INTERVIEW WITH

Dr. ANTHONY FAUCI

H1N1 ORAL HISTORY PROJECT

Interviewed By Sheena Morrison

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Interview with Dr. Anthony Fauci
Interviewed at NIH,
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H1N1 Oral History Project
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Dr. Anthony Fauci: AF
Sheena Morrison: SM
Patty: Patty

Sheena Morrison: The following interview was conducted with Dr. Anthony Fauci, director of the National Institute of Allergy and Infectious Diseases within the Department of Health and Human Services. It was conducted on behalf of the National Library of Medicine for the Making History: H1 Oral History Project. It took place on March 23rd, 2010, at Dr. Fauci's Office in Bethesda, MD. The interviewer is Sheena Morrison.

So let's begin with biographical stuff.

Anthony Fauci: Okay.

SM: How long have you been in your current position?

AF: I am the director of the National Institute of Allergy and Infectious Diseases, and I have been in my position since November 1984.

SM: Okay. And can you give me an overview of your agency's role in the federal government's planning and response effort to the 2009 H1N1 outbreak? And how did you facilitate this as Director?

AF: Okay. So, the National Institute of Allergy and Infectious Diseases has the primary responsibility for study of the basic and clinical research in all infectious diseases and diseases of the immune system. Since influenza is a major infectious disease for decades and decades, the NIAID has been a major player in the basic clinical research associated with understanding the pathogenesis of influenza: the clinical trials in the development of vaccines for influenza; the developing of drugs for influenza, as well as the evolution and epidemiology of influenza viruses throughout the world, predominantly in humans but to some extent in animal carriers such as in birds and in pigs, et cetera.

So, the influenza pandemic of H1N1 of 2009 fell right within the realm of the responsibility of NIAID of studying influenza viruses as they evolve. I'm sure you have a question about what our role was in the development of the vaccines; I'm sure you have a separate question for that. So, rather than give you all the information on one answer, I'll wait for that question. Unless you don't ask it later, I'll be happy to answer it now.

SM: Alright. Can you recall where you were and what you were doing when it became clear that this novel H1N1 virus was highly transmittable?

AF: You want me to give a dramatic story like I was in the bathtub just listening to a radio? [Laugh]

SM: Perhaps sitting at your desk or--?

AF: No, I actually am being facetious. I know exactly where I was: I was sitting at my desk. And I remember seeing on one of the news alert type email (the bulletins you get, both from regular news and from the CDC,) that there were a couple of cases of a virus in Mexico. And then soon thereafter, viruses in Texas and in California in

individuals with influenza-like symptoms that were non-typeable. And as an infectious disease person, that is always a big red flag that may not have been a red flag for the man in the street who hears about the non-typeable vaccine, excuse me, a non-typeable virus. But to those of us who do infectious disease that means, "Hmm, maybe it's the evolution of a new virus, a new influenza."

And then, in a very rapid succession of events, it was identified actually by a new surveillance system that the CDC had set up in several places throughout the country, including in California. And they were able to recognize it as an influenza A, an H1N1, but one that has never before been on record in its sequence and its properties. So, that was the beginning.

I remember I was in my office when I first saw it. And then, over a period of a few days, things evolved rapidly. We were getting back and forth from the CDC and were in reasonably continual contact with the CDC during the influenza periods about what was going on with influenza. We read all of the material because now our scientists that we fund feed into the data bases that the CDC uses, et cetera. So, it's a very smooth interdigitation of

collaboration. So a), I first saw a small announcement. Then things started to happen: phone calls back and forth with the CDC, et cetera.

SM: So at what point did things, did your particular role—?

AF: My particular role became apparent very rapidly because the sequence of events that occur when a new virus is isolated is that you isolate the virus. The CDC did a magnificent job of doing that very quickly, within a period of days to weeks.

Once they got the virus growing, they gave it to us at the NIH to distribute to our grantees to do molecular analysis; to do pathogenesis studies; to do animals studies. In addition, they gave it to several of the pharmaceutical companies that the Department of Health and Human Services has contracted with over a period of time.

The contracts were already in place to develop seasonal flu vaccine. Since this was the end of the season of flu--it was in April, and then this started happening at the end of April and the beginning of May that the seeds stocks were

given--at that point, right from the beginning as soon as the virus was isolated, NIAID and me personally got very heavily involved.

Let me tell you how the institute got involved, and then I'll tell you how I personally got involved. Institute gets involved because it is the tradition that when vaccines need to be tested, we have a very tried and true decades-old vaccine and treatment evaluation unit. It's called the VTEU's, which are used throughout the country: eight of them that are set up to do vaccine trials.

