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 1 of 2

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Q: This is Sam Robson here today with Tim Uyeki. Today's date is April 29th, 2016, and we're in the audio recording studio here at CDC's [Centers for Disease Control and Prevention] Roybal Campus in Atlanta, Georgia. I'm interviewing Tim as part of the CDC Ebola [Response] Oral History Project. Tim, thanks so much for being here with me today and for the record, could you state your full name and your current position with CDC?

Uyeki: My full name is Timothy, middle initial is M, and my last name is Uyeki. My title at CDC is chief medical officer in the Influenza Division, National Center for Immunization and Respiratory Diseases, CDC, but I think what you're interviewing me about is my role as the clinical team lead for the CDC Ebola response.

Q: Absolutely, thank you for that.

Uyeki: In the fall of 2000, after I had finished EIS [Epidemic Intelligence Service], there was an Ebola virus disease outbreak in northern Uganda, and the epicenter of that was in Gulu District, which borders southern Sudan. CDC sent three different teams as part of the WHO [World Health Organization] response. Because I had worked previously in

Uganda, I was very comfortable with Uganda—I knew the country, and English is not a problem in Uganda—I was very lucky as just after I had finished my EIS two-year fellowship that I went off as part of the CDC team to join the WHO Ebola outbreak team. I was in Uganda for about seven weeks. I guess I went in November, late November of 2000, and came back sometime in early 2001. I remember having either or both Thanksgiving and Christmas dinner in Uganda up in Gulu District. That was a very, very interesting experience. Prior to the 2013 to 2016 Ebola virus disease outbreak in West Africa, the Gulu outbreak back in 2000 to 2001 was the previous largest Ebola virus disease outbreak. We had approximately 425 suspected, probable, and confirmed cases with approximately a case fatality proportion of fifty-five to sixty percent. I was involved in a lot of surveillance activities, but I was with the second team, so I went after the outbreak had already peaked and was coming down because of the control measures that were implemented. Those are the same as what were done for this outbreak, which is you isolate, you want to isolate the symptomatic patients in an Ebola treatment unit and you want to monitor the exposed contacts for twenty-one days so if they become symptomatic they need to be tested and then isolated. I was involved in a lot of field surveillance, but several of us were performing activities in the field that are not done by CDC staff nowadays. For example, if someone dies in a village, a rural village, what's very, very important is finding out if they died of Ebola virus infection because of the implications for controlling the outbreak, monitoring of the contacts. You need to test that corpse for Ebola virus infection. CDC's Viral Special Pathogens Branch had set up a field laboratory. Not only from patients that are sick do you need samples, but you also need samples from people that die unexpectedly in villages. So, we were performing cardiac

punctures on corpses and so you get a sample of serum that can be tested by RTPCR [reverse transcription polymerase chain reaction] for Ebola virus RNA [ribonucleic acid] by the field laboratory. So it was a variety of activities, particularly surveillance activities.

Q: Does that mean that you were collecting samples?

Uyeki: From corpses, yes. We also would take skin snip from the back of the neck and send that—these are from corpses—and put that into formalin preservative, and those would be analyzed and tested back in Atlanta. The serum specimen would be tested right there by the field laboratory for Ebola virus RNA.

That was an amazing experience. I hadn't worked on Ebola since until I got a call from Inger [K.] Damon, who was the incident manager, and I distinctly remember getting a call on August 1st at 11:55 am, and Inger asked me to work on the CDC Ebola response as the clinical team lead and to get on a conference call in five minutes at noon. I accepted, and then that began my work on Ebola for CDC. I should also say that earlier in the spring, I had been asked to go to West Africa to work on the Ebola virus disease outbreak in the early days, but I was unable. I was not available at the time, so I was actually more than happy to work on Ebola when Dr. Damon asked me to join the CDC Ebola response. I would say that it was very humbling because I definitely do not consider myself an expert on Ebola virus disease and I still don't, but at least I'd had a little bit of experience albeit back in 2000, early 2001.

