CDC Ebola Response Oral History Project

The Reminiscences of

Timothy M. Uyeki

David J. Sencer CDC Museum

Centers for Disease Control and Prevention

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Timothy M. Uyeki

Interviewed by Samuel Robson
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Interview 2 of 2

CDC Ebola Response Oral History Project

Q: This is Sam Robson here with Dr. Tim Uyeki. Today's date is May 20th, 2016, and we're back in the audio recording studio at CDC's [United States Centers for Disease Control and Prevention] Roybal Campus in Atlanta, Georgia. This is our second interview for the CDC Ebola [Response] Oral History Project. Tim, thank you again so much for joining me, talking about your experiences with the Ebola epidemic again.

Uyeki: My pleasure.

Q: Mine as well. One question I had was, we talked about the beginnings of your involvement in the Ebola response, how you got that call from Inger [K.] Damon. But how, really, did it come about in the first place, that CDC would have this role in coordinating the exchange of clinical information between doctors at different facilities?

Uyeki: I think that was not necessarily a planned activity. I'm not sure it was thought about. As some background, earlier in 2014, in the spring of 2014, I was asked to be the clinical team lead for the CDC MERS-CoV response, Middle East respiratory syndrome coronavirus response. Specifically, I was asked to focus on so-called medical countermeasures for MERS-CoV infection, which means basically, investigational

therapies if any are in development, and candidate vaccines in development. I was a clinical team of n=1 person. I also ended up co-chairing an HHS [US Department of Health and Human Services] interagency working group on MERS-CoV medical countermeasures. I was quite involved in that. I think it's because of my work on that, that's why I was asked to work on the clinical team, probably to focus on medical countermeasures for Ebola virus disease, or Ebola virus infection.

Earlier in the spring, I had been asked to go to West Africa, to work on the Ebola virus disease outbreak, in the early stages. But I was unable to travel. That was because I had previously worked on the second-largest Ebola virus disease outbreak, now, which occurred in 2000 going into 2001, in northern Uganda, in Gulu District. I had to work with World Health Organization colleagues and CDC Viral Special Pathogens colleagues and others. I think that might have been why I was asked: the combination of having some—not much experience, but at least some—a little bit of experience in the field, working on an Ebola virus disease outbreak. And then focusing more on clinical and medical countermeasures stuff. I think I was really brought in to focus more on investigational therapies, initially.

But the clinical team for the Ebola response ended up focusing on both therapeutics—so to use for treatment of patients who were sick with Ebola virus disease—as well as persons who had some kind of exposure, so-called high-risk exposure to Ebola virus. And then, what kinds of interventions there might be used for post-exposure prophylaxis. Initially, also to work on candidate Ebola vaccine issues.

The clinical team for the CDC Ebola response worked on all of those. But later, it became pretty clear that a separate team would be needed to work on Ebola vaccine issues, and particularly to work on this large clinical trial in Sierra Leone, the so-called STRIVE [Sierra Leone Trial to Introduce a Vaccine against Ebola] trial. But the clinical team still retained activities related to the use of an Ebola vaccine for post-exposure. We were not involved for prevention, but we were involved in using vaccines for post-exposure after a high-risk exposure.

But in the early days—so this would have been August, September, even October of 2014—we were very much involved with all of the activities that related to development of Ebola vaccines. That means on conference calls, and sharing of information—actually, trying to collect information, gathering information from our regulatory partners at FDA [US Food and Drug Administration], our Department of Defense partners, our NIH [National Institutes of Health] partners, etcetera, etcetera. We had lots of calls with manufacturers, trying to look at the data. Trying to look at protocols, and then also looking at the animal—the in vivo data.

We were looking at all of that. On our clinical team, we had at least one person on our team who was an expert in regulatory issues, with the CDC regulatory affairs; we had people who had expertise in different vaccines, not necessarily Ebola vaccines, but other vaccines; people that worked on vaccine safety issues broadly for CDC. A lot of people probably don't know this, but we were working on Ebola vaccine issues before the

Vaccine Task Force started working on this. They actually pulled people from my team to work on that, which I was not happy about. But we at least retained the ability to work on post-exposure interventions with Ebola vaccines.

I think really the reason I was brought in was probably to work on all the experimental therapies and vaccines. But even if you have an experimental treatment, of which we had very, very little—and we had limited data, back in the summer of 2014, the majority of clinical management is not whether you get one drug or another—experimental drug—but it's actually supportive clinical care. It's intensive care, it's critical care nursing and so forth. From my perspective of the clinical team, we were focused on clinical issues, anything that pertains to clinical management, and most of that did not involve whether a patient received an investigational therapy or not.

It turned out that most of the US patients received an investigational therapy. In fact, most of them received more than one. But this was all essentially under emergency IND [investigational new drug] requests, single-patient requests by the treating clinicians, to FDA for rapid emergency approval to use a product that in fact might have had zero data in humans, and then working with the manufactures and trying to get that product to the hospital for the patient as soon as possible. There were data requirements that the clinician then had to report, both to FDA and to the manufacturer. It was really coordinating all that information as it evolved over time, providing that, and trying to facilitate the clinicians who were managing that patient, get them the latest information, and then sort of connect them up with FDA and the manufacturers so that the patient has

the ability to get access to that product. But again, most of the clinical management is not whether they got this product or that product.