So, we immediately needed to know--since the companies were developing a vaccine at the contractual agreement with the department--we needed to know how to use it. And the fundamental question that NIAID would answer is what is the right dose? Is it 15 micrograms? Or, is it like the H5N1 from several years previously, which required a much higher dose to induce an adequate immune response? Was it two doses of 15? Was it two doses of 30? Is the dose the same in the young, the elderly, the children, the infants? What about pregnant women? What about people who have other issues, such as those who have HIV Aids and asthma, et cetera, et cetera?

So, we needed to determine is it immunogenic? Does it induce a good immune response? And if so, what's the proper dose for that? And we immediately launched on a series of clinical trials. So, that was my institute from the very beginning jumping on the problem of working closely with the CDC for filling our role of how we use the vaccine. The companies make it; we figure out how to use it.

I got personally involved in two ways: One, as the director of the Institute, I follow closely and direct several levels up all of what's going on out there. But I have program directors who, on a daily basis, do that.

But the real personal involvement was that the Department of Health and Human Services immediately formed the H1N1 pandemic flu team, which was represented by me from NIH; by the FDA, which at the time was Jessie Goodman who was involved in from the FDA; Tom Freidan was not yet the CDC Director, so it started of with Rich Besser, and then Ann Schuchat and other people from CDC, and people from the Department of Health and Human Services: Nicky Lurie, Laura Petrow, Jenny Baccus, et cetera. So, there was a core team that literally met every single day on a conference call

about what was going on, and what we needed to do. So, I got very personally involved because I was part of this core HHS/NIH/FDA/CDC team.

SM: So, initially you said that your institute jumped right into preparing--?

AF: The clinical trials for the vaccines.

SM: But at that time, there really wasn't any funding. So NIH used its own money?

AF: Absolutely. We moved money around quickly to get the job done.

SM: And what other mechanisms were in place for these agencies to communicate? Was it simply the conference calls, or were there other mechanisms?

AF: Well there were other mechanisms. The conference call was the verbal interaction, but we would get a report every single day from the CDC. And the CDC had a real-time internet website updating on what was going on. So it was real time information flowing in all the time, every single

day. So it was the website from the CDC, material that gets sent and printed out (but most of them was online stuff), and it was the relatively continual conference calls that we had.

SM: And for your institute, did you have something in place as well to coordinate what was happening?

AF: Well, everyday there would be a phone call. I mean, there was material. I would get a daily written report from the Division of Microbiology and Infectious Diseases updating me on clinical trials and updating me on everything that was being done. So we had a daily update report, and every week, there would be a summary report.

SM: Was there anything early that would indicate that this particular virus was different from any other virus?

AF: Oh, absolutely. The molecular structure immediately told us that it was different.

And background immunity in the population, there was none in young people, in children, in young adults. There was an interesting bit of background immunity in the elderly,

which strongly suggests something that we now know for sure molecularly: that the viruses that were circulating in the 50's and even the 1918 Spanish flu pandemic virus had some serious similarities between that and H1N1 of 2009. Because at first, there was antibodies that were present in the older population that suggested that they might be relatively protected. And in reality, they were. Because if you look, as the picture unfolded in real time, kids and young adults were getting infected, but the older people were getting infected but at much, much less a rate than the younger people, which is a epidemiological strong suggestion that they had some background immunity.

So, what occurred in sequence? First, what was happening alerted us that there was some cross-reacting immunity. When you looked at the sera of the elderly people, we found that they actually had antibodies that did cross-react with H1N1, where the younger people didn't. And then, when finally you get a complete sequence of all the viruses over the years, and you went to the informatics computers, you found out that they were significant similarities molecularly between H1N1s that was circulating in the 50's, that were circulating in 1918, and the H1N1 of 2009. So, it was a nice scientific story that unfolded over months.

SM: So, this is a novice asking right now. In your opinion, was the novel...was it the result of a shift, or--?

AF: No, we know exactly what it was. It was a re-assortment in a pig vehicle (namely, a pig, a living pig) of multiple viruses, multiple influenza viruses: human influenza virus, bird influenza virus, and at least two types of swine influenza virus that came together in a pig population.

And you can do--the beauty of molecular biology is that you could look at what's called molecular fingerprints--and you could do a mathematical modeling of how long it was in a pig population before it jumped into the humans, which was in March or so of...Probably earlier than March, but a couple of months earlier. But it first got recognized in March, April. And we know that that virus was likely in pigs for at least ten years before it jumped into the human.

SM: Ok. What were some of the major issues that you were confronted with during the first wave? And were these similar issues that you dealt with by the second wave?

