Bax, Adriaan 2021

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Dr. Adriaan Bax

Behind The Mask

June 30, 2021

Barr: Good afternoon. Today is June 30, 2021. My name is Gabrielle Barr, and I'm the archivist with the Office of NIH History and Stetten Museum. Today, I have the pleasure of speaking with Dr. Adriaan Bax. Dr. Bax is an NIH Distinguished Investigator and chief of the Biophysical Nuclear Magnetic Resonance Spectroscopy Section, which is part of the Laboratory of Chemical Physics at NIDDK [National Institute of Diabetes and Digestive and Kidney Diseases]. Today he is going to be speaking about some of his COVID research and experiences. Thank you for being with me.

Bax: Very nice to be part of this. Thank you.

Barr: When did you—and others who are part of your lab—begin conceiving and preparing for your study that looked at SARS-CoV-2 transmission via speech-generated respiratory droplets?

Bax: Actually, an interesting story. It was early 2020 that I talked to my former postdoc [postdoctoral researcher], Fang Li, who's now a professor in Wuhan. She was obviously very nervous about what was going on in Wuhan. I was not really following the whole thing, but I started panicking when I realized it was a lot more serious than we were aware of here in the United States. Fang, my postdoc, explained that people got sick—many people got sick—but very few were coughing or sneezing even though it was clear that it was a respiratory virus that was going around. I knew nothing about viruses really, certainly not about respiratory viruses. Normally we assume those are being transmitted by coughing or sneezing. When Professor Li told me, "no, nobody's coughing or sneezing here [in Wuhan] but lots of people are getting sick," this posed an interesting question. I discussed it with my wife, who's a linguist, and she pointed out that there's tons of speech droplets. I've seen speech droplets flying around when people speak—you get those big droplets coming out of people's mouths. It didn't sound very likely that was a transmission mechanism because these fall to the ground, but she assured me there's actually a science of studying those droplets. Indeed, there are many, many more droplets that are too small to see. It then sounded like it was pretty obvious that speech droplets could be a transmission mode. We figured, okay, as long as people are aware of speaking being so dangerous, we should be good to go and be able to contain this whole pandemic. We figured if we could just visualize speech droplets in a video, that should be like a public awareness alert, and that should help. There was no real science involved in this. This just started out as a public awareness service, effectively. We weren't even going to publish it [as a scientific journal article], so we only started out making a video for YouTube and put it anonymously online. This was apparently frowned upon by the NIH Communications Office [Office of Communications and Public Liaison (OCPL)]. Basically, we were naively thinking that as soon as people see the enormous number of speech droplets that come out of people's mouths when they speak, [they will] realize that speaking is not a good idea. This happened at just about the time that in Italy the pandemic really took off, at the end of February, 2020. Because of the pandemic, everybody started speaking more, not less. It was feeding on itself. It seemed so obvious what was happening. Then the whole thing started here in New York, where the same thing happened. When the infections got going, people stayed home, which may not have helped very much, actually, because they started speaking more. Everybody panicked—more speech droplets, more infections. The whole thing sort of cyclically started exploding. We felt that was a pity—if people were only aware of what causes transmission, that would have been able to stop the whole thing. That's sort of how we rolled into it.

Barr: That's really interesting. How did you decide that you wanted to do a video rather than capture the speech droplets in some other way like high resolution images that you would post online or something else like that?

Bax: It turns out there are already high-resolution images—photographs—of those droplets online. Actually, the oldest paper—that's really interesting—goes back to 1938. It's by the people that studied the flu pandemic from 1918. There are beautiful pictures from 1938 showing tons of speech droplets. Nobody cites the paper, and it seemed everybody was blissfully unaware of it. We only stumbled upon this accidentally, but it's been long known. It's very frustrating to see that all this good knowledge—really old-style physical chemistry [and] physics measurements that were done in the early and middle of last century—have been totally forgotten. Today, everybody is focused on molecular medicine and all the advanced things, but this old-style knowledge has sort of gotten lost or forgotten. It's really a pity.

Barr: Have there been a lot of other papers about speech droplets since the 1938 paper?