I think it evolved very quickly that if you're going to be dealing with clinical issues, and clinical management, you have to know all kinds of things. It's the diagnostic testing, it's the routine laboratory testing, it's the testing for hematologic parameters, metabolic abnormalities, etcetera, etcetera. Then, it's what specimens need to be collected for Ebola virus testing at CDC.

And then learning. So much of it was a learning process, as we go. With each new patient, you learn more. The reason why this was important was, in contrast to the many thousands of patients that were cared for in West Africa Ebola treatment units, or ETUs, there was really limited testing going on there. Whereas in the US and Europe, most of these patients were in sophisticated biocontainment facilities, and we had the ability to do a lot more laboratory testing, detailed testing, daily testing. Although, there still were some limitations about the extent of the testing that could be done because Ebola is—you know, it's quite a dangerous blood-borne pathogen. For example, there was limited ability to perform microbiologic testing. And whatever testing you were going to do, really has to be inside the biocontainment unit. And most of the biocontainment units didn't have sophisticated microbiological cultures. For example, you can't culture up and identify any bacteria. You're limited to what you can process and what analyses you can do. Because certainly there's concern, and some of these patients did have secondary bacterial infections that probably did contribute to their disease severity, and actually to

their final outcome, in some cases. I think, overall, it was very important to collect a lot of detailed clinical and laboratory data and virologic data, frankly, from these patients in the US, as well as in Europe, and to share this information among ourselves.

This all started with the first two patients that were admitted to the Serious Communicable Diseases Unit at Emory University Hospital on August the 2nd and August the 5th of 2014. Myself and another colleague basically were trying to help with the specimen collection and transportation. But I functioned as essentially the liaison between CDC and the Emory clinicians who were managing the Ebola virus disease patients. Then it kind of evolved as we got more Ebola virus disease patients in the US, that I ended up serving as the liaison to the University of Nebraska Biocontainment Unit, and then to Bellevue Medical Center, and to the NIH, and then to Texas Presbyterian Hospital in Dallas. Obviously, the NIH can do their own testing. But I still served as the liaison to CDC. With all these patients, I was in daily telephone contact. Any time there was an Ebola virus disease patient admitted in the US to a healthcare facility, I spoke to the lead clinician or clinicians managing the patient every single day. Sometimes, this was in the middle of the night, as well. The reason for this was both to collect and coordinate information, detailed information, but also to help synthesize it and inform the CDC leadership for the Ebola virus disease response and others in the US government.

In general, my personal feeling was to share as little detailed information as possible with non-clinicians, because the people who were managing the patient, who really need to know this, are the clinicians in the units, not decision-makers. But there were many

requests for detailed information. This is something that happens with every response, that people want information, but I don't think that there's any reason why people need to know this information.

Q: Who, specifically wanted that information from you?

Uyeki: Certain parts of the US government, and my position was to push back on this, and was to try to serve as a buffer between the clinicians and high levels of the US government. Then I was told they were going to go right to the clinicians, and I strongly suggested not to bother them, they're too busy.

Q: I understand if you can't, but can you be more specific about what parts of the US government wanted that access?

Uyeki: National Security Council. White House. Yeah. It's one thing to talk to a White House clinician—and I've done that in the past on other kinds of diseases. But I think so-called, for situational awareness, you don't need to know that. You just need to know the patient is quite sick, or is on mechanical ventilation or not, or the patient is clinically stable or improving, or was discharged, or died. I don't think you need to know any other details.

What I would try to do is, anytime there was a new patient—and particularly, for example, at Texas Presbyterian Hospital in Dallas, and then at Bellevue Medical Center,

and even when the first NIH patient was admitted—is to assemble clinicians, especially from Nebraska and Emory, who had good experience, albeit a very small number of patients. But just to share information, try to answer questions. I was more the facilitator and the moderator of that. Similarly, on these calls—sometimes they were weekly calls, sometimes every few weeks. Really, it depended upon whether there was a patient that was actually admitted in hospital. Sometimes there were four patients in the US or Europe, or actually, even more at one time. We would discuss these different aspects of it, and really discuss very detailed information. So, I was the organizer of that, and then served as a moderator.

Q: Can I ask where that idea for conversations between the clinicians really came from? Was that your idea? Were they already having some conversations, and reaching out to each other? Or how did that really come about?

Uyeki: Well, since we were already doing that in the US, and I was coordinating that, once there became a patient in Europe, it was important to really share that information. I think you can learn a lot by learning about the experiences of clinicians who have worked in West Africa. But because there was much more extensive testing done, and also use of some of these investigational therapies done in the US that then were also used in Europe, or different ones were used in Europe, we wanted to share that information.

