

Dr. Anthony S. Fauci

This is an interview with Dr. Anthony S. Fauci on August 9, 2002, about NIAID and NIH work in biodefense. The interviewer is Victoria Harden, the NIH historian.

Harden: Dr. Fauci, I want to begin by taking you back to the summer of 2001, before the terrorist attacks. Now, I looked on the NIAID Web site and saw press releases relating to AIDS that summer. In August, for example, you published a paper on HIV-induced changes in B cells, and NIAID had mounted an initiative to increase minority enrollment in AIDS studies. And no doubt there were many other issues occupying you last summer. Could you describe for me your recollection of your NIAID and NIH concerns before the September 11 attacks?

Fauci: With regard to bioterrorism?

Harden: No, in general. What was your mind on last August?

Fauci: Well, my mind was on a few things. Obviously, we have a very intense interest in the HIV/AIDS, and we were particularly interested in something that we still have a considerable interest in and are working very hard on, which is the extrapolation of our efforts with HIV/AIDS into the international arena. There's been a lot of concern about the -- appropriate concern about HIV in developing nations, particularly with the newer U.N. AIDS numbers that show that there are now 40 million infected individuals, and the pace of the infection and the trajectory of the

infection in developing nations, including in Eastern Europe, Russia, India, China, that the projection, is that there very likely would be maybe 40 to 50 million new infections in the next 10 years, and perhaps up to 70 million deaths in the next 20 years. So, international HIV was very much on our mind. We also were concerned because we've had an effort now over the last few years on how we were going to rev up our work on biodefense. In fact, prior to the summer of 2001, we had initiated the first smallpox vaccine dilutional study, which was a pilot study to determine if you could dilute the 15 million doses that we have in our stores or in our reserves, in the federal government reserve. And we did a pilot study that started actually in the spring of 2001 and went through the summer in preparation for doing the larger study, which ultimately showed that we could actually dilute our stores of vaccine.

Harden: Why were you concerned about smallpox vaccine at that point?

Fauci: The reason we were concerned about our smallpox vaccine stores is that, as part of our biodefense plan -- and there had been a plan for at least a couple of years and we were looking at the category A agents -- that smallpox, together with anthrax and hemorrhagic fevers and tularemia and botulism and plague, etc., was an important microbe that we felt we needed to defend against, and since we knew that we had a relatively naive population, we asked ourselves the question, what would happen if we had a smallpox bio-attack now? And now was in the spring of 2001.

Harden: So it was assumed in government circles at that point that indeed there was weaponized smallpox.

Fauci: Oh, absolutely, absolutely. And we felt extremely vulnerable with an unvaccinated population and only 15 million doses in our stores, and we were talking then about the possibility of making a new generation of smallpox vaccine. But the question that was asked of us by me and by our group is, what happens if we need it right away? We can't do with just 15 million doses. And that's why we started the dilutional studies, which antedated by several months September the 11<sup>th</sup> as well as the anthrax attacks.

Harden: How did the work that had been done in the 1950s on anthrax infections and vaccine at Fort Detrick and the Russian outbreak in 1979 figure into NIAID's research support for work on anthrax?

Fauci: Well, it was a very -- it was a major factor. Among the threats of microbes in bioterrorism, anthrax was one that was absolutely clearly documented that there was weaponized anthrax that had been made not only by people who we consider adversarial to us, namely the Soviet Union at the time, but also we knew that, at some time in our history, that we were making it in a weaponized form ourselves, as was the United Kingdom, as was a variety of other countries that are on the allied side of the Cold War. The ease with which one could get anthrax, because it's a naturally occurring infection, is such that it would be foolish to think that

there were not people or groups that either already had material made by others or could make it themselves. So anthrax was very, very prominent on our radar screen of things that we needed to be concerned about.

Harden: Interviewing you about this new challenge can't help but remind me of earlier interviews about the early days of AIDS research. Could you compare the state of basic knowledge about bioterrorism and the state of basic immunological knowledge in which the AIDS epidemic started? Are we further ahead facing this than we were in 1981 with AIDS? How do these things . . .

Fauci: I think it's a case of apples and oranges because when we started off with HIV/AIDS, there was the phase prior to the microbe, and then, namely, prior to the discovery that HIV was the cause of AIDS. And then there was the post-HIV, which is the era we're in now of having a microbe and being able to develop a diagnostic test to develop antivirals to begin work on a vaccine, which is still not complete at this particular point in time. Understanding the immune system took a positive shot in the arm when a lot of very competent investigators and young investigators on their way up began to study the immune system vis-à-vis HIV/AIDS, so it was a scientific evolution with regard to immunology. But how that impacted how we handled the AIDS epidemic from a standpoint of public health isn't necessarily a one-to-one ratio. We really needed to get the diagnosis, get the drugs, and hopefully get a vaccine.

Right now, it's much more complicated because we have (a) microbes that are multi and heterogeneous and varied. We don't have a single virus that we're worried about. We have multiple. The other thing is that we have a totally unexpected arena in the sense of we don't know if and when or where it will happen. Although the AIDS epidemic initially took us by surprise because it was a new microbe, once we knew what it was and where it was going, you could actually plot what was going to happen. We were sitting here years and years ago, before the big problem in Africa, before the big problem in Asia, and I remember we were talking about, we're getting hit here in the United States badly during the early '80s and mid-'80s, but this is a sexually transmitted disease, and when you have a sexually transmitted disease, this is going to spread throughout the world, particularly in countries in which the risk of a sexually transmitted disease being transmitted among individuals might be higher than in a different population with a different culture. So there was some degree of being able to predict what would be going on. Unfortunately, our predictions were correct, but we at least knew the general direction of where things are going. When you're dealing with biodefense now, you really have a black box. You can guess and make some pretty good intelligent guesses about what the microbes might be, but you have no idea when, where, and in what form those microbes would be released. Are they going to be aerosolized? Are they going to be an infected person

mingling in the population? Is it going to come in a letter? Is it going to come in a ventilation system in a building? So it really is a much different situation than we had with HIV/AIDS, which was really rather well defined.