Bax: Yes, people have kept studying this. It's all so interesting. There were some very nice, thorough studies in the 1960s and also later on, but people started focusing on the very small droplets because of newer instrumentation that is readily available. There are instruments known as optical particle counters and aerodynamic particle sizers, which are really made for atmospheric aerosol observation. Those can count very small particles—very small droplets. They are not so effective at catching speech droplets—that mostly are bigger. Speech droplets you actually can catch with regular light photography or with the kind of laser setup we use in our lab. We can see a ton more than what you can see with this very sophisticated instrumentation. It's surprising and somewhat frustrating that, yes, there is definitely interest in those very small droplets, but the intermediate size turns out to be the most important for transmission of the virus.

Barr: Before we get too much into the other questions, why are the intermediate sizes the most important in terms of transmitting the virus?

Bax: The intermediate size is still small enough that it can stay floating in the air, but it also contains a lot of fluid to begin with so the particles are larger and therefore can carry more virus in them. Of course, there also are the very small particles. There are more of those, and they float around for a very long time, but they're so small that there's very little chance they contain virus. It's actually this intermediate size that's generated while speaking, and it's only a small fraction of your speech droplets that are in that size range—both big enough to contain virus but also small enough to keep floating in the air. It's a little bit too large to see by the conventional modern equipment. It's a little bit of an accident almost. There's a blind spot [with particle sizers] that the laser imagery that we were conducting was able to fill in.

Barr: Just out of curiosity, about how many speech droplets do people produce in a conversation in an hour with a normal person?

Bax: An hour is uncountable. It is, roughly speaking, about a thousand per second.

Barr: Oh, wow! That's a lot.

Bax: Wow, exactly! That's a ton of them. Every word you say, there's actually hundreds to thousands of droplets flying, but not all of them are relevant. Some of them are so small they're unlikely to carry any virus, even if I were infected. Some of them are so large, they're going to fall down to the ground very rapidly because they're heavy so they're not going to infect anybody. Just the intermediate size—and there's, I'd say, anywhere between 10 and 100 per second that would be in the size range—floats around for a couple of minutes before it lands on the floor. Those can have a ton of virus in them.

Barr: That's interesting to know. Can you relay how you, and others you worked with, went about conducting your experiment—including mentioning the kinds of tools and equipment you employed, as well as the metrics you all used to evaluate your result?

Bax: That's also an interesting question indeed. I had absolutely no clue on how to go about this and how to go about making those droplets visible. But I have a colleague here in the lab, Dr. Phil Anfinrud, who's also a section chief [Ultrafast Biophysical Chemistry Section, Laboratory of Chemical Physics]. He's a very bright, ingenious physical chemist by training, and he has a fantastic laser setup in the basement of our building. When I talked to him, I figured we might be able to see droplets, perhaps by making them fluorescent or by doing something with him. We should be able to see this with laser light. He actually proposed a much simpler solution—just to use light scattering. In retrospect, if I would have known, I could have just bought a powerful flashlight for a hundred dollars. A very bright flashlight can do almost the same thing as our laser setup, but we use this ultra-bright laser. We were able to get fantastic images very, very easily with that setup he had. He actually modified his laser setup to make a sheet of light rather than a beam of light.

Barr: How does one go about making a sheet of light versus a beam of light?

Bax: You start out with a beam of light, and you send it through a cylindrical lens that basically expands the beam of light in one dimension to make a sheet of light out of it. This then creates a very bright , thin sheet of light. It's a little bit like if you close the curtains at home and the sun is very bright outside, you get a little sliver of light coming through a crack in the curtains into your room. You can see the dust hanging in that light sheet. You may have seen that at one point at your own home. It's a nice way to observe the abundance of dust, and it's basically how we observe speech aerosols but using a much brighter light source than sunlight.

Barr: How bright is this light that you used?

Bax: Phil's setup was about maybe 10 times brighter than sunlight. Not humongous but about a factor of 10 brighter than the sun on a very bright sunny day.

Barr: The room is completely black?

Bax: Totally black, correct. That's the tricky bit, to get the background to go to zero so any dust in the air would light up. Working in a dust-free environment is also important for this purpose because otherwise all we're looking at is dust in the room. Light scattering cannot distinguish speech droplets from dust that hangs around everywhere.