That's a good question. I think it probably evolved from—for many, many years, I've been involved with clinical issues related to influenza, severe influenza, either caused by

seasonal influenza, or pandemic influenza, or zoonotic influenza; in particular, human infections with avian influenza A viruses. I've certainly contributed to WHO [World Health Organization] in terms of a lot of clinical management guidance, antiviral treatment recommendations, and then also worked on that clinical management for MERS-CoV for WHO. It's sort of the same people that I've worked with at WHO, and it was sort of the same idea. We've had these teleconferences that WHO has organized, or other groups have organized for WHO. I think that the idea was to do a WHO-CDC teleconference, or a weekly teleconference, or whatever was indicated. But the WHO clinical group was so busy with focusing on clinical response in West Africa that essentially, I was asked to organize and coordinate that. And so I did that. I guess we called it the US–Europe Clinical Network on Clinical Management of Ebola Virus Disease in Higher-Resource Settings. It evolved as it went. You organize one teleconference, and then, oh, there's another patient here, admitted to a hospital in Spain. Or here's another one admitted to a hospital in Germany. Oh, here's one admitted to another US hospital. You just kind of go with it and just keep organizing it. None of this was planned. We had no idea that there would be any patients. After you get a few, we had no idea how many. So I don't know. It just sort of evolved.

Q: Gotcha. Because I was a little interested in how novel that process was, of coming together and sharing that data. It sounds like in the past with influenza, or with MERS, that practice of coming together and sharing information across national boundaries, and oceans between physicians—there was precedent for that. That was something that—

Uyeki: There was some precedent, but that was under the sort of organization by WHO, in particular, one particular group. CDC doesn't typically do that. I've participated as a representative from CDC on a lot of these different teleconferences. But in this situation—I don't know, it was just the right thing to do, since I was already doing it in the US, and then WHO asked me to do it. I was happy to do it. I thought it was important to share information.

Q: No doubt. You've kind of described yourself as a facilitator, as creating the space for the conversation to occur, but to what degree were you actually participating in exchanging information with people?

Uyeki: I guess it's related to what I do for influenza. I was not managing these Ebola virus disease patients. But I was certainly learning with them and assimilating information with them. Everyone's tracking information that's either being published, or being presented at a conference, or something. It's sort of learning along with everyone, and yes, I was assimilating information and trying to help share information. But I wasn't generating that data. I was more trying to link people up. But I would moderate these teleconferences. I would ask a lot of questions. But I don't know, I sort of view my role as, again, the organizer and moderator. But I'm not the one managing the patient.

Q: Right. Okay, that's helpful. You gave an example last time of, when you're paying attention to all of this information, learning the typical disease progression for Ebola, and

how in one patient in particular, you noted, hold on, given the progression of symptoms, I think this person was actually infected earlier than what we were originally thinking.

Uyeki: Oh. That was based upon what the patient's history was, when their symptoms started. And then learning about how the patient actually presented, what signs and symptoms were present, and what laboratory findings were present at that time. My sense was that what that patient is reporting as the duration of symptoms of the illness, is probably shorter than the actual length of the illness. In other words, the illness onset date was probably several days earlier than the patient thought. The reason for that is, in contrast to what the thinking used to be, everybody gets a fever. And the fever is your illness onset, is signaling your illness onset. Well, it's pretty clear that not everybody gets a fever or reports being feverish, and that the first signs and symptoms of illness with Ebola virus infection is not fever onset. It might be very, very nonspecific. Some of this is really in retrospect, but if you go ask patients, when did their fever start? What were their symptoms at the time? Then you ask them a little more. You keep asking them. And again, I'm getting this second- or third-hand, because other people have interviewed the patient. But in some of these situations, I was actually communicating back and forth with the clinician that would go in that patient's room and re-interview the patient, ask the questions. So some of it was not so much third or fourth-hand. Some of it was. You find out that some of these people would report, maybe they weren't sleeping so well. Some of them felt a little more fatigued, but they just attributed it to something else. They attributed it to too much work. One attributed it to jetlag. Who knows? But it's quite possible that in fact, that was their illness onset: that fatigue, maybe some insomnia. That

was actually when their illness symptoms started, and the fever didn't occur until a few days later. But these are all kind of estimates.

Q: Right. I like that as an example of you contributing to the conversation, and being part of that, in addition to just facilitating. Do you remember any time—so they go back, and they re-interview a patient. Does that have practical effects on the care that they give to that patient?

Uyeki: It doesn't have effects on the care, but what it has huge implications for is contacts, and following the contacts. We think that patients with Ebola virus disease are not very contagious to their close contacts or others, until they develop illness; until symptoms start, their fever starts, and so forth. So, if actually, your illness onset was a few days before you think it was, unless you really tease that out, you may not pick up the contacts. It is true that exposures that occur early on in the clinical course, probably the patient is not as infectious. As the patient becomes sicker and sicker, the patients will have high levels of Ebola virus in blood, but not initially. That's actually one of the reasons why you test the patient repeatedly. If they test negative in the first seventy-two hours or so of illness, you can get a negative result by testing blood. And that's why you need to retest them after seventy-two hours of their illness onset.