Harden: I was out of town on September 11<sup>th</sup> last year, so I have no firsthand knowledge of just what happened here. Would you relate the sequence of events that day when you first learned about it? What happened at NIAID? What happened on the NIH campus?

Fauci: Well, it was very interesting and, ironically, historic that I heard about it because I saw it. I was in New York on September the 11<sup>th</sup>. I was going to a meeting in Midtown Manhattan, and I was just coming out of the Queens-Midtown Tunnel from La Guardia Airport. And as we were driving up in a cab, in the distance there was some just little puff type of vague smoke that you could see, but it wasn't even anything you paid attention to. In fact, I didn't pay any attention to it. I thought it was an air conditioner on top of a building that was the problem. And I got to the meeting that I was going to, and that took about 15 minutes in the cab, got up and walked in, and I saw everyone just crowded around a big-screen television, and I said, "What's going on?" The meeting was completely disrupted. And there it was, the World Trade Center building tower with a lot of smoke and flames coming out of it. And as I walked in, we waited about 15 or 20 minutes, and then boom, the second plane hit the second

tower live on television. We walked to the other side of the building and looked out and saw the smoke coming up from downtown by the financial district where it had occurred. So it was an eerie form of looking at something on television, having inadvertently seen the beginning of it and not even realizing what it was, and then looking out the window and seeing it from another angle. So it was a very dramatic situation for me. I immediately got on the phone and called my office about this, and the phones were just completely jammed. No one could get any phone call out. So I sent an e-mail and then finally was able, on my cell phone, to get through and speak to the people in the department, and with Secretary Thompson's office, who was obviously trying to get mobilized to get the Department of Health and Human Services push packs and things up there. I was already there. I really couldn't do much. The question was, could I go down there and help out from a medical standpoint, and that would have been nice, but it wasn't practical because everything was already tied off and the police and the fire department really had things, at that time, under reasonable control about who was going to be let in and not. When it became clear after a while, a very short while, that this was a terrorist attack -- there was no question in anybody's mind, two planes hitting at the same time in a devastating way -- I immediately started thinking about the fact that this makes the biodefense aspect of what we do even more important and more imminent and more compelling. So,

when we got back, we sat down with my group, and I got back on a late train that night. I couldn't fly out. It was logistically very difficult to get out of New York City. When I finally got back in the middle of the night or early hours in the morning, we had a meeting literally within a day or so with the people in our infectious disease group, reassessing where are we in biodefense, what's going to go on here, and we had immediately meetings with Secretary Thompson at the Department, anticipating that this is going to be the first in a series of attacks. And we reassessed our program and we started turning things on, the afterburners a bit more about what we were going to do. And then when the anthrax attack came shortly thereafter, then it was very, very clear that we were in the middle of a war, and a different kind of war, and a war in which we were one of the primary groups of people who'd be fighting that war, namely the biomedical research community, in being able to prepare the country in biodefense the same way the CDC is the surveillance community and the threat-assessment community and the group that is going to be the first responders. So everything changed. It was kind of our mission was transformed into something that we had never experienced before, where we were actually, truly felt like we were at a war, and we were an important division in the armamentarium in that war.

Harden: This is twice in your career, then, that you have had to make a sudden shift.

Fauci: Absolutely. I mean, I immediately thought, actually, of the conversations that we had a long time ago when I told you that I decided one day to just change the direction of my career and get involved in HIV/AIDS. This was a little bit different because there was really no choice. It wasn't like, well, should I or shouldn't I? There was absolutely no choice. It was the responsibility of the Infectious Diseases Institute since biodefense is so fundamentally ingrained in infectious diseases. We already had an emerging infection program that was a substantial program, and I looked upon it . . . In fact, I remember sitting with my staff at an Executive Committee meeting literally within days of the September 11<sup>th</sup>, and then more intensively after the anthrax attack, and told them that as far as I'm concerned, a bioterrorism microbe is just another form of an emerging and reemerging disease. In fact, we even sketched a little slide of that showing that, if you look at the continuum . . . I remember I showed you that slide of the cover of the *New York Times* magazine with the person masked and saying, "The Flu Pandemic of 1918," and then the AIDS epidemic that became recognized in 1981, and I had mentioned to you that in my father's lifetime, who was at the time in his eighties -- it was now '92 -- that he had experienced two catastrophic emerging diseases. One was reemerging, with influenza, and the other one was truly emerging, with HIV. Now we put a third panel on that slide, which is deliberate release of microbes in bioterrorism, and that was the picture in *Newsweek* and the

*Time* magazine of the anthrax attack. So it just continues that spectrum of emerging and reemerging diseases. But now we're dealing with something that is and will likely in the future be deliberately released.

Harden: Let's also, before we go on in the actual events, think back over your training in your career. When you came through medical school and decided to go into infectious diseases and immunology, it was at a low point, actually, in funding.

Fauci: Right.

Harden: Infectious disease has been conquered.

Fauci: You bet.

Harden: Did you see in your medical school clinical rotations any cases of anthrax? I'm sure you didn't see any smallpox.

Fauci: No, no. We vaccinated a bunch of people.

Harden: What types of things did you see?

Fauci: I was -- I think I'm one of the few -- I wouldn't say few, but the people of my generation were people who actually did vaccinations as part of our medical school training because I was in medical school in the '60s. We stopped vaccinating in 1972. So anyone who went after 1972 would have no experience in vaccinating individuals. No, I never saw a case of smallpox in New York City. I may have seen a case of cutaneous anthrax in someone who was referred who might have gotten infected secondarily from exposure to some wool. I don't recall . . . In fact, my memory is so

vague, I don't know whether it was a film of someone with anthrax or whether it was an actual cutaneous case of anthrax, but it certainly wasn't any more than one.

Harden: What about botulism, tularemia, \_\_\_\_\_?

Fauci: Tularemia we saw. Yeah, we saw some tularemia. We see or saw tularemia in people who have gone hunting and skinned some rabbits. Botulism, I saw a case, a pediatric case, when I was in medical school.