Barr: You probably do this for other experiments, but how do you keep away the dust?

Bax: Dr. Phil Anfinrud has in his lab a setup with HEPA-filtered air. One part of the lab is being refreshed with very highly filtered air that is dust-free. Whenever we move into that space, we've got to wait about 20 minutes for all the dust to settle. Then we can start speaking.

Barr: That is very interesting. What were some of the observations that you and the others who were part of this project made?

Bax: The first observations that we made were that the number of droplets, indeed, were enormous. I was blissfully unaware of that. The size range was also obviously very large. We saw large droplets and much smaller droplets. With the setup we had, we could not see breath droplets, so just breathing wasn't good enough. Those droplets are yet another factor of 10 or so smaller, and we were not able to see them; it wasn't sensitive enough for that. But the speech droplets being larger and so many of them—we saw literally thousands per second of speaking.

Barr: Were there certain sentences that you said over and over again as you tested? Or were there differences in terms of what you said? Did you notice different droplets based on what you said?

Bax: Yes, we tried a whole bunch of things, and basically everything we said would produce droplets. One phrase that we used a lot was “stay healthy,” and that was a very droplet-producing phrase. It was also sort of, at the time of course, quite on the mark. For a lot of the testing, to keep it standardized, we used “stay healthy.” We also used the phrase “spit happens”. It’s the “p” from “spit” and “happens” when your lips are parting. That actually pulls a film of fluid between the lips, just when the lips come apart. The exhaled air bursts these films into little droplets, so the letter “p”—and the letters “b” and “t”—they generate most of the droplets from the front of the mouth.

Barr: Interesting. Were there different speakers that you looked at or did one person do all the speaking?

Bax: The original measurements were all done with Dr. Phil Anfinrud being the speaker. If you use multiple speakers, very quickly it becomes human subject research because now we’re comparing different individuals. For that, one needs IRB [Institutional Review Board] approval. It’s a whole different hurdle that we normally don’t deal with in the Laboratory of Chemical Physics. It requires all kinds of approvals. For publication purposes, we start with one speaker, but of course, everybody spoke. It didn’t make any difference in the end. We were criticized in a paper by Professor Didier Pittet, an infectious disease physician affiliated with the WHO [World Health Organization]. To address that, we made a video that had all four of us speaking. That was actually published in The Lancet in August or September 2020, I believe. We needed to get a waiver from the IRB to allow that to be used in a publication.

Barr: I didn’t realize that even if the researchers were the ones being part of the experiment, they have to get an IRB [approval]—that they’re treated like a [human research] subject.

Bax: I’m afraid so. NIH is stricter than academia. At NIH, one needs approval or a waiver that you’re exempt from that kind of approval. We ended up getting the waiver.

Barr: What were some of the challenges that you and your team faced with doing this study?

Bax: Technically, the challenges were all solved by Dr. Phil Anfinrud. Basically, the recording of the data and the counting of the particles. How many particles do we have? For the technical challenges, he had a very good postdoctoral associate, Valentyn Stadnytskyi, Ph.D., who played a key role in that. The hardest part turned out to be writing up and selling it to the medical community. Making a YouTube video took us two days but getting our findings published was a lot harder. [NIH] Director Francis Collins was very supportive, so that helped, at least with the first paper. Then we had a follow-up paper that tried to measure how long those droplets stay in the air. Again, those measurements were done very, very quickly. We felt it was urgent that we publish that as fast as we could. The measurements were not perfect, but they were certainly good enough to show that, yes, those droplets hang around for many, many minutes. That got published fairly rapidly. My daughter, who is an M.D., actually was sent home from Penn Med School [University of Pennsylvania Perelman School of Medicine] at the time because the school was closing down. She turned out to be very helpful with both writing it up and doing a lot of the literature research—giving it a little bit of a medical flavor, if I may call it that. It turned out to be a very, very productive team where everybody complemented one another.

Barr: Definitely. Why was it so hard to sell to the medical community, and what did you do to try to sell them on this idea?