It has some implications that you need to monitor contacts of the patient a little bit earlier. Practically speaking, they probably don't transmit to those individuals, but you would really not want to miss an outlier, where some transmission occurs early. But no

doubt that the sicker the patient gets, the higher the Ebola virus load in their blood, and in other bodily fluids; they're much more infectious.

Q: Right. I have another question. And that's, as you're getting this information from all of these different sources coming in, was there a place where you were kind of compiling this new information and this new data? I don't know if you had like a—obviously, it wouldn't be as crude as this, but like a Google Doc, where you have, like, a common source were people can refer to information about treatment?

Uyeki: Well, I kept notes—written notes. But on these clinical teleconferences, with the US-European network, we did not want to circulate a lot of notes. People did take notes. I took notes. But we didn't want to circulate them, and the reason is, there were more people listening into these calls than just the clinicians managing the patient. We did not want to share, frankly, confidential information, and some detailed information. For internal purposes, we did take some notes. I kept notes on any discussions, or any new developments, but we didn't formally keep it in one place, a record of that.

I was just thinking about that last thing we discussed. The reason why, in particular, one patient was important to tease out when the person actually had illness onset was because that person actually—well, it's actually not just one patient. Several people were moving around prior to the illness onset and potentially could have exposed other people, not just their household contacts. Again, it turns out that people in the early stages of Ebola virus disease are not very infectious. But we didn't know that, for some patients. So it's

important to do the investigations so you make sure you're following up the contacts. You really want to define when the illness started.

But in terms of information-keeping, it was mostly what I did was keep written notes in notebooks.

Q: Right, personal notes.

Uyeki: Yeah.

Q: What motivated this desire by you and these other clinicians to really keep some of this data close to the chest, and not be sharing it willy-nilly with everyone?

Uyeki: The people who need to know the information are the people managing the patients. Certainly, this would have implications for management of patients in West Africa. But the kind of resources that are available were very limited. Some of this, of course, was evolving knowledge. These experiences were certainly shared with a wide range of clinicians, through WHO clinical meetings. There were a number of WHO clinical management of Ebola virus disease meetings during 2015 and—trying to think—in 2014? Sorry, in 2014 and 2015. And that did include clinicians from Liberia and Sierra Leone and Guinea. The idea was to share this information and then it would be shared to their colleagues by the participants. In addition, there were a number of publications—single-case reports, or case reports of two-patient series, or three-patients. The clinicians

wanted to publish the very detailed data in the peer-reviewed literature. This serves two purposes. One, it gets it out to everybody. And the other is that it protects their ability to—you know, these are mostly academic clinicians, and so they want to publish it. The information was shared among clinicians managing patients, both in higher-resource settings, but also in West Africa. But to some extent, the ability to use this information was more limited in West Africa, because the kind of interventions were extremely limited. Even fluid management was very, very limited and challenging, except in a very small number of Ebola treatment units. The information was shared, but again, some of it's very confidential. We don't want to disclose patients' identities. We want to really protect patient information. Even outside of the US, it's very, very important to protect patient information. One has to be careful. One has to be careful, actually, about information getting out that could be misleading or interpreted incorrectly. I think sharing it through these WHO teleconferences as well as the WHO meetings was very important. And then, getting publications out. It was frankly up to the clinicians how much information they wanted to share. It wasn't sharing of every single bit of data on the patient, and every day and every hour. It was summarizing key points. I think that was very useful.

Q: Right. Thank you. That's what I was trying to get at a little bit, was, it seems to me that you have a very strong ethic of maintaining patient confidentiality, and in the environment of a very public response, that becomes challenging.

Uyeki: Well, the sad fact is that it's not just unique to Ebola virus disease, but in particular, Ebola virus disease. If you were a patient in the US or Europe, there was no confidentiality. The media press just jumped on it. Patients' names were—you could find the names. If you know how to do literature searches, you could find the name of almost every European or US Ebola virus disease patient. If you can't find their name, you can certainly find where they were hospitalized and the dates of hospitalization. You can find a lot of other information. I think, actually, protection of patients' confidentiality is extremely important for any disease, whether it's infectious or non-infectious. Unfortunately, the sensationalism around, and the thirst for telling stories by the media press violated patients' confidentiality. I think that's just wrong.

This was really a challenge for us on these clinical teleconferences. When you have a lot of people listening in—it's not just one clinician, but it's a room full of people, each line—and then a lot of public health people that are not managing a patient, and other people were listening in, probably who I have no idea who they were. I've experienced this before in running clinical teleconferences—there is a balance between sharing a lot of detailed information and then protecting confidentiality.

Q: Thank you, I appreciate that.

