have not, or those who have tested negative, but they swear that they definitely did. The testing in the early days was not really that accurate.

Karp: For this databank, we need a confirmed diagnosis. We are not, for this databank, taking people who think they might have had COVID.

Barr: How did you go about promoting this resource to both researchers and clinical partners?

Karp: It was announced on various NIH websites, it was picked up by various media outlets, and so it was publicized through those—the usual NIH ways of announcing new initiatives. And especially, there's a lot of interest in COVID, so it was on the NIH COVID announcements. As I said, we talked to a number of media people about it, so we were able to get a fair amount of publicity for it.

Barr: Roughly, do you know how many clinical partners NeuroCOVID has currently, and are you accepting partners from all over the world?

Karp: We are accepting partners from all over the world. Right now, we have about 40 institutions at various stages of registering with us. It takes a bit of work to actually submit data to us. You need to get approval of your local institution; it has to go through some IRB [Institutional Review Board] approvals; and then we have to work out the mechanics of transferring the data. Right now, we have about 40 sites worldwide that have contacted us and are in various stages of preparing and submitting data. We're just at the point now where our first sites have cleared the process and are about to start submitting.

Barr: Do you know roughly about how many samples or the amount of data that you all have collected? Ultimately, how much would you like to acquire?

Karp: We are just at the point now where we're starting to take data in, so we do not have it yet. I don't have the numbers in front of me of how many patients are coming in from the 40 sites that we've contracted and worked with so far. But we are open to however many we can get. The bank really does doesn't have any restrictions on the amount of data that we can take in.

Barr: That's great.

Karp: We're welcoming all comers.

Barr: Are there certain neurological conditions to date that are more represented than others?

Karp: No. We're really getting queries, largely from neurologists since we're neurologically focused, but also from places that have been seeing large numbers of COVID patients that would like to contribute their data to understand the neurologic aspects of it. I wouldn't say at this point we have any predominant conditions other than we're just focused on neurologic conditions.

Barr: Yes. I read that all these samples and data get de-identified for those who are researching. So how do you keep track of all that information? And how do you track the biosamples that are everywhere in the world that connected with you all?

Karp: The de-identification occurs at the site that's submitting to us. We're using a system which is fairly commonly used called a GUID . It's a global universal identifier. The people who are submitting the data enter some information into a computer algorithm that generates a unique code for that individual. Our bio and data repository only gets the code. We don't have any original identifying data that was used to generate that code. That code is unique, and it lets us track data from a single individual across time. If a person were to have symptoms now and then want to report follow-up symptoms two months later, we would be able to know it was from the same individual. We can link the samples to the data from that individual. If a person went to two different sites that are enrolled in our databank, because the site would enter the same identifying information on the individual, it would let us be able to link data coming in on the same individual even at two different sites.

Barr: Oh, that's nice.

Karp: Similarly, one of the things that we're doing is we're including pregnant women and neonates. This type of identification system will also let us link the mother's data to their infant's data.

Barr: That's great. That's really, really nice. So how do researchers access this material?

Karp: Once it's available, it will be on a publicly available website. The application process for accessing the data will be available publicly.

Barr: Do you know of any studies or diagnoses that have come from researchers looking at the information he from NeuroCOVID so far?

Karp: We don't have any data in yet. So not yet. But we're hoping that there will be within another year or so—months to a year.

Barr: How did you decide to include pregnant woman and neonates? Not every databank has done that with COVID.

Karp: I have a long interest in the equitable inclusion of pregnant women in research. I think they are often ignored, often out of unrealistic concern for their or their infant's safety. Especially in this type of research, where there's really no risk to the mother or infant, we want to make sure they're included. We really do not know much about the effects of COVID, especially on neurologic development, in infants born to mothers who are exposed to COVID. So, I thought that was an important aspect to include.

Barr: Yes, definitely. Have any new questions emerged since this resource was created that you hope that the biobank can answer such as, "Do certain variants cause more neurological issues than others or are there different types of complications?" or any other types of questions that you hope that the biobank can answer?

Karp: The two main new questions that emerged after we set it up, are the one that you raised, which is "Are variants like the Delta variants going to be different in the neurologic complications?" The second one, of course, that we knew was coming or we hoped was coming, were the effects of the vaccine. We don't know yet whether or not the vaccine will lessen the incidence of neurologic complications; if it will reverse the course of

some neurologic complications or affect them. We just don't know. So, the two confounds that we are collecting data on—we'll collect data on vaccination status, date of vaccination, what symptoms were before, what symptoms were after. Of course, we'll have some information on when testing was done. We may not have testing, [from] early in the course of this of the pandemic, on what variant or what the type of coronavirus was, but we will get that going forward to the extent that we can. So those are the two main issues that have emerged.

Barr: What have been some challenges and launching NeuroCOVID and maintaining it so far?

Karp: The maintenance is not an issue since we have experience maintaining databanks and biobanks. The challenges in setting it up really have been deciding on what elements to collect, what data we wanted to collect. Because we wanted to collect as much as possible, we faced the barrier that you can't possibly collect as much as possible. It becomes unworkable for the person trying to get the data in. Choosing what to include and what not to include [and] trying to make it user friendly, have been a challenge, and [so has] getting the word out.