Harden: Would you say that your experience was pretty average and common for most physicians training?

Fauci: Yeah, absolutely.

Harden: So we would have, in this current situation, a problem with people just recognizing what they're seeing to start with.

Fauci: Right.

Harden: And this is just a part, I presume, of the challenge that you are working on, to help people diagnose.

Fauci: Right.

Harden: All right. Let's do move on a little bit. The first diagnosis of inhalation anthrax was made on October 4<sup>th</sup>.

Fauci: Right.

Harden: In Robert Stevens, the editor of the tabloid publication in Boca Raton, Florida, and he died the next day. Now, how did you learn about this? Did you learn about it on the news, or had there been prior discussion

about it with CDC, NIAID, DHHS?

Fauci: No. I heard about it on the news, and then when there was that situation, it was unclear what it was, and the Department got some criticism for saying we're not sure what it is. It could be someone who was drinking out of a stream, which is -- I don't think at all that Secretary Thompson should be blamed for that because I think someone just told him, "Oh, these are the five or six different reasons how you can get anthrax," and I think if that's the worst sin he ever commits in his life, he'll go straight to heaven when he dies. So that wasn't a mortal sin. But what happened very soon after that is that we started having meetings immediately, CDC, myself, Secretary Thompson and his group down at the Department. So he formed a team pretty quickly, pretty quickly, of people who were going to be handling the biodefense, to his great credit. It was like almost on a dime.

Harden: How were the responsibilities -- I mean, there are obviously clear responsibilities for CDC and NIH and FDA, but were there any discussions that either overlap or collaborations that you \_\_\_\_\_ at that time?

Fauci: Well, you know, in the beginning it was more of a group of senior advisors who would discuss where we're going with that, so it wasn't -- even though it was understood that my responsibility as a director of a research program was, what do we need research? We need the vaccine,

and that's the reason why we immediately accelerated the second phase of the dilutional study. We made an immediate, intermediate, and long-range plan for smallpox. We talked about what drugs we have. Do we have vaccine against anthrax, the problematic situation with the anthrax vaccine that has the baggage that goes along with it because of the perceived toxicities, whether they're real or not. It was something that was unclear at the time. What about other microbes? So we spoke about what the responsibility of the NIAID would be for the research protocols, what the CDC would be doing with their surveillance and their involvement in being first responders. But it was beyond that. It was really a group of individuals that were the advisors to Thompson. We would be not only talking about what we do, but would provide some advice about the whole situation of where we should be going. So it was a multitasked group, so you didn't just speak only about your research, you spoke about the broad general problems back and forth.

Harden: Can you bring the Department of Defense or any of the other agencies into this? Were they \_\_\_\_\_ these discussions?

Fauci: Oh, yeah. Oh, absolutely. Peter Jahrling and Art Friedlander were very much involved in the beginning. I was on the phone and talking with them, meeting with them, still do to this day, the people in the Department of Defense, particularly in the Army, USAMRIID, who have great experience in that, and two of the names were Peter Jahrling and . . .

Harden: You just said it.

Fauci: Friedlander, Peter Jahrling and Art Friedlander. Right.

Harden: Okay. By late October and November, public fears were starting to shift from anthrax to smallpox.

Fauci: Correct.

Harden: And on November 2<sup>nd</sup>, you testified before a subcommittee of the Senate Appropriations Committee about smallpox and what plans were being made to combat it. Would you describe your perception of this, how this shift, what was going on in the public and what the Congress was asking you and wanted to know at this time?

Fauci: Oh, yeah. What went on, it was just exactly what we were talking about that I mentioned in the spring of 2001, prior to September the 11<sup>th</sup>, is, where are our vulnerable spots? And there was a big, fat, vulnerable spot with smallpox because we have a naive population and we have 15 million doses. So we sat down and said, "We've got to have an immediate, an intermediate, and a long-range plan. The immediate plan is get the dilutional study done so that we'll know whether or not we have not 15 million doses but 75 million doses. While you're doing that, let's put out an RFP for contracts to make the second generation of the smallpox, the one that \_\_\_\_\_ Baxter International ultimately got to make the tissue-culture-derived smallpox vaccine as opposed to the calf-lymph-derived, which was the original one; and the finally to do a long-range plan of

getting an attenuated smallpox vaccine or a smallpox vaccine that was in the form that you would avoid complications to immunosuppressed individuals, because the one prohibitory factor of all of this is that this vaccine, the live vaccine, the vaccinia, the classical one that we used, is not safe for people who are immunosuppressed, and we have a lot more immunosuppressed people in the population: we have close to 900,000 HIV-infected individuals; we have transplant patients; we have people on steroids. So if we ever needed to vaccinate the population, in the long run it would be wonderful to have a completely safe vaccine. But in the meanwhile, we were jumping all over the immediate plan, which was the dilutional study, and the intermediate plan was to get the production rolling on the second generation of tissue-culture-derived smallpox vaccine.

Harden: All right. Now, let me clarify on these. The dilution, the vaccine that would be diluted was calf-lymph vaccine.

Fauci: That's right. It's call dryvax.

Harden: Dryvax.

Fauci: Right.

Harden: The tissue culture, is that vaccinia or variola?

Fauci: Yeah. No. That's, it's all vaccinia. There's no smallpox in any smallpox vaccine.

Harden: And you would not -- if you were looking for an attenuated smallpox

vaccine, you'd still use vaccinia.

Fauci: Right, you bet. And one of the major candidates is one called modified vaccinia ankara, MVA, and the reason we know that's safe is that's been used as a vector to insert the genes of other viruses, including HIV, to make a vaccine. So it has been given to a large number of cancer patients because they would put the genes of the particular cancer protein into the MVA and vaccinate the cancer patients against their own tumor antigen, and none of those patients had any problem, so that was proof already that MVA is clearly safer than vaccinia. The question that we're dealing with now is, is it going to be as effective as vaccinia, the classic dryvax vaccinia, in protecting against smallpox were an attack to occur?

Harden: One other follow-up question on anthrax at this point. I noted just recently Italian and French researchers had reported in *Nature* that they developed a technique to identify chemicals useful as therapies in late-stage anthrax.