Uyeki: But what we did, finally—again, it took quite a long time, for a variety of reasons, not to mention securing approvals and consent from patients and families, as well as institutions and governmental approvals—but we were able to collect some detailed

clinical data and laboratory data, and to aggregate that, and to summarize that in the peer-reviewed literature. The first goal was not to identify any patient, but to present summary information so that no patient could be identified. To summarize the information in a way that would be useful for other clinicians. The unfortunate thing is that this took quite a long time before we were able to actually collect all the data, analyze it, and actually publish it in the peer-reviewed literature. But the key thing was, the essential elements for clinical management had been shared freely at WHO meetings and clinical teleconference calls and by word of mouth. Those that needed to know were informed. But to actually get it out there took quite a long time. In the end, once it was published, I don't think the data are going to be that useful, because this was really at the end of the whole West Africa outbreak. But it will serve for both medical response planning and preparedness for future Ebola virus disease outbreaks, and other hemorrhagic fever outbreaks, both for planning in developed countries, as well as I think lower-resource and middle-income countries.

One of the key issues is to, frankly, improve clinical management in low-resource settings. Maybe we can't provide the degree of care that we can in higher-resource settings, but there are certain things such as proper fluid management and correcting electrolyte abnormalities. For example, hypokalemia, or low potassium levels. Correcting potassium levels may be extremely important. But proper fluid management, I think this could actually greatly improve survival. But another challenge is certainly protecting healthcare workers from nosocomial infection, acquired in Ebola treatment units. There's a lot that needs to be done, but we can use the lessons learned from the experience in the

US and Europe to improve clinical management of patients with Ebola viruses, even in low-resource settings, as well as other settings. But we have a long way to go. Again, the big contribution was the sharing of information prior to publication. To me, it was really anticlimactic that finally we were able to publish the information, and it will help others, hopefully, in the future. But I think that the key was sharing of information more informally.

Q: Briefly, just to make sure this has legs, an example of the kind of information that gets published—what would that be? Like, what comprises the data? Is this people's viral loads, and people's disease progression, and that kind of thing, or—

Uyeki: Oh, hematologic parameters, so white blood cell count, hemoglobin, platelet counts, routine laboratory chemistry such as potassium levels, sodium levels, albumin levels, creatinine values, liver function tests, transaminases, so forth. Then, yeah, viral load over time. But we just tried to summarize it. Also, what proportion of patients required invasive procedures or advanced organ support such as mechanical ventilation, that would be either non-invasive ventilation, or invasive mechanical ventilation. How many required a central line? How many required total parenteral nutrition given intravenously? How many required renal replacement therapy for kidney failure? So forth. Duration of time that they required advanced organ support for outcome, so forth, like that. Some of that has implications for critical care support planning.

Q: That is really helpful, thank you. I'm going to switch gears, actually, a little bit with this next question, but I know that another one of your jobs as clinical team lead, you mentioned last time, was coordinating the transportation of specimens. Do you have any specific memories of that part of your work that stand out to you?

Uyeki: Well, you just do what you need to do to get specimens to CDC so that our colleagues in the Viral Special Pathogens Branch laboratory can perform the testing, it can be done as soon as possible, and those results are transmitted back to the clinician. There are always challenges in shipping specimens, and—

Q: Do you remember any challenges in particular?

Uyeki: —cost of specimens. I'd really have to think about that. It never happens as quickly as you want it to because specimens need to be flown overnight. It depends on where the specimens are coming from. If the specimens are at Emory, you don't have to fly a plane. They are three blocks away. If the specimens are coming from Omaha, Nebraska, or New York City, it's a different story. And from Dallas, Texas. It's much more challenging. Getting things done in a timely way. But I was never the one packaging up the specimens or collecting the specimens, I was more trying to help coordinate the collection and processing—or collection and transportation. I can't think of any good stories offhand about that.

Q: Oh, that's okay. That's okay. Stories of logistics are not always the most interesting, anyway. [laughs]

Uyeki: I have some good stories about going back to 2001 with trying to coordinate anthrax specimens getting sent to CDC, but that was a different pathogen, and a different era.

Q: Sure. Well, I wish—maybe in a future oral history, we should explore that. [laughs] How about—another thing that you mentioned that you did in our last interview was, there would be suspected Ebola patients in the United States as well, and you would be involved in having conversations about them and what to do about them, etcetera. Do you have any instances of work in that realm that come to mind?

Uyeki: We had a domestic clinical inquiries team, which was separate from our clinical team, and they were handling all the requests or inquiries coming in from state health departments or local health departments or clinicians about how to assess a suspected—actually, the term is "person under investigation"—for Ebola virus infection in the US. I would only be brought in when there was going to be a teleconference with public health partners and clinicians, if it was a more complicated or highly suspected kind of patient. I was involved in quite a few of those teleconferences, and sometimes they occurred late at night.