AF: Well no, they were different. The issues were we had a virus that was spreading at an unusual time; you don't see influenza spread rapidly in April, May and June. That was one interesting phenomenon, and that was related to the fact that you had a naïve population of kids in school. But when you have warm weather--windows open, humidity--viruses don't spread very well.

So, we had the bad news that the kids were not immune. The bad news is that it was a new virus. The helpful news is that summer was coming. The weather was warm, the weather was moist. Cold-dry is good for flu; warm-moist is bad for flu. So, instead of there being a major explosion throughout the country, there were many explosions: like in Saint Francis Prep in Queens, and some of the New York Schools that had to close, and a little bit here in Washington, DC, et cetera.

Then when the summer came, the virus didn't do what influenzas do. They usually go underground essentially and

disappear--figuratively underground, not literally. They disappear: very, very little flu. It went down, but it didn't disappear. It smoldered around and infected kids in camps and soldiers who were recruits in Army Bases, because influenzas love when you crowd immunologically naïve people together. And in the summer, which is fundamentally a bad time for flu, you still have crowding. So instead of having explosions, it kind of subliminally hung around.

And then the really different thing that happened with the second wave is that unlike seasonal flu, which even though the kids come back in September to school (the end of August and September), the seasonal flu from the previous year is usually so underground that it isn't until December, January, and February when seasonal flu explodes in the schools. That didn't happen this time. Since the flu was lurking in the background, as soon as the kids came back at the end of August, the beginning of September, there was an absolute explosion of influenza in the second wave, months earlier than it usually happens. It happened in September and October. By the time November and December came it was gone. I mean, not gone, but close to gone. Whereas in the regular flu season, it does this until December, and then it goes up and then comes down.

So, it was a couple of unusual aspects in both the first and the second wave. The first wave occurred when flu shouldn't occur. What is it doing occurring in April? Doesn't happen, but it did--didn't get too serious because of the weather, the kids getting out of school. Then it happened in an unusual time in the fall, very early as opposed to late.

SM: And we still haven't had a peak seasonal flu.

AF: We had no seasonal flu. Not peak, none.

SM: None? It didn't happen?

AF: It knocked it right off the radar screen.

SM: Well, you touched on this a little bit. What were some of the underlying assumptions that guided your decision making process in the spring, and how did they change by the fall?

AF: They actually didn't change. The underlying assumption is that we needed a vaccine and we needed it quickly, and

we needed to know how to use it. So, I implemented clinical trial as quickly as we possibly could, and we got the information as quickly as we possibly could. From NIH's standpoint, things went very, very smoothly. We were tasked with doing the trials and getting the information. We got the information we needed, and we got it right on time.

The difficulty was that the virus and the vaccine didn't grow very well. It wasn't a research problem; it was a production problem. So, we came out looking pretty good on this. Others didn't through no fault of their own. The virus just didn't grow very well. So when that peak came in the beginning of September and October and then went down, the vaccine in its full force was not ready until November or so--October, November, December. We knew how to use it because I had done the clinical trials in the summer and in September and in October. So we knew exactly how to use it. The only trouble is we didn't have it.

SM: You had just enough to do the trials.

AF: We had enough to do the trials but not enough to significantly distribute it to the population.

SM: As many federal agencies moved from a transitional leadership in the spring to its current leadership by the fall, what kind of impact did this have on your institute and your efforts to implement your response [indecipherable 19:49]?

AF: You mean the administration? No, none, none.

SM: The fact that in many of the agencies there weren't, like, there wasn't an ASPER, there wasn't the director of the CDC, director of [muffled 20:02]?

AF: See, what people don't understand is that organizations like the NIH and the CDC are very, very deep in people with a lot of experience that don't change from administration to administration, or from year to year. So, there was really no negative impact on the fact that we were in a transition.

SM: You've been in a role of readying the country for influenza pandemics prior to this current outbreak. Is there any different in the degree of senior level White House involvement in the response effort when compared to

the government strategy to deal with H5N1 or other emergent infections?

AF: Well, the difference... I mean, there was one potential. I had been at the helm of many seasonal influenza vaccine developments, which is a very predictable smooth process, rarely gets White House and departmental involvement.

The preparedness for pandemics: Over the last several years I've had two major experiences. One was preparation for a pandemic that never happened: H5N1. A lot of involvement at the level of the Department of Health and Human Services, particularly during Tommy Thompson's regime and Michael Levitt's regime during the Bush Administration. The preparation was superb. We didn't have to execute it, and it was because of that superb preparation, and even the current administration admits that, that things went so smoothly this time with the real pandemic.