Bax: I think it's mostly a question of speaking different "languages." The medical community was totally focused on their own area, and I don't think they wanted to be bothered by a bunch of physicists. They had very preconceived notions about what speech droplets are and what aerosol is. That droplets actually turn into aerosol was apparently totally surprising to them. Whereas for us, it is so obvious that you don't even want to mention it. It's so trivial that you don't want to sort of speak down to people, but apparently a lot of the confusion came out of this lack of understanding of trivial physics by the medical community, like in the paper by Pittet. It's been a bit of a pity. If that would have happened earlier, I think, the world would have made more headway with mitigation efforts.

Barr: Do you have plans to continue the study, and if so, what are some of the new angles about air droplet transmission that you'd like to explore?

Bax: Interesting question, actually. There's a new angle that I think people have missed. I'm not sure how much I can get into detail here. You know that most people get only mildly sick, and some people get very, very sick or they die. If they get very sick, it's when the infection goes to the lungs. As long as the infection remains in the upper respiratory tract—in the nose or the mouth, you don't have to worry very much. Once it gets into the lungs—especially if it gets there before the adaptive immune system has kicked in—you can be in big trouble. Especially for old people, where the immune system is not going to react with the same kind of speed as for young people. Now it turns out that most of the process—starting in the nose and how the infection ends up in the lungs—is not fully understood. The medical community blames aspiration—that's when effectively the snot drips down into your lungs at night when you're asleep. We actually believe that it's speech droplets that cause the self-infection. Because you speak a lot, especially when there's a lot of disease and panic around, you're in the center of your own speech droplet cloud. So, you're going to inhale your own droplets—that contain virus—from your mouth, but you're inhaling them into your lungs. The chance they're going to infect your lungs is very small because these droplets normally don't make it to your lungs. But if you sit in your own cloud for the whole day, the entire time that you're speaking there's a much higher probability that you're going to infect your own lungs than of somebody else infecting your lungs. So, we believe that self-infection with speech droplets actually may have a lot to do with it. We started a study with Gallaudet University where people who use sign language—we expected—would not get as sick because they would not self-infect because they're not speaking vocally. Usually, they use sign language instead. Collaborating with Professor Poorna Kushalnagar, Ph.D. at Gallaudet and Carson C. Chow, Ph.D. here in NIDDK [National Institute of Diabetes and Digestive and Kidney Diseases], we carried out a survey of COVID-19 patients in the deaf community. Indeed, there is a significant correlation—people that don't speak don't get as sick as people that do speak so we believe that provides support for this self-infection hypothesis. We're just in the process of getting that published. There're two angles to this. It offers an immediate way of stopping yourself from getting seriously sick if you know that you've been exposed or as soon as you start feeling the first symptoms. You would stop speaking or you speak with a mask. If you speak with a mask, your droplets will not turn into aerosol and cannot be inhaled into your lungs. Either don't speak after you get exposed, or at the first sign of symptoms, you wear a mask. It's actually been known that people that wear masks don't get as sick. There are published studies of grocery workers and people on cruise ship. [It's been] published in prestigious journals that people that wear masks don't get as sick, but nobody understood why. We believe that it's because it stops self-infection.

Barr: That's really interesting. I never thought about infecting yourself. I'd always heard masks in relationship to other people infecting you but not yourself.

Bax: It's not proven yet. The data strongly suggests that it's the case. It's for sure that it happens. How significant is it? Does it make a 50 percent contribution to severity, or 90 percent or 10 percent? We can't really tell. It's probably more than 10 [percent], otherwise we would not have seen the effect on the deaf community. I'd say it's a least 50 percent but is it 100? Probably not. There are other ways. Aspiration is a direct hit. Also, if I get this first speech droplet from somebody and it enters into my lung with a virus in it, and it gets me infected, it starts as pneumonia. It's a low probability but it does happen, so there are other ways. But self-infection may be a big part of it.

Barr: What implications do you think your research will have on other viruses? Do you think that speech causes the transmission of other viruses?

Bax: To some extent, probably, yes. I think for measles it's actually long been known that speech is a big factor. I remember as a five-year-old kid I got infected with measles. The village physician instructed my mom that nobody was allowed to talk with me inside my room. I was in a little bedroom with the window open, and she would talk to me through the closed door. I remember as a kid this was totally crazy that people would think that sound waves would carry virus. Obviously, it's not the sound waves; it's the droplets. I'm sure the physician didn't know about the droplets, but it was known back in the village that you don't speak in a room when somebody has measles.