Just trying to understand what information was available, what exposures the individual had had in West Africa, what were they doing? When was the onset of their illness? What signs and symptoms did they have? Most of the time, there wasn't any testing that had been done, but sometimes if there had been some limited testing, what were those results? And then trying to assess. Most of the time, these people were really deemed to be low-risk, because they actually were not having direct contact with a person who had Ebola virus disease or even a suspected—or that was sick. Just being in a country where there are Ebola virus disease patients, even a big outbreak, doesn't mean you're actually exposed to Ebola virus. As we know, the vast majority of these individuals—persons under investigation in the US who got tested—did not have Ebola virus infection at all. The number one diagnosis was malaria. We picked up a lot more malaria. Those people might have been treated earlier than they would have, had they not been picked up as a person under investigation for Ebola virus disease.

We did have two imported cases of Ebola virus disease, one who presented in an emergency room in Dallas, Texas, and actually presented twice, and the second time was when that patient got admitted. The other individual was someone who had been working in an Ebola treatment unit in Guinea, and realized, once he started to develop some symptoms, that he might in fact have Ebola virus infection, and he self-presented. He called ahead of time to an emergency room, to let them know.

In fact, the screening that was going on at airports that then local public health and state public health were following these persons under investigation, there weren't actually any

Ebola virus disease patients picked up that way in the US. But you never know. It certainly brought to light—we knew this beforehand, but it certainly brought to light that there's certainly a lot of other etiologies for febrile illness that have nothing to do with Ebola virus infection, and that you can pick up, including very common human infections, including respiratory virus infections.

Yeah, I can remember some very interesting and urgent teleconferences, including late at night. But most of the time, I wasn't really convinced that the person really had had an exposure to Ebola virus, and therefore it was pretty unlikely that that person was actually going to have Ebola virus infection. But I do recall, a few times, getting phone calls that were very complicated situations. One was from the wife of an Ebola virus disease patient who had contacted CDC, and I think someone had not been able to follow up, and I just happened to be talking to a person who was going to assign out that responsibility, and I just said, "I'll take care of it." It ended up being, again, the wife of a patient in Sierra Leone. I was trying to help this person out, and this ended up being someone who—I work with the State Department—the State Department made a decision to medically evacuate that individual back to the US, because that person had permanent resident status in the US.

Another time, I got a call from a woman who actually was a physician, and she was trying to tell me about her family members in Sierra Leone, of whom I believe three died of Ebola virus disease, and a couple survived. She was seeking help in trying to get access to an investigational therapeutic. We were not able to help by individual request. I

sort of felt very helpless. I wanted to help this person, certainly including this person was a physician, but had had her family devastated by Ebola virus disease.

As it turned out, CDC did get a [separate] request. It was sort of a request by the Ministry of Health [and Sanitation] of Sierra Leone actually to Canada, but in some sense also to CDC, to assist. They made a request because there was a very senior clinician in Sierra Leone who unfortunately was diagnosed with Ebola virus disease and was quite sick. The request was for an investigational therapeutic that was actually developed in Canada. I ended up coordinating this shipment, or whole issue along—I was communicating with Sierra Leone colleagues, Canadian colleagues, and actually it was very complicated to just get one treatment course of an experimental medication for a single patient in Sierra Leone. What was extraordinary was the cooperation and collaboration with everyone involved. We were all trying to do this as urgently as possible. I was trying to figure out how to do this as quick as possible. But now I can remember—I haven't thought about this for a while. But there was a limited, a very, very limited amount of this product in Canada. If I recall, it was in Winnipeg, Manitoba. It was flown down to Toronto, so it was actually hand-carried by—and this product needs to remain frozen, so it was carried on dry ice by a laboratory scientist. It was carried down to Toronto, and we were trying to arrange for a plane that was going to medically evacuate this individual to—or actually, a different patient, to divert to go to Toronto, to pick up this medication, and then go to West Africa. But we were unable to coordinate that. Unfortunately, there was no facility that would accept the patient. Then it finally dawned on me that we were just losing time. I suggested that this person continue from Toronto and come to Atlanta, and I had to

actually write a letter and scan a letter on CDC letterhead, and do this essentially in, I don't know, a matter of probably ten to fifteen minutes, to expedite this laboratory scientist so he didn't get stuck in US Customs and Immigration. We could actually time it so he could get on a plane in—so he flew from Toronto to Atlanta, and I told him to stay in a hotel overnight, and then he was going to fly back.

Once he arrived, then I coordinated this. I had a CDC staff person go pick up this package, bring it back to CDC and get it stuck in the freezer, and then we replaced this with frozen cold packages so it wouldn't be on dry ice, but it would be frozen cold packages. But the point was, we would keep it frozen overnight at CDC. I wrote more letters, and then I was able to get an EIS [Epidemic Intelligence Service] officer, who was on her way to Sierra Leone, to actually hand-carry this. I wrote more letters, which ended up being needed, because she flew, I believe, from Atlanta to Frankfurt. The Frankfurt authorities there wanted to inspect this package, and we did not want this package to be opened. It's a good thing I wrote this letter on CDC letterhead and signed it, but I also did not want to disclose what was in this. I didn't want people to freak out that this was an Ebola treatment, because I was concerned that it might not be allowed on a plane.