So there was one somewhat suppressed pandemic that never occurred, but it launched a major pandemic preparedness plan that was implemented during the Tommy Thompson/Mike Levitt era and the Bush era. Now, we took that plan and

then we implemented it during the current administration because it was a good plan and it really got us hitting the ground running. So there was no difference except that the administration got involved in the preparation in the previous administration, and got very much involved in the implementation in this because we had to implement, because we had a real pandemic.

SM: Right. You're right. You are to the point.

AF: I don't screw around.

SM: [Laugh.] Okay. One of NIH's primary roles in the U.S. government pandemic preparedness plans is to conduct scientific research and clinical trials needed to develop and test pandemic influenza vaccines and therapies. Was there any phase of the process from characterization of the virus to identifying a candidate strain and conducting the clinical trial that could be identified as either a breakthrough or a barrier in expediting the manufacturing of the vaccine?

AF: No, there were no... What we did was unrelated to expediting of the manufacture of the vaccine. Our role was

purely--give us enough vaccine to do the clinical trial, and then we would tell you how to use it, what's the right dose, how many doses, when to give it, and whom to give it to. And we did it, and it had nothing to do with the manufacturer. There were no barriers. It was smooth because, as I mentioned earlier, we have clinical trial process that we do every year. So, we just plugged it right in, and we just did what we do. You know, Kentucky Fried Chicken, we do chicken right; we do it all the time. Ando so--

SM: That's the Vaccine and Treatment Evaluation Units, right?

AF: Right, exactly.

SM: So was there a working relationship with vaccine manufacturers?

AF: Oh yeah, oh yeah, absolutely. They gave us the product. So, you know, and then we shared all of our data with them--it was a very transparent process--as soon as we got the data. Usually, you wait until you write a manuscript and you publish it and do things like that. We

were totally transparent with our data. We gave it to the CDC, the FDA, WHO, and the companies as soon as it came out.

SM: Do you think this kind of transparency actually solidified the agencies as a whole and in a way that wasn't present prior to this?

AF: Well, you know, I wouldn't say it wasn't present prior to this. We hadn't had a pandemic prior to this. We had a preparation for pandemic, but we didn't have a pandemic. So, I would say that we are very pleased with what happened because what we had planned for, we executed. The planning was good, and the execution was good. I mean, this would have been considered, historically, a huge success story, which it actually was, were it not for the fact that the virus didn't grow very well, and we didn't have enough vaccine early on. But every other step of the process worked beautifully.

SM: Yeah, and in fact, the government got a B+ from outside--

AF: Right.

SM: The beltway.

AF: And I think if we had had the vaccine in time, we would have got an A+.

SM: Or, not predicted.

AF: Right.

SM: Okay. So, can you tell me a little bit more about how the Network of Vaccine and Treatment Evaluation Units were employed?

AF: Yeah, well, what they do is that they are at the ready. We contract with them, and they are ready to do a vaccine trial on a moment's notice as soon as we say, "Here is the material." So the process is very simple: we ship the material to their sites, and the sites are Rochester, New York, Texas, Atlanta, all over the place. And what we do is we ship them the vaccine, and we say, "This side is gonna do this one. You gonna do it in infants." The ones who have good pediatric access use infants. Then, the other ones will do adults, and the other ones who use pregnant

women. So we essentially have a plan, a war plan, you know, like a map: You guys do this, we'll send you that; you guys do that, et cetera. But they are prepared for that. It's almost like they've rehearsed that a hundred times.

SM: So they are just there waiting?

AF: They're there waiting for this to happen.

SM: Has there been any data from the studies, from NIH studies or any other NIH supported research that has helped to better understand the nature of the virus and how it causes diseases in human?

AF: Oh, absolutely. Like I told you from the beginning when we first started talking, when the virus was first isolated, it was given to us, and it was given to the companies. We gave it to our investigator that we fund through our grants and our contracts to do the research that you are asking about. And we found out its virulence. We found out its transmissibility in ferrets. We found out what the molecular signatures were of transmissibility and of virulence. We found out does it easily re-assort with other viruses or not? And if so, what is the end result?

So, we examined this every which way but Sunday, and we knew a lot about it after a few months.

SM: Okay. I asked you whether you thought it was the result of an antigenic shift or drift. Well what are some of the things that researchers have discovered about the H1 virus that sets it apart from other H1N1 viruses? What makes it unusual?

