Dr. Kenzie L. Preston

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Higingbotham: Hello, today is October 14, 2022. My name is Haley Higingbotham. I am the assistant archivist at the Office of NIH History and Stetten Museum. Today I will be interviewing Dr. Kenzie L. Preston. Dr. Preston is a Scientist Emeritus and a special volunteer at the National Institute on Drug Abuse's [NIDA] Intramural Research Program. Today she will be speaking about the trajectory of her career including her education and research. Dr. Preston, thank you for speaking with me.

Preston: Thank you for giving me this opportunity.

Higingbotham: To start with, would you please tell me a bit about your childhood?

Preston: Okay. I come from a smallish Midwestern town in