This nice EIS officer, once she presented the letter and once she was able to get cleared, so that they didn't restrict her from bringing this product on the plane, and in fact, they didn't inspect it. Actually, she arrived in Sierra Leone and was met at the airport there. I helped coordinate that. We got it to the hospital—to the Ebola treatment unit.

Unfortunately—it was stuck in—so, a part of it was stuck in the freezer, but one—this was a product that's administered in three doses. And so one dose was put in the refrigerator to thaw. So the success was, we actually got it from Winnipeg, Manitoba, all the way to Freetown, Sierra Leone, frozen. We maintained the frozen product. They were then able to thaw it in the refrigerator. The very, very tragic thing was the patient died in the morning, before the patient could receive the first dose.

Then the question was, you have this treatment. We don't know if it's going to work or not. There's some evidence to suggest that it might work; it had been given to some US patients. Or, sorry, at least a related product had been given to US patients. Some patients in Europe had received this. But then, you have a scarce product that might benefit a patient, but then a huge demand for it. And then the question is, who, then, gets it? Then it's fraught with politics. Who's more important to get it? As it turned out, I'm not one hundred percent certain, but I believe the person who ended up getting this product was the mother of the woman who had called me to plea for assistance from Sierra Leone. She had lost at least three of her family members.

But the decision of what patient then gets that product, that was not our decision. I was simply helping coordinate the shipment, or the hand-carrying of this product. To me, that was really an example of tremendous international collaboration and coordination. Again, this was trying to do this as urgently as possible. But nevertheless, it takes a lot of time, because we're talking about getting this product on planes from Winnipeg to Toronto to Atlanta to Frankfurt to Freetown, Sierra Leone. In some sense, it was a success. We got it

there frozen. But it was a failure in that the patient died before the patient could receive it.

Q: Right. Thanks for sharing that. It's a great example of the kind of like, crazy hoops that you would have to find yourself jumping through in order to solve a problem.

Uyeki: This happened all the time. I can also remember writing letters on CDC letterhead for some survivors of Ebola virus disease in the US who then went back to West Africa to do work. We did not want them to run into problems coming back. Because they'd had Ebola virus infection, they'd developed Ebola virus disease, they'd recovered from Ebola virus disease. They're not going to get Ebola virus infection. They're not a risk. So if they have a fever coming back at airport screening, it's not Ebola, it's malaria or something else. We didn't want them to have to get held up by the screening and the monitoring, and so forth. One physician, despite my letter, did run into some problems, some complications. But in some of the other people, the letter apparently was helpful. But I have a great deal of respect for these survivors who went back to West Africa to continue providing care for Ebola virus disease patients after they recovered from the same disease that they were caring patients for.

Q: I suppose we have only about fifteen minutes left. There is much more to talk about, actually. Shall we talk about the patient with the Ebola hiding out in the eye, and your work on that?

Uyeki: Sure. Of the nine survivors of Ebola virus disease that were cared for in the US, two of them developed—well, actually, it's probably three of nine—developed ocular complications. But two that I was really involved with, because the other one is really followed by colleagues at the National Institute of Health for follow-up. But two of them did develop complications, ocular complications that were managed by ophthalmologists. One was managed in Massachusetts, and then one was managed at Emory. That survivor at Emory has actually experienced the most complications of any survivor in the US, and also was the most critically ill of any survivor in the US, or for that matter, probably in the world. He developed actually complete loss of vision in one eye. But that happened over time. At one point, he developed extremely high intra-ocular pressure. He was under the care of ophthalmologists at Emory University. One procedure was done, because the pressure was so high in the eye, was to remove some fluid. But also, that was tested for Ebola virus at CDC's Viral Special Pathogens Branch. Not only was it RT-PCR [reverse transcription polymerase chain reaction] positive, but in fact, they were able to isolate Ebola virus. This had never been done before, so in some sense, it was a real game-changer.

In previous Ebola virus disease outbreaks, we knew that ocular complications could occur. There's very few cases reported in the literature. Because these outbreaks were generally—had occurred historically in rural areas, there was very poor follow-up. There really wasn't a whole lot known about ocular disease in Ebola virus disease survivors. But when you go back and look in the literature, there was a patient, many years ago, who had survived Marburg virus disease and actually developed ocular disease in one

eye, and had an invasive procedure, and Marburg virus was isolated from that eye. So it's not that surprising that Ebola virus was isolated from ocular fluid. But this was roughly a couple months or more after the patient recovered from, or at least was discharged from Emory University Hospital. This raised the whole issue of concern of persistence of Ebola virus in immunologically privileged sites. We had known that a virus could be detected in semen for prolonged periods, but no Ebola virus disease survivor had ever had their ocular fluid sampled. So this was, in some sense, both a game-changer, but also, it raised challenges about how to manage that survivor's eye. Actually, this individual is just an astounding sort of case report. He's, again, probably the most critically ill Ebola virus disease patient that has survived. And then, second, everybody thought he was going to lose vision in his eye, and in fact, he's regained the vision. But he's had other complications.