Barr: That's fascinating! That's a really interesting memory.

Bax: This is really historical knowledge that has gone by the wayside and is no longer trained in medical school. Whether it applies to influenza, I don't know. It depends where [in the respiratory tract] the virus is active and where it replicates. There's been an NIH study—you may have interviewed those people, [Kevin] Byrd and [Blake] Warner—in Nature Medicine that came out just recently. They showed coronavirus to be very abundant in saliva, especially in pre-symptomatic and asymptomatic carriers. Once people are really sick, like I explained, they have it in the lungs. They're probably in the hospital, but it's the asymptomatic and the pre-symptomatic carriers that drive this pandemic. They turn out to have massive amounts of virus in saliva, but whether it's true for other respiratory diseases, I really don't know.

Barr: That will be interesting to learn. Will you please discuss your study that looked at whether humidity from masks may lessen the severity of COVID-19?

Bax: That's an interesting, serendipitous finding that we made. When I was doing my measurements on droplets in the box, we would use the increase in humidity of the box—the container where the droplets float—as a measure for how much air I would exhale into the box. When trying to do the same measurements with a mask to see if my mask would stop the droplets from getting into the box, it turned out I needed a lot more breathing and speaking to get the same humidity increase into the box. Trying to understand what happened there, it was immediately obvious that the mask is absorbing a lot of the moisture each time you exhale and evaporating that moisture when you inhale. Meaning that the apparent moisture that enters your lungs is much higher, so the humidity of the inhaled air goes up tremendously when wearing a mask. All we did was try to measure this quantitatively. It has long been known that humidity plays a role in respiratory diseases, especially low humidity. It can dry out your mucosal layer in the lower respiratory tract and make the mucociliary clearance less effective. Meaning that if you inhale something it might actually be able to infect you rather than getting moved out by this conveyor belt clearance mechanism we have in the lungs. It's a small observation, but it was interesting. I think in retrospect everybody knows that if you wear a mask that it gets sticky, and it gets moist, and it is sort of a nuisance. But it's probably helpful, especially for older people that can have the mucosal layer dry out in the lungs much easier than young people. Humidity is supposed to be effective, and that's why steam inhalation is often used for people with a respiratory tract infection. Again, this is kind of centuries-old, you know, grandma's wisdom—but it probably works through this mechanism of mucociliary clearance.

Barr: Do you think either of your studies had any impact on public health policy?

Bax: That's always a big question. We were hoping that it would have an impact early on by recommending the use of masks. It's very obvious that masks would stop speech droplets from entering the atmosphere. Whether our work had a role in that… Perhaps [former NIH] director Francis Collins helped propagating the idea. Tony Fauci was supportive and actually advocated the use of masks to protect other people. Perhaps the visualization efforts that we made had some role in that.

Barr: If I went to YouTube would I be able to find the video that you all produced?

Bax: I can send it to you. It's embarrassingly primitive because it was done in a rush. It literally took less than two days to do the experiments and make the video, but I'll send you the links. https://www.youtube.com/watch?v=qzARpgx8cvE

https://www.youtube.com/watch?v=_OSz5Gr7gG0

Barr: Okay, that sounds good. Have you been involved in any other COVID research or initiatives at NIH or outside of NIH?

Bax: Yes, we have. Of course, when the campus closed, the only way to get access to your lab was if you were involved in COVID research, and the same is true for the postdocs. There's actually very interesting science to be done. My more conventional area of research involves nuclear magnetic resonance (NMR). We're using that to look at various proteins that play a key role in the SARS-CoV-2 virus, including the protease. The Main Protease is an enzyme that's also a great drug target. We do NMR studies of that. Another postdoc is focusing on how the virus actually enters the cell, what the exact fusion mechanism for the membrane of the virus is—it has to fuse with the membrane of the host cell for it to get into that cell. We've got a very nice molecular-based model now based on his experimental measurements to explain that. There's a third guy studying why virus in the air decays. Why does it become less viable when it floats in the air? There're all kinds of different angles, and there's been a whole bunch of neat science coming out of this.

Barr: Seeing that you're trained in physics, how do you try to inform yourself about some of the other aspects that maybe you're not an expert in—like some of the biological aspects of the disease and things like that?