Inger called me and asked me to be the clinical team lead for the CDC Ebola response and to join a conference call in five minutes with a number of groups, a number of US government colleagues and others to discuss potential use of investigational therapies or experimental therapies for Ebola virus disease patients, and that was the start of my work on the clinical aspects of Ebola virus disease for the CDC Ebola response. The very next day, August 2nd, the first patient with Ebola virus disease managed in the US arrived at Emory University Hospital. We knew this patient was on the way the day before and this was trying to start discussions about what investigational therapies might be available. That was the very beginning of a lot of discussions with FDA [Food and Drug Administration] colleagues and others about what drugs might be available and so forth. I was also the liaison between CDC and Emory University Hospital clinicians. Ended up, throughout 2014 and 2015, there were eleven patients with Ebola virus disease that were managed at US healthcare facilities, including three biocontainment units at the University of Nebraska, Emory University, the NIH [National Institutes of Health] Clinical Center, and then two hospitals, Texas Presbyterian Hospital of Dallas and then Bellevue Medical Center in New York City. Bellevue had been preparing for potential admission of an Ebola virus disease patient and they were set up, whereas Texas Presbyterian Hospital of Dallas had made no preparations. I ended up being essentially the liaison between CDC and all of the clinicians managing these eleven Ebola virus disease patients. In addition, I worked very closely with the State Department, their medical operations unit, because they were responsible for medical evacuation of Ebola

virus disease patients that were either Americans or American citizens who had permanent US residency status. It was quite an experience and quite interesting.

Q: What are some of the initial things that you have to deal with when Patient One comes in August 2nd? What are some of the—for instance—therapies that you are considering might be appropriate for him or her?

Uyeki: Well, in addition to the admission of an Ebola virus disease patient on August 2nd, a few days later if I recall, it was August 5th, so three days later, the second Ebola virus disease patient was admitted to Emory University Hospital—both of these individuals had been evacuated from Liberia. Basically, this was quite a learning experience with all of the clinicians involved. They had never managed an Ebola virus disease patient and there is no proven treatment for Ebola virus disease, although there is one monoclonal antibody cocktail that is likely to have clinical benefit, but the randomized trial of this therapeutic called ZMapp did not enroll enough patients. It was under-powered statistically, and even though a survival benefit was suggested, it was not statistically significant. We still don't have a proven treatment, and basically clinical management for Ebola virus disease patients consists of supportive care, and so that's really managing any of the complications or metabolic abnormalities that a patient might manifest and supporting the patient until their immune system can recover and fight off the virus infection. It really comes down to really excellent nursing care and critical care management.

In the US we had eleven Ebola virus disease patients and two died, so that's a tremendous achievement compared to the reported mortality for Ebola virus disease patients in West Africa. It's also when we look at the European and US Ebola virus disease patients, of which there were twenty-seven, only five died, so the case fatality proportion for those managed in Europe and the US was 18.5%, so that's much better. Although most of them received some experimental therapies, we really have no idea if they had any clinical benefit at all. This was all uncontrolled, compassionate use, emergency use, and not controlled. It's sort of the art of medicine. You give the patient what you think might be helpful, but we also have to realize that some of these potential therapies might actually have harmful effects as well. There were some side effects and at least in one patient might have contributed to clinical deterioration in the patient.

It was basically since the beginning, trying to focus on, what potential experimental therapies are available? What's the in vitro data available? What's the animal data that are available? It was really an evolving process. The other aspect that our clinical team worked on was what about in people that had a potential high-risk exposure, such as a needle stick while working inside an Ebola treatment unit? That's a rather high-risk exposure to Ebola virus, or at least potential exposure. What could be administered to those people for post-exposure prophylaxis? Our clinical team also focused on that.

A lot of what our team did was linking and trying to coordinate information and helping the clinicians learn from each other. The first two patients were admitted to Emory University Hospital, but then we had patients admitted to the University of Nebraska

biocontainment unit. My role was to really link the clinicians up with each other. I organized and coordinated, and I guess I was the moderator of these clinical teleconferences. One really important aspect was sharing of information from clinician to clinician, and that was not only in the US, but I organized the US-European clinical network on clinical management of Ebola virus disease patients. Not only was detailed patient information shared among US clinicians who were managing patients, but also across the Atlantic with our clinical colleagues in Europe. These allowed discussion of very detailed information on a confidential basis, and I think I ran something like eighteen to twenty of these international teleconferences. In addition, we would share information by smaller conference calls or one-on-one calls and then e-mails.