This patient did receive some experimental therapy, and other therapeutics, topical therapeutics. Also received corticosteroids for a long time to quiet down some of the inflammation in the eye. He eventually recovered most vision, almost to baseline. So that was actually a huge success story. One, that the patient survived, and secondly, the patient's vision is nearly—it's not quite normal, but it's nearly normal. That was pretty astounding.

The other US survivor that I was involved with that had unilateral ocular disease was able to be managed as an outpatient. Failed topical therapy, but took oral corticosteroids for a

number of weeks, and actually, vision improved and complications resolved. So that was great.

Q: How would you describe your involvement in these cases?

Uyeki: I worked closely with the ophthalmologists. A lot of discussions, and also with the Emory infectious disease physicians about—a lot of discussions about how the patient might be managed, what experimental therapeutics to consider, and so forth. Eventually, I collaborated with them in writing up case reports on both of these patients so that could be shared with the world.

Q: You also had some contact with the patients themselves, right? Some conversations, etcetera?

Uyeki: I've been in communication with eight of the nine US survivors.

Q: Wow.

Uyeki: Actually, I've been in contact with all nine of them by email, and I've met most of them, not all of them. Some of them I've met multiple times, and a number of them are physicians. I've talked to them on the phone, I've talked to them in person. We've had email discussions, and so forth. For a number of reasons. We were monitoring the male survivors for—or most of them, not all of them. One was being managed by NIH.

Everybody was being monitored for persistence of Ebola virus in semen. I was working with the clinicians who were following them up as outpatients, and then with the patients themselves, to try to get specimens for testing at CDC, and then communicating results to them. There was sort of a game-changing event which occurred in a survivor in the UK [United Kingdom] who had developed meningoencephalitis and was very sick. That was about nine to ten months after her initial Ebola virus disease course, in which she was severely ill and survived, and frankly recovered very slowly over time. But then developed meningoencephalitis, and actually, infectious Ebola virus was recovered from cerebrospinal fluid. That was, again, quite a game-changer. Again, it raised this whole issue of persistence of Ebola virus for many, many months in perhaps an immunologically privileged site. In that patient, in that survivor, a relapse of the virus. That raises a lot of questions for public health, but also for the patient and how do you manage the patient. Because of that, the CDC director, Dr. [Thomas R.] Frieden, asked me to contact all the survivors in the US and inform them about that, and then just communicate about follow-up if they were to become sick. That was another opportunity to communicate with all of them. It's actually been quite rewarding to meet most of them in person and have discussions with them. A couple of them have said to me, when I first met them, "You probably know a lot about the details of my case." My reply was, "Yes, I do." [laughter] But, you know, that's all confidential.

The other thing, just to mention briefly, was when we did have, unfortunately, two secondary cases—both in nurses—who had cared for a critically ill Ebola virus disease patient in Dallas, Texas. That was an extremely stressful time because before that

happened, this was a critically ill patient being cared for at a facility that was not a biocontainment unit. They were completely unprepared for managing an Ebola virus disease patient. I was trying to help coordinate information-sharing from Emory and Nebraska physicians with them, and link them up with FDA and manufacturers, and discussions about investigational therapeutics.

The other thing was coordinating with Emory. One of the Ebola virus disease survivors from Emory ended up donating plasma that was transfused to five other patients in the US. I look at that individual as being a very noble and generous and compassionate survivor. He thought that if there could be some benefit is his plasma, because it likely had antibodies to the virus, that that might actually help improve the outcomes of another patient in the US who was very sick with Ebola virus disease. We had that individual donate repeatedly, and when we had a new patient, we collectively—the clinicians and myself, tried to contact that survivor. He moved around a lot in the US. Sometimes he was driving somewhere, and we're trying to get him to stop at a blood bank in a certain state, and get that blood then transported to another state, where the patient who's to receive that transfusion is being hospitalized. Another time, we only had about twenty to thirty minutes. This individual was about to get on a plane to go to a certain state, a certain city. We ended up getting that person to fly to a different city, and then get an escort right away from the airport to a facility where he could donate blood and the plasma could be extracted, and then that could be brought to the hospital where a different patient was.

Some of this, again, is just, whatever comes up, you just do what you need to do and try to coordinate and facilitate. But a lot of it is, once you start working with people, and they know you, and they trust you, and then it's easy to get on the phone, even if it's three o'clock in the morning. There was a huge amount of collaboration, coordination, people really working together. Because everybody's trying to do the right thing and actually try to help. This was a very rewarding thing, working with a lot of people, both inside CDC, but a lot outside of CDC, and a lot of people actually outside the US. There's a huge amount of cooperation and collaboration going on. People working, trying to help out, and I think that was the best of it. Despite limited sleep for many, many months.

Q: No doubt. I know you have to run to a call, but I want to thank you so much for donating yet more of your time, Tim, to this project. It's been fascinating hearing your stories. Thank you.

Uyeki: Thanks, Sam. It was a pleasure.

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