Fauci: Right.

Harden: And apparently a lab in New Jersey has also produced this. Over the last year, what kind of NIAID or is there any NIAID coordination across the world, or is it basically doing what normally is done with just individual collaborations?

Fauci: Well, the coordination across the world is easy because of the extraordinary transparency and data and studies that get executed and written about and discussed at meetings. And just like in any discipline,

including HIV/AIDS, you know literally within days, or even before it's announced, because there's so much collaboration. So that's on track, then, and will stay on track. What NIAID is doing is that we have been funding for some years investigators who are looking at and have successfully identified, crystallized, and developed inhibitors already for the three major toxins of anthrax, the lethal factor, the edema factor, and the protective antigen, and we have our grantees who are making major advances in figuring out ways to target those particular toxins, which are an important part of the pathogenesis of anthrax.

Harden: I'm going to step out and ask a radically different question at this point. As all this is going on, there are pressures on you to consider becoming the NIH director.

Fauci: Right.

Harden: You're now talking to the son of the president you turned down twice.

Fauci: Right.

Harden: You want to tell me about this?

Fauci: Sure, no problem at all. Secretary Thompson, right from the very beginning, had been asking me several, several times to consider being the NIH director. He wanted me to be the NIH director very badly. He and I developed a very, very good and close relationship, and I have an incredible amount of respect for him, but I told him no. And the reason no is because of what I was involved with was HIV, what I was involved with

was in emerging diseases, and we had not yet gotten to the point of the September 11<sup>th</sup> event. And I just said no, I don't really want my name to be put forward because I'm not interested in leaving the active involvement in HIV and emerging diseases. And he had asked me -- again, we'd become friends that he could do this; it wasn't an awkward thing. He would ask me every month and a half or so, "Can you change your mind? What can we do?" etc. And I kept on saying no. But then right after September the 11<sup>th</sup> -- and it must have been September the 13<sup>th</sup>, I think -- he called me down in his office and he said, "Tony, we really need leadership now. You're going to be the guy that's going to be doing the biodefense also. We really need leadership in infectious diseases. We need leadership in the broad area of the NIH. Would you like to at least consider, reconsider taking the job?" And I was actually struck by the fact that he really was not trying to be melodramatic, but he said, "The country really needs you. Would you consider it?" And I told him, I said I would consider it, but I would consider it on one condition, that I would not give up the National Institute of Allergy and Infectious Diseases, that I be named, not the acting director, but the director of the National Institute of Allergy and Infectious Diseases because I must continue to provide the direct leadership in HIV/AIDS, in emerging diseases and biodefense, and then I'd be happy to do the NIH job, which I felt certain that I could do both because I know the Institution so well. It isn't something that I have

to learn. I know it like the back of my hand. Well, he was absolutely tickled pink and delighted that I said that. He was very, very happy about it. So he brought that down and discussed it with the White House. The White House -- there were a number of complicated issues there, but probably the most prominent one is that they were uncomfortable with someone running an institute at the same time as they were actually running the NIH. And I can remember that we went up to Pittsburgh together--Tommy Thompson and I and President Bush flew on Air Force One to inaugurate some special surveillance program, that the people in Pittsburgh had a very creative way of monitoring the possibility of a bio-attack. And on the way down from Pittsburgh, we had some very nice conversation with the President. It didn't come up with the director, but we spoke a lot about a lot of different things that I was doing.

And then after the flight, when the President went off in Marine One, on the helicopter, Thompson came over to me and says, "Is there any way that you can rethink about it, because we really want you to be the NIH director, but it's really problematic about doing both jobs." And I said, "You know, quite frankly, I'd do it for you if they were all, both jobs together, but I just really cannot leave the direct involvement in what I'm doing." So, obviously, there must have been a conversation where the President said, "Fine, if he wants to do one, we'd be happy to do it," but his advisors . . ." I don't think it was the President, to be honest with you.

I think the advisors around him, but the President functions at a level above that. I don't think he's working out who's doing those kinds of things. But I think he got some strong indication from his advisors that they thought it was not well advised to have someone do both. And I was actually perfectly comfortable with that, I really was, because I wanted to do the job that I was doing and I would consider doing the NIH job merely as a service to the NIH, not that I aspire to that, because my track record has proven that I haven't aspired to that because I've turned it down so many times. So when the ultimate decision was that it was not going to happen, I actually felt extremely comfortable, so it was just another chapter in the NIH thing.

Harden:

I just don't know anybody else in the country who could run the NIH out of his back pocket and run the Institute, and I don't know that there's anybody who would have doubted you could have done it, but that's another thing. In late November and early December, you published articles in *JAMA* and *Nature Medicine* on bioterrorism, saying that you thought that it was likely that additional attacks would occur and that bioterrorism research was -- not should be, but was -- an important part of the research agenda for the biomedical research community. And this to me indicates that you were ahead of the curve here already that this was the new agenda that the biomedical research community needed to be looking at. Would you comment on how your thinking about this --

obviously, NIAID had \_\_\_\_\_; you've already described this -- but how you saw this new era developing by the end of the year. Did you see it [as you recalled], AIDS sort of took over the NIAID budget. Is this what you were seeing happening?