Another aspect was getting specimens from these patients or either suspected cases or confirmed cases to CDC. Trying to coordinate the specimen collection and then shipment to our Viral Special Pathogens Branch diagnostics laboratory to confirm Ebola virus disease infection, but then to monitor the infection because this has implications for clinical management in terms of hospital discharge. When has the patient cleared Ebola virus from the blood? Therefore, you have to follow this patient, even as they're improving, you have to continue to test the patient's blood—we also tested urine specimens—because you do not want to discharge a patient even if they're clinically improved if they still might have evidence of Ebola virus in their blood.

For the patients at Emory, there's no need to do air shipment or ground shipment. Basically, I would coordinate the specimen transportation, and between myself and

another colleague we transported ninety-nine percent of all the clinical specimens from the four Ebola virus disease patients that were managed at Emory as well as other specimens from survivors that were being evaluated at Emory. But for patients outside of Atlanta, it was organizing the—coordinating the transportation of those specimens to the CDC and then communicating the results of the testing done at CDC with the clinicians as soon as they were available.

Another important aspect was certainly communications with the clinical community in the US. Participating in clinical outreach and communications activity or COCA calls, conference calls, along with other CDC colleagues, and then to maintain a web page of detailed clinical information and guidance on the CDC web pages. But also to inform the leadership for the CDC Ebola response, including Dr. [Thomas R.] Frieden, about the status of Ebola virus disease patients in the US.

We had a very large separate group of clinicians at CDC that were helping do consultations on persons who were sick in the US who were deemed suspected cases of Ebola virus disease, or more specifically, persons under investigation. I would work with them on some of the cases that were more suspicious for Ebola virus disease than others. Many of these patients actually had malaria, but I would be involved in some of these clinical teleconferences with state health departments and other CDC colleagues if there was a highly suspicious person under investigation.

Another aspect, another activity by our clinical team that I was very much involved with when there was a patient with Ebola virus disease was helping with getting an experimental or investigational therapeutic to the hospital. Working with FDA, working with the clinicians, working with the companies to get a product that might have potential clinical benefit approved and then delivered onsite.

I was really working a lot with a variety of groups for each patient. For some of these patients, while they were hospitalized, not only did I organize daily clinical teleconferences, but I also organized sometimes twice daily clinical conferences; morning and late afternoon. Some of these calls were actually going on in the evening and late at night depending upon status of the patient and so forth. Some of these patients—we had two secondary cases unfortunately in nurses in Dallas, and we decided to move those patients. One was transferred to the NIH Clinical Center and one was transferred to Emory University Hospital, so I was very much involved in both of those situations. Just trying to keep all of the clinicians in the US—well actually, US and European clinicians who had managed at least one Ebola virus disease patient—sort of keep everybody up to speed with the latest information. Sharing whatever latest information that was available that might be of some use on a confidential basis.

Q: Can you give me an example of a specific piece of information that, this is something that people need to know, let's share this in the teleconference?

Uyeki: Well, we certainly talked about—we had discussion of various complications and when interventions might occur. For example, some patients became critically ill and had respiratory failure and had to go on mechanical ventilation. Some developed kidney failure and had to go on renal replacement therapy. Basically, a lot of patients initially had a peripheral intravenous catheter, but then some benefited by having a more invasive line, what's called a central venous catheter. This is all intensive care management and it involves decisions about maybe implementing some of these interventions earlier than maybe later because the patient may be deteriorating very, very rapidly. You might want to intervene earlier than later. So basically, it was sharing that kind of information. Also, what particular investigational therapies were used, what dosages and what frequencies and how long to treat. Basically, a lot of this was brainstorming, thinking out loud. All I was doing was serving as like a facilitator, a moderator of information. I wasn't the one telling people what to do. I was basically facilitating clinicians who had managed a patient to share information with clinicians who suddenly just admitted a new patient. A lot of it was really helping with information sharing, keeping everyone up-to-date.

Q: At the same time I imagine you, as this coordinator, creating this forum for people to share, would develop this really neat view of the forest instead of the trees, right? This view of the overall and be able to find, this is something that's really important. That is something that's really important. Can you talk a little bit about that?