Barr: In what ways have you tried to make it user friendly?

Karp: We looked very carefully: We went through question by question to try to really make sure that we were only asking the things we really felt were critical to know. And [we were] using common data elements with a decision tree to the extent possible. So, if you answer one question "No," you don't get any further questions related to that issue. We try to use a kind of logical progression through the questionnaires and really home in on what the person's particular problems are.

Barr: Yes. Someone said that it can take hours to do some questionnaires.

Karp: We tried to get it down to much less than that, and we also can accommodate electronic data transfer. So, if the information is in a medical record or in another databank, we can just transfer it electronically and map it onto ours. We put in place procedures to do that as well to make it less onerous on doctors or hospitals that wanted to submit data.

Barr: How did you account for those whose English was not their primary language or those with disabilities in terms of your questionnaire?

Karp: A lot of the questionnaires are available in other languages, especially Spanish. That can be easily incorporated. We can provide assistance in filling them out for people who have other sorts of disabilities. Most of the data entry is being done by health practitioners rather than patients themselves, so they are available to assist with that.

Barr: You said that you wanted to collect everything, but it's unfeasible to do so. What were certain areas that you ended up deciding on concentrating on?

Karp: I would not say we really cut out any major issues. We just maybe collected fewer or less in-depth questions than we would have otherwise. We have very wide interests in neurologic complications. We are not particularly focused on stroke or headaches or seizures or cognitive problems, because if we try to focus too much, we might miss what else is out there that's less frequent, but also concerning and impacting people's lives.

Barr: What has been your role in creating and managing this project as well as others at NINDS?

Karp: What we were involved in at NINDS is developing the initiative itself, taking in applications, and funding it. This is part of what we're funding. Then we work alongside with NYU in administering it. Basically, we worked with them to define what data elements we want to collect. When a new site comes to us and says they want to participate, we talk to them jointly with NYU. We have regular meetings with NYU to keep it going and to talk about the status. We also work with them to put in an external expert advisory board. So, we have NeuroCOVID neurologists with COVID expertise, nationally and internationally, who give us feedback on the databank and what we should be collecting—what kind of research questions we're going to want to ask with the data—so that we can make sure we cover what's really important.

Barr: Have you been involved in any other COVID-19 endeavors at NIH or outside of NIH?

Karp: I haven't been involved with anything else outside of NIH. Within NIH, I'm also working with the Post-Acute COVIDS syndrome group [PASC], the PASC initiative.

Barr: What are you doing with the PASC initiative?

Karp: I serve as a program lead and a neurologist. They wanted to make sure we had subject-matter expertise and people who represented NIH on the various committees. The PASC initiative is going to be accomplished through a series of awards to centers across the U.S., but we need some NIH representatives with that as well. I am one of those NIH representatives, particularly, to provide some neurologic expertise as well. So that's an initiative which is focused on the post-COVID syndromes—the long haulers—trying to understand what it is, what are the risk factors for it, how frequent it is, and things like that.

Barr: I forgot to ask, how long is the NYU award for, and can it be renewed?

Karp: It's currently funded through 2024, and it would be possible to renew.

Barr: In addition to being a scientist and a physician who has been working on COVID issues, you're also an individual who's been living through the pandemic like everyone else. What are some of the opportunities and challenges that COVID has presented for you personally.

Karp: The opportunities have been to expand research opportunities and get involved in trying to do something that would hopefully help the country and help people cope. At a personal level, I've been fortunate in that I've not been infected. My immediate family has not been infected. Very few of my friends have been very sick from it. We've been very fortunate and very careful. The main difficulty I've had is I was not able to see my grandchildren for over a year. I still have not seen my son for nearly two years in person. That's been my personal challenge.

Barr: Has there been something that you enjoy doing that has helped you manage the pandemic better?

Karp: The main thing I've been doing personally is we have an outdoor swimming pool that was open all winter. So, I was able to get out and exercise all winter. That was really important even when other gyms and things were closed, and, we had our little pod of friends who we did things socially—unmasked—with. Those are the types of things that were really very important during the worst of the pandemic.

Barr: Yes. What has been most rewarding for you working on NeuroCOVID and the PASC initiative?

Karp: I would say that the most rewarding part is just knowing that you're doing something to help people who are dealing with the severe effects of COVID and post COVID. It has been so disruptive to so many people's lives and health. Just being able to contribute in even a small way is very gratifying.

Barr: Yeah. How long do some of these neurological issues, on average, last for some of the people who have had COVID? In some it seems like it disappears right away. In some, it lasts for a long time, and it seems to disrupt their lives forever.

Karp: That's what the PASC initiative is set up to answer. We really don't know. Some people say that they seem to get better after their vaccine. Some people don't. Some people say that they are extremely fatigued and have difficulty thinking for months. Other people seem to recover within weeks. We just don't know. And that's why we need data like this to really understand what we're dealing with.

Barr: Yeah. Well, is there anything else that you would like to share?

Karp: I really think you've covered a lot of territory here, and I really appreciate the opportunity to talk to you about our NeuroCOVID work.

Barr: Absolutely. I wish you and all your colleagues all the best in their work. It'll be interesting to see the results that come from NeuroCOVID.

Karp: Thank you.