Fauci:

Well, it was not as easy as that, because it would really depend on what the commitment of resources was going to be, and it's a good story. It's a true story of what happened, we had a plan, and it was kind of given the resources. We had about 200 less; we had less than \$200 million in biodefense in fiscal 2002. In fact, it was around \$100. In fact, it was less than \$100. And we felt that we could mount a reasonable program and focus on the importance of it or we can do the Mercedes Benz version of it. We could make it something that we could accelerate rapidly; we could get people involved, there could be a major, major component of the Institute. But the only way that would occur would be if we have considerable more resources. So we had the backing of Tommy Thompson to make that happen, to his really enduring credit. He said, "We need to make this happen." And I warned him. I said, "Mr. Secretary, we can't have this destroy the other important programs like HIV/AIDS and emerging and reemerging diseases. So if we're going to do it, we've got to do it with new money." So we worked, he and I together, in those months in November and December, before the budget was formulated for 2003, worked very closely with the Office of

Homeland Security, something that's not very well appreciated by people, particularly a fellow named Richard Falkenrath, who was the person who was in charge of the scientific aspects of the Office of Homeland Security, and together with Governor Ridge also. And they said that they would help us push for getting OMB to agree without slashing the rest of the NIH budget, but really, truly making it new money, to put a substantial amount of money in the research endeavor for NIH. And he asked me, on a reasonably short turnaround, "Will you be able to document that you would spend this money well?" And at that point, I got my staff -- again, great credit to people like John LaMontagne, Carol Harmon [sp.], Pam McGinness and people like that -- to sit down, and we put together, through into the night, through the weekends, rolling up our sleeves, kind of like in the old days of HIV/AIDS where the time clock didn't mean anything. You were here until the middle of the night. And we sketched out a strategic plan and a research agenda and we put it together, and we went back to the White House, the Office of Homeland Security, together with Secretary Thompson and said, "We would be able to well spend this money, and if you gave us X amount of money" -- it turned out to be \$1.5 billion extra -- "we would sketch out a plan that we would be able to justify it and we would give you good science," and that's how the birth of the evolution of the jumping biodefense from this to that in the research agenda for NIH came about.

Harden: I was going to ask you who else on your staff were involved, and so I thank you for giving me that. Now, by December, this that you were describing had come about, and a DHHS news release announced seven new research initiatives and quoted you as saying you'd been deluged with calls from scientists who wanted to help, and I'd like for you to describe this outpouring from the scientific community. I understand you had 700 proposals.

Fauci: Absolutely. What happened is that I think the juxtaposition of the extraordinary emotional impact that September the 11<sup>th</sup> had on everyone in the country, and then the anthrax attack, really spurred in the scientific community that feeling, of, 'well, wait a minute, this is our ballgame here now.' We can't do anything about a plane flying into the World Trade Center, but we can do something about bioterrorism and biodefense. So I started to get an incredible number of calls from people who were not only encouraging me in what I was doing, because at that time we were all over the press and we were trying to calm the nation of saying that they would be willing to do anything. It was just amazing, the calls that we were getting. We were getting scientists to say, you know, "I'll work as a volunteer to help you out." I mean, "You want us to do research? Tell us what to do. I'm an expert in this. I'd be happy to do it. What do we need to do?" It became very clear to me that the mobilization of the scientific community would be rather impressive once we got the resources to

support them. I never quite experienced anything like that where people would be sending me e-mails. “We know you’re busy, you don’t need to reply, but anything I can do to help, let me know.” It was just very respectful of my time, realizing that we were working 20 -- I mean, literally, there was a period of time there that even surpassed anything with HIV, because during the anthrax period, we were truly, without hyperbole, working 20-hour, 21-hour days. I mean, there were two hours and three hours of sleep for a week and a half, two weeks in a row. It was just extraordinary. Even in the heyday of HIV, there wasn’t that intensity, because we didn’t know when the next attack was going to come. I mean, it’s easy now, retrospectively, to look back and say, you know, we had 18 confirmed and 22 total possible cases. We had 11 inhalational and five deaths. That was that anthrax episode. But while it was going on, we didn’t have any idea whether the Metro in Washington would be the next target and there’d be thousands of people who were dying, so it was a race –it was all adrenaline on everybody’s part.

Harden: And tell me a little more about what all you were doing in those 20-hour days. Not just writing the research agenda, obviously. What was . . .

Fauci: No, no. It was part of that inner circle with the Secretary and what we’re going to plan, what we’re going to do, what the agenda is going to be, what the next step is, what the holes are, what the gaps are, how we would handle the press. It was constant meeting with the White House. It was

just back and forth, back and forth. It was quite intense.

Harden: Walk me through the major lines of discussion that led you to the strategic plan, the way it played out, and especially how the concept of responding to bioterrorism evolved into the larger biodefense position.

Fauci: Right. Well, it was an example, I think, of how experience in putting programs together on the part of my staff -- and, again, I mentioned the group. It was John LaMontagne, it was Pam McGinness and Carol Harmon [sp.] and their staff. There was even some contribution from the Division of AIDS people, Tramont and his people, the Intramural Program. Cliff Lane was very heavily involved again, my old colleague from the HIV days, and a bunch of other people who worked under them. We sat down and I said, "Okay, here's our task. We have to put together a program that's credible. We've got to put together a program that builds on what we have but that thinks out of the box." I remember having said that 15, 20 times in a few-day period. "We've got to think out of the box. We can't be thinking in terms of what we know is doable by the standard, traditional way. Push the envelope. Make out there's nothing in your way. What kind of program can we put together?" And I have to tell you, you have to keep beating people to do that because they're so used to thinking in terms of the practicalities of what you really can do, and I had to constantly remind them that this is a different ballgame. This is a different ballgame; this is a war. So where can we go? What can we do?

And that's how we came up with the plan.

Harden: Okay. You published the strategic plan in February 2002, the same month that you convened the blue-ribbon committee to advise NIAID on a biodefense research agenda for the category A agents. Now, I looked at the membership of the committee, which was quite large, and even included Ed Kilbourne of swine flu and the whole, quite a large variety of experts. Would you describe how you chose those participants? And what happened during that two-day meeting?

Fauci: Yeah. Well, we chose it because we wanted people who were experienced in epidemic type things, the Ed Kilbournes for the influenza. We wanted to have scientists who were fundamental basic scientists as well as people who had executed clinical trials. We wanted people who were young with new ideas, and we wanted some of the grey-hairs who had been through things like this, who had been involved in some of the eradication programs of different -- the polio eradication programs, etc. We wanted a mixed group. We wanted to have multiple disciplines. We needed people who knew virology, who knew bacteriology, who knew public health, who knew epidemiology, and we wanted the whole spectrum. We put them together and we said, "This is the plan, a strategic plan and a research agenda we put together. Let's go through it. We'll go through it page by page. We need your advice, what you think will work, what you think won't work. It was a great meeting. It was a very intense, two-day

meeting.