Uyeki: I think you learn a lot about Ebola virus disease, sort of the details, characteristics of these patients, the clinical course. For example, on one hand you can read about what

are the signs and symptoms of Ebola virus disease, but actually they don't come on all at once. We talk about oh, a patient with fever and diarrhea, but the diarrhea doesn't typically come on day one of illness. People have this image that Ebola virus disease patients, because Ebola is one of the so-called hemorrhagic, viral hemorrhagic fever diseases, that people are bleeding profusely from all over. Some people do. Those are critically ill, near death. But most patients with this particular—that had Ebola virus disease from *Zaire ebolavirus* infection, which was the Ebola virus species that was the cause of the West Africa outbreak, the amount of gross hemorrhage was actually a low proportion. What's important to understand is sort of the evolution of the signs and symptoms. The first few days of illness, you may just feel malaise. You may lose your appetite. You may or may not have a fever, and the gastrointestinal complications or gastrointestinal symptoms come on somewhere. I mean, there is a real range, but they may come on somewhere around day four to six. Actually, the profuse, watery diarrhea is a big problem with Ebola virus disease because not only do you lose fluid, but you lose a lot of electrolytes, in particular potassium, and that can lead to cardiac arrhythmias and actually you can die from that. You can die from shock because you've lost so much fluid through the diarrhea.

Again, there's sort of a progression, a timeline, and there is a range, but I can remember hearing about some signs and symptoms and findings and lab findings in one of the US Ebola virus disease patients and hearing that the patient's only been sick for about one day and given what was presented to me, it's impossible. I shouldn't say impossible, it's very unlikely that this all occurred all at once, and likely the person has had Ebola virus

disease for probably about four or five days and probably infected for longer than that. You can sort of get a sense of the timeline of the progression of signs and symptoms and then the complications. I had some discussions late at night on conference calls, including separate calls with Dr. Frieden and e-mails about some patients. I think it's a learning process, so it's sharing of information and then learning. It's a collective kind of thing.

Q: Can I ask about that specific case when you see an individual and it's highly unlikely that they just came down with Ebola, they were probably infected earlier—perhaps they were infectious earlier. Is that something that also comes to the fore and maybe something that you learned through looking at this person's progression is going to affect what people need to look for in terms of chains of transmission?

Uyeki: Well we know that people really are not very contagious at all until they become symptomatic. Someone who is infected, but is not yet sick, even with mild illness, is not thought to be infectious. It's once the illness starts, in particular once the fever starts, you become more and more infectious. But the early days even of Ebola virus disease, you're not very infectious, and that's something that's important for testing because if you test someone after they've only been sick one, two, or even three days, they might test negative, and that's because the level of virus in their blood may not be high. As they get sicker and as they progress, the level of virus circulating in the blood will be much higher and will be detectable. People are not so contagious even in the early stages of disease, but as they get sicker they're more contagious.

[break]

Uyeki: One of the other things—well, I was involved with many things, but I was involved with the planning for the Monrovia Medical Unit. From the very beginning, working with an interagency group for trying to decide what kind of care might be provided. What kind of interventions might be utilized. What kind of supplies and equipment might be available in the Monrovia Medical Unit. That training was done, and as part of that training, I don't think they had organized any discussions with people that actually had come back from West Africa, that had worked in Ebola treatment units. So I contacted the Public Health Service leadership and offered to arrange some clinical teleconferences. I got friends and colleagues who had worked in Sierra Leone, Guinea and Liberia in Ebola treatment units early on in the outbreak, and had them discuss the clinical features of Ebola virus disease and the kind of patients and complications that they were seeing. Their experience as working in these ETUs in West Africa. In addition, I had colleagues from Emory and Nebraska on to sort of talk about some of the details of the Ebola virus disease patients in the US.

The reason why it was a nice complement was because in the US and Europe we can run a lot more laboratory tests and do a lot more assessments and interventions that's not possible for most ETUs in West Africa. We can learn a lot more about the experience of patients in the US and Europe managed in these tertiary care medical facilities or special biocontainment units that can augment the experience learned in caring for thousands of Ebola virus disease patients in West Africa. I organized those teleconferences both for the

teams that were going to staff the MMU, both before they left the US, as well as some teleconferences to present cases while they were in Monrovia. We had case presentations from some of the clinicians that had managed cases there. So I think that was beneficial both ways, sort of two-way sharing of information.

Q: I want to thank you now because I want you to have enough time to get to your call. Thank you so much and I look forward to our next talk.

Uyeki: Yeah, thank you.

END