AF: What makes it unusual is that it is molecularly completely different. I mean that's the thing. It is different from the standard H1. H1 is around every year, and that's part of our routine vaccination is H1N1. This H1N1 was very different and was not in our data base. We had not seen it before. We have seen things that may have resembled it, which is why I said is the reason why the elderly people probably have some cross-reactivity. But we have never seen a virus just like that before. So that's the defining, distinguishing feature. It was a brand new virus.

SM: Okay. Can you tell me--what were some of the safety concerns surrounding the administration of the H1N1 vaccine

and the seasonal flu at the same time? Why was there a concern?

AF: There was no concern about safety. The concern of the seasonal flu and the pandemic flu vaccine given at the same time is that if you gave it at the same time, did you need to space it by a week or a month or two months? Would one lessen the response to the other? In other words, if practically speaking, it would be great to bring people in and say, "Here is your seasonal flu; here is your pandemic flu" at the same time? There was a theoretical concern that if you did that, that the response to each would not be optimal, that you would have to separate them. So we did the study, and we found that when you did it at the same time, or followed by a month, there was no difference in the response.

SM: Okay. So, if you had to name, say, six principle players who were actively involved in shaping policy around the pandemic response efforts, who would they be? Yourself included, of course.

AF: It would be me (I'd be one of them for sure); Jessie Goodman; Secretary Sibelius; Ann Schuchat; early on, Rich

Besser when he was CDC acting, and then Tom Freidan thereafter; eh, Robin Robinson; Nicky Lurie. I would say that was the core group.

SM: Okay. Do you have a timeline of the events that you use for yourself to track the events as they occurred--where your response was related--that I could use and keep for posterity's sake as part of the archives?

AF: What do you need?

SM: Well, for instance, like BARDA. They had their strategy; it's also a timeline.

AF: Yeah, I could tell you, and you could write it out.

SM: Okay, alright, that's fine.

AF: We found out about it in April. We were given the virus in May--end of May, beginning June. We distributed it to our scientists, and then over a period of the summer--July, August, September, October--we did our clinical trials, got our answers, and that was it. And now we're done.

SM: Are you working on anything right now related to H1N1?

AF: We're still following up on a lot of individual grantees who are looking at pathogenesis things, molecular fingerprints and things. But the main effort of the job that we were tasked with, we started it very quickly when the virus was given to us. We got the seed stocks in the summer, and we did the clinical trials and finished them in time.

SM: Did your office play a role in deciding to launch the campaign? Once it was determined that the virus was here and vaccine production was underway, doing the pilots, there had to be a consensus as to whether or not it was right--?

AF: To vaccinate people?

SM: To vaccinate.

AF: Yes, it was. That was the team that I told you spoke every single day by phone. I was a very important part of

that. As everybody, there wasn't one more important person than the other. The whole team was important.

SM: Okay. Are there any documents that you recommended that we archive?

AF: You know, I don't know. Patty what do you think?

Patty: Some papers or whatever or anything that was published?

AF: Can we think about that?

Patty: We can think about that and get back to you.

AF: Maybe the original schedules for the clinical trials, maybe those would be good. We could send that to you.

SM: Okay. Acknowledging that hindsight is 20/20--I mean, you've already stated that you had a perfect experience in terms of your role--but overall, is there anything that you would have done differently?

AF: As the Director of NIAID, there is not anything I would have done differently. What I would have done differently, which I tried to impact, but it didn't happen was to--you want the truth or want the politically correct thing?

SM: No, I want the truth.

AF: I was very uncomfortable with the secretary's office promising that by October, every American who wanted the vaccine would get it. Because that's what the companies said, that we would have 120 million doses by the fall. And having dealt with the vicissitudes of vaccines development, I knew that was a risky proposition to definitively promise that we would have these many doses on this day. And I often said in the discussions, "Be careful, don't have us out on the limb saying there is gonna be a dose for every one who needs one at a particular time because it may turn out that that's not gonna happen." But unfortunately, my advice wasn't listened to. Not that it was rejected. It's just that I don't think people appreciated the vicissitudes of vaccine development. So, it wound up that we--in fact, functionally, people would deny that--but functionally, we over-promised.

SM: Why do you think that that was the case? I mean--

AF: Because people like to be able to make the statement. You know, somebody sticks a, "Well," whomever..."Madame Secretary"...whoever..."are we gonna have enough vaccine in the fall when this comes back?" "I'm sure we will." As a matter of fact, the right answer was, "I can't guarantee it."

SM: Okay, that comes up a lot. Yeah. So if there's anything else, is there anything you will like to add?

AF: No, I think we covered it pretty well.

SM: Okay, and if I need to contact you for clarification?

AF: Sure, you can get back to me.

SM: Alright. Thank you.

AF: Great! You're welcome.

SM: You're a man of your word!