Harden: Those CDC category A agents include plague, tularemia, and the viral hemorrhagic fevers, as we have said, which can . . . Well, the tularemia and the hemorrhagic fevers, many of them can be transmitted by insects or other arthropods. Now, in the 1970s, much of NIAID's medical entomology research was shut down in favor of expanding molecular biology, molecular approaches to disease problems. Would you describe the current situation with expertise in the field of medical entomology, where it's located now -- is it industry, academia, or where? -- and whether the current state of knowledge is proving adequate to deal with these things.

Fauci: I think we have always felt concerned that it isn't as if we necessarily shut entomology down. It's that the next generation of entomologists who would have been entomologists were attracted to the molecular biology and the gene cloning and things like that, so fewer people were going into the field. It isn't as if there was a deliberate pushing them out. It was that there wasn't interest in that because that didn't look like the wave of the future. So we don't have as many as we would like to have right now, but there are enough and enough experience and enough corporate memory, particularly people at the CDC. I mean, they have some good people down there. We have some good people in our Rocky Mountain Laboratory in Hamilton, Montana. If I had my way, would we have more

now? Sure, of course. But that's just the way the field went, and I don't think it was through any fault of anyone. I think it was just the evolution of the field.

Harden: Are you all actively recruiting more entomologists?

Fauci: Not really. We are certainly making it clear that we welcome projects on that, but we're not -- we don't have a formal training program for that.

Harden: Because of some of the extreme danger posed by some of these agents, biodefense research must be conducted in BL3 and BL4 facilities, and I have seen several different things, but I believe NIAID is going to add new facilities here and at RML, and I'm not sure where else.

Fauci: Twinbrook.

Harden: Twinbrook. Would you describe all these facilities that are in the works?

Fauci: Yeah. First of all, let me just make a small correction. Biodefense research does not have to be conducted in BSL4 and BSL3 facilities. It's the nature of what you do, because you can be working on a project that requires no containment, or BSL2, and it would still be directly related to biodefense. It's only when you actually take a microbe that falls in a certain category and deal with the live microbe either in a test tube or in an animal model that you need containment facilities. But there's a lot of biodefense research that is important that doesn't do that.

Fauci: Having said that, we certainly knew that if we were going to recruit the best and the brightest into the field of biodefense, we would have to have

facilities for them, not only intramural facilities but extramural facilities.

So what we did is we had a two-pronged plan. It was to build up the structural infrastructure within the intramural program as well as to provide the capability of having BSL3 and BSL4 in our extramural programs. So let's take intramural first. We have on campus an underutilized, if not used, BSL4 that was originally put together for multiple drug-resistant tuberculosis. It's rarely used at all.

Harden: Is this Building 41?

Fauci: Yes, Building 41. There is a BSL4 up in Frederick that the Department of Defense has; there's one in Atlanta that the CDC has, and there's one in Texas that is independently owned. That's not enough to do the kinds of research that we would want to do, severely restricted. So we are building a BSL4 in Hamilton, Montana, in our Rocky Mountain Laboratories; we are building a building here on campus, which we're calling, for lack of a better terminology, Building B, right here on campus, literally across the parking lot from this building that will contain a BSL3, not a BSL 4. In Frederick, in collaboration with and in conjunction with the Army, the Department of Defense is renovating their own BSL4, we will be building an NIH BSL4 up in Fort Detrick, and we're putting a BSL3 in Twinbrook. In the extramural situation, we have a request for applications for what we're calling regional centers of excellence in emerging microbes and biodefense, and we plan to have three or four this coming year and another

two the following year, then up to 10 of these. Some of these will have BSL3 and some might even have BSL4, so we're planning on expanding the containment facilities not only here on campus and in our satellite campuses like in Rocky Mountain Labs, but we're also planning on making available, where appropriate, for extramural investigators in these regional centers.

Harden: The NIH has not really -- there was some controversy over the tuberculosis research in Building 41 by the neighborhood-- but we haven't really had that sort of concern in the past. I have heard of a few grumblings around here. I wonder what you've heard and what you're doing to . . .

Fauci: Yeah. Actually, I think it's understandable how the community would be concerned when they talk about containment facilities. They don't know what it means. And it's our job -- and we're hopefully doing it well and will continue to put a lot of time in -- to try and educate the community in the fact that a BSL3 facility on campus in fact is really quite safe. The very nature of what it is, the containment, makes it, by definition, very safe. There's always a question of gee, why do you need to do that here, and the reason we need to is what I said before, because we are at war and we are an important part of the defense in that war, and this is a government facility. We'll be very respectful of the community around us and we will involve them in the decisions that we make. But this isn't a

question of if; it's going to happen and we want to do it with the buy-in and agreement of the community.

Harden: I want to come back to that, I have a historical footnote. I have to say this and then a question about tularemia. As you no doubt know, in 1911, it was one of your predecessors, Dr. George McCoy, who discovered the tularemia organism while he was searching for plague in California ground squirrels, and tularemia was subsequently named after one of his colleagues, Edward Francis, and the county in which it was found, Tulare County. That's the historical footnote so that we know the organism is *barencicella tularemis* [sp.], if I pronounced it correctly.

Fauci: *Tularensis*.

Harden: *Tularensis*. Thank you. Yes. I'm not reading my own writing. My question for you, though, is, in your opinion, how likely do you think tularemia or botulism are to be used as agents? Do we know whether they're weaponized or not?

Fauci: Yeah.

Harden: Oh, we do? The others?

Fauci: Kanatzhan Alibekov, who is now known as Kenneth Alibek, who's a colleague of ours, was the deputy director of Biopreparet, the Soviet Union's biowarfare facility, got a medal, actually, in the '70s, a medal for developing an aerosolized form of tularemia, so we know as a fact that it has been weaponized. Now, the Soviets say that they destroyed it all and

it's taken care of, but they may have, in good intention, tried to destroy it all, but in fact, with the dissolution of the Soviet Union, it's entirely conceivable that small aliquots of that got taken away and sold to people who would buy it and use it for nefarious reasons.