Bax: If nothing else, this pandemic was a great stimulus to beef up on my knowledge and understanding of virology. It's been interesting and educational to find out what else is going on outside of what I call "spin physics." I've talked to many colleagues that have been extremely helpful in explaining the basic principles of respiratory diseases—the host defense system, the immune system—it's been an eye-opener. In a sense, it's sort of rewarding if we can do anything to help in this crisis that appears now, fortunately, mostly behind us. But it's probably going to come back again in the fall. All signs are, right now, that this Delta variant is going to create havoc come November or December [of 2021].

Barr: What ways do you think that people such as yourself and those in your lab—who have more of a physics approach—how do you think that is particularly advantageous to looking at the disease? There's a lot of different ways of looking at it.

Bax: Perhaps it complements, right? It's like I said, if you talk about aerosol, very few people with an M.D. have any understanding of aerosol. For us, we have very little knowledge about the immune system and about many of the processes there, but both are important to this disease and how to deal with it. There's been a lack of communication—although we've tried hard—but everybody's very busy right now because of this pandemic and there is less time to talk. I've actually had a great time talking with an expert at Baylor College [of Medicine], a gentleman by the name of Daniel Musher, M.D., who's a world expert in respiratory diseases. He's sort of been my mentor in bringing me up to speed.

Barr: That's interesting. What are some personal opportunities and challenges for you that COVID has presented?

Bax: The personal challenge was originally the shutting down of the campus—the disruption of the regular research. Also, the pressure to get our droplet work out in the open, to make clear to people what is going on, what we believe was important—whether or not it was important. There probably were enough other people that could have done that, but at the time I sort of felt pressured to get the information out as fast as we could. At the same time, I felt responsibility for my group, my postdocs—keeping them employed and interested, so that nobody ends up dropping out. It's been a tough year. Personally, of course no vacations, less socializing—but that's what everybody deals with. That's not really been the most disruptive aspect.

Barr: How did you ensure that everyone in your lab continued to be safe but also continued to have the experiences they needed for their jobs, to move on to their next position, their education, or whatever they may need?

Bax: We took advantage of the rules, knowing that having research dedicated to COVID would give some priority for at least part-time work on campus. We only needed to adjust the work that others were working on, like the postdoc working on viral fusion—membrane fusion of virus—originally worked on HIV. The SARS-CoV-2 work is so similar that he could very rapidly switch. The other postdoc working on the main protease was his own idea. When he saw that this pandemic was coming down on us, he was proactive and picked this project all by himself, before the shutdown. In the end we were able to steer pretty much everybody to a project that, in one way or the other, is associated with the SARS-CoV-2 virus and allowing them to get back in the lab earlier, at least on a part-time basis. That's been sort of helpful, and of course it's motivating for the postdocs as well—if they know that they're working on something that is not just of academic interest. I think it's been motivational for all of them.

Barr: Has there been something that you enjoy that has made the pandemic easier to cope with?

Bax: There's nothing I've really enjoyed about this pandemic, expect for perhaps spending a little bit more time at home. Now I work a lot of time from my basement. I think my wife likes it when I'm home. My daughter, like I mentioned, spent a couple of months working with us, so that was a good experience. Although I think she believes I'm the worst mentor she ever had—the toughest mentor—but I guess you're always tougher on your own people than on others, so I hope she forgives me.

Barr: Is there anything else that you would like to share either about your work or about your experience as a person living through the pandemic?

Bax: Nothing in particular really. Let's hope it's all going to get behind us sometime soon. It's been a big effort by a lot of people. I'm happy to see the vaccines because those really seem to be a real solution. Also, soon [there] will be effective drugs, so even if vaccines are not 100 percent effective, the drugs should be coming out next year if the approval process can get expedited. I'm quite convinced that some of the inhibitors are very efficient at fighting the virus so I'm pretty optimistic that a year or two from now this is not going to be a problem anymore.

Barr: Well, let's definitely hope so. Thank you—and thank you for all the work that you and your team and lab do.

Bax: Alright. My pleasure. It's a pleasure to be working at NIH where they let us do this kind of stuff!

Barr: Definitely.