Harden: In November 2001, you testified that NIAID had made a significant investment in the burgeoning field of microbial genomics.

Fauci: Right.

Harden: And by May, researchers had unraveled the anthrax genomes. Now, would you discuss the significance of whole-genome sequencing technology and computational methods?

Fauci: Yeah. Well, this is something that we've said long before September the 11<sup>th</sup> and long before anthrax, that just as the Genome project is going to open up the key to the nooks and the crannies of understanding the humankind, the sequence of a microbe is essential, really, to expose all the potential targets for diagnostics, for therapeutics, and for vaccines. So we have a program now that ultimately will essentially sequence all of the pathogens that are important to us. Certainly included in them are pathogens that would be associated with bioterrorism. So, for example, if you know the precise genome of a particular microbe, you'd be able to know how certain proteins that are the toxins, the metabolic necessities of a particular microbe, the antigens that are expressed on the surface that could be used as a vaccine component -- it opens up limitless possibilities.

So we look upon the Genome project for pathogenic microbes in the same light as the human genome people look upon the sequencing of the human genome and then the subsequent proteomics and informatics and all those other things that go along with it. It's really the same thing.

Harden: So this will be a major part of the biodefense research agenda.

Fauci: Absolutely.

Harden: All right. Now, let's come back to smallpox. There was the discovery of the additional stockpile of smallpox vaccine, and you've already talked about the research on dilution. It seems clear that it's possible now to offer vaccination to most of the U.S. population, and you've outlined the risks as well as the benefits. I also understand -- I just read that NIAID was planning to conduct clinical trials of vaccine stocks on two- to five-year-old children.

Fauci: Right.

Harden: And what I'm getting at is this. You published an editorial in the *New England Journal of Medicine* calling for a broad public dialogue.

Fauci: Right.

Harden: I haven't heard much of a public dialogue. Where does all this stand?

Fauci: Yeah. The public dialogue is actually -- following my editorial, there was quite a good response to that, and there were five separate cities -- San Francisco, Atlanta, New York, and a couple of other cities -- and then culminating in a final meeting in Washington, D.C. at the National

Academy of Sciences to openly discuss all the things I wanted to hear discussed in my editorial when I called for it this past year.

Harden: But these were scientists?

Fauci: These were scientists [and] public people. It was open to the public. It was a public town-hall meeting type approach, so it was everything from the newspaper people there to policymakers, to scientists, to just John Q. Public or Mary Q. Public, whatever. And the discussion was open and transparent, so I'm actually pleased with how that happened.

Harden: What do you think the policy will be eventually?

Fauci: I know what it's going to be, but I can't talk about it right now, because the President, when he comes back from Crawford, Texas, where he is now on his August vacation, will very likely announce what the policy's going to be. I'll be happy to come back to you and tell you at a time how we came about that.

Harden: Good. We'll get back to that. The drug -- and again, if I pronounce it correctly . . .

Fauci: Cidifovir.

Harden: Cidifovir, thank you, has been found to have some effect against smallpox.

Fauci: Right.

Harden: You want to comment on research on this drug and other new therapies?

Fauci: Yes, absolutely. In fact, there's another example of, again, going historically back on our own conversations, of the positive spinoffs of HIV

research. Cidofovir was developed originally by Gilead as a drug for cytomegalovirus in HIV-infected individuals, and we found out by chance, just by screening drugs, that in fact it has very good *in vitro* activity against pox virus, orthopoxvirus, including smallpox, so there's smallpox, camel pox, monkey pox, vaccinia. All orthopoxviruses. And a study was done in an animal model by Peter Jahrling in which he infected monkeys with various pox viruses, including smallpox, and showed a very dramatic effect of cidofovir. It's given intravenously in a single dose. The difficulty, it has some toxicities to it, so we now have worked on it and have successfully developed it. It's in testing now in animal models, an oral version of cidofovir that is much more powerful, interestingly, and somewhat paradoxically, than the intravenous version, and hopefully it will not have as many toxicities. So we're well on the trail of not only pursuing cidofovir and its analogs, but also screening for other antivirals that might be effective against smallpox and any of the other viruses that we're concerned about.

Harden: So, how far down the line would it be before they would be in the pharmacies in Iowa?

Fauci: We already ordered cidofovir for the stockpile, the national stockpile, just on the basis of the animal data.

Harden: Very interesting. Now, you've talked a little bit about this, but in the numerous times you've testified before Congress since September 11<sup>th</sup>,

tell me about the kinds of questions the congresspeople, the Senate and the House, what did they want to know? Were they concerned about their own personal safety...?

Fauci: A combination of both. I mean, obviously, the vast majority, if not all of the senators, are there, and congressmen, in a very altruistic way concerned about their constituents, first of all. They also have personal concerns, and they always ask you personal things, like what they should do, what I would recommend that they do. But for the most part, it was what about their constituents. And it was a combination. The hearings were briefing them on things that they had not heard before about what are these microbes, what are their potential, what is the risk, what is the danger, what is the effect of them, and then, what are you doing about it, what are your plans, how safe are we, how big is the risk -- the standard questions that virtually everyone asks. I mean, I go home and visit -- you know, my sister asks me these questions all the time. What is the risk? Is it... we don't know what the risk is, but it's certainly not zero. Why are you concerned about smallpox? I'm concerned because the population is a naive population. If you vaccinate, what are the toxicities? Those same questions, and over and over we've done that.

Harden: Do you have confidence in the public to understand this and not panic?

Fauci: I have confidence in the public's ability to understand what a risk is. I think we don't give them as much credit as we should. I think there

obviously are going to be some people, no matter how many times and how you tell them, they're just not going to understand what you're talking about, but that's life, that's human nature, that's the general public. But for the most part, the broad general public, I think if we continue to get out front on TV, in the media, on the radio, and explain this over and over and over again, I think it will sink in. They'll understand the importance of it and they'll understand the risks.

Harden: Now, a recent *Washington Post* article this week was saying that not enough of that's been done. Now, NIAID has a very large public information program and has a record of doing an excellent job in this. Is NIAID attempting to do anything ?

Fauci: Oh, absolutely. We try to educate people on the things that we're responsible for, and now I'm also working with Secretary Thompson and his Office of Communication headed by Kevin Keane, who's really a good person, about how we're going to roll out these kinds of announcements. Like when the announcement is made about what our policy is going to be on smallpox vaccination, there's going to be a very well-orchestrated publicity approach to try and get the people to understand just what this means for them.

Harden: Okay. Let's talk, as we're coming to the end, about the proposed new Department of Homeland Security. This department, of course, would include scientists conducting research on biodefense, and there have been

a lot of proposals: let's transfer money, let's transfer people out of NIAID and other places. And I know a number of the scientific professional societies are very concerned about this. They don't want it to happen. Would you like to describe the discussions that are going on here and what you think's going to happen?

Fauci: Well, you know, the original first cut was to so-call transfer -- transfer the money, transfer people from whatever agency, the CDC, the NIH, over to the Department of Homeland Security. Obviously, that met with a lot of resistance. We have had a lot of discussions, and obviously the President has come out saying that he wants it this way. But I think now that we're massaging it a bit, there's the realization that he can get what he wants without necessarily having to do it literally the way it was originally rolled out. Obviously, I have to, on the basis of my own job, my own position, to defend President and his decisions, and I do that. But that did not stop me from negotiating and discussing very intensively behind the scenes with the White House about what we felt would work. I must say -- this is sort of a historical documentation for history -- the White House was extraordinarily accommodating to me about making sure that we want to get the job done. What we really do need, we must have some control over the prioritization of what is important -- we being the Department of Homeland Security. If we're going to be the Department of Homeland Security and we're going to be responsible for the security of the

homeland, we cannot leave completely the biodefense agenda to somebody else. That's not an unreasonable proposal. Even though we know, as scientists, that we can do it better than anybody else, their request is not unreasonable. So how can we work that out without literally transferring everything over to the Department, because the original proposal was to transfer the money and the people and then to contract it back to the NIH. So it was almost, we give it to you and then you give it back to us. So we're going to take the \$1.7 billion, but then we're going to contract it back to you to do exactly the same research you're doing now. So in the negotiations we said it makes sense for you to have a role in the prioritization, so the bill -- and I don't know how the bills are going to be passed because we're in the summer recess right now and we don't know what's going to happen when they come back. But something that I think will fly is to indeed give the Secretary of Homeland Security the overall prioritization of the research on biodefense. What are the important issues? Is smallpox what you want to go after? Is Ebola what you want to go after? Then have the actual research agenda be derived and executed through the NIH by the Department of Health and Human Services, who shall consult with the Department of Homeland Security. So overall prioritization, Homeland Security; execution of the research agenda, planning of the research agenda, NIH/DHHS. They seem to agree with that, that they thought that that was workable. Whether or not that's

going to get into the law, stay tuned in the fall and we'll find out.

Harden: Okay. Let's close with one other international question, or my last question, and then I'll ask you if you have other things you're thinking of. We're hearing more and more about the possibility of war with Iraq and the use of bioweapons by Saddam Hussein.

Fauci: Right.

Harden: Where is NIAID and you in these discussions and in responding?

Fauci: Well, yeah. The only thing I can say at this point in time, which is interesting . . . This has indeed got me into an arena that I had not been in before. I've been through a lot of this with HIV/AIDS, but one of the things that's going on right now is that I find myself now, having gotten top-secret clearance, to be very heavily involved in understanding what the top-secret discussions and plannings are vis-à-vis not the biological aspect, but the actual defense aspect against possibilities of attack, be they terror in general or bioterror. And there is concern about Iraq, as you know. You can read that in the newspaper, so I'm not divulging anything that I heard in confidence and as a top-secret clearance. But it is very clear that if -- and this is, again, not anything that I'm giving that's secret because it's on the front page of the *Washington Post* -- if in fact we preemptively strike Iraq, there is obviously a concern that Saddam Hussein would use weapons of mass destruction, including biological terror weapons. If he can't logistically get it to us, he might get it to our

allies like Israel. So there's a concern that if there's going to be a decision made to preemptively prevent him from doing that, there is the possibility that an attack will occur, so that is obviously something that you factor into the equation of the importance of what you need to do.

Harden: So, we will leave it at that point. Discussions are ongoing.

Fauci: That's right.

Harden: This is all I have to bring us up since last summer to where we are now. What else do you want to say in terms of things that we should know and be thinking about?

Fauci: I think the details of what actually happened you, as usual, covered wonderfully well because you did your homework very well, as usual. One of the things that, again -- I mentioned several things that were quite different and unique about this, but the thing about it that's very, very clear is the extraordinary intensity and closeness of the interaction between NIH, me personally, NIAID, and the Secretary of Health and Human Services and the White House. The access to and discussion with the White House on this has been, I think, exemplary. You have a whole new respect for the competency of the people that work in the White House, including the President, about understanding what is going on here. So this isn't something where you're dealing with multiple different levels below. You actually are dealing right up front with the Secretary and with the people in Homeland Security, and the President is briefed

daily on this.

Harden: It really is a shift, isn't it? We've never had a situation in the United States before where we had science, biological science especially, so clearly at the center of an international crisis like this.

Fauci: Right. One of the things that we have discussed several times at the White House is very clear. The President understands it; certainly Vice President Cheney understands it; Colin Powell understands it; and, absolutely, Tommy Thompson understands it, and that is, we are dealing now not only with the public health, which would be our responsibility, don't you worry about it, but public health also simultaneously becomes national security. So when public health becomes national security, then scientists like myself find ourselves walking in an arena and in an environment that we don't usually walk in.

Harden: And we have a long way to go to bring public health back up to where it should be, don't we?

Fauci: Yeah.

Harden: All right. Well, I thank you very kindly.

Fauci: You're welcome.

Harden: And I will tell you that I not only do my homework, but I get the best editor in the country here, and so she will be working...

Fauci: Well, it was very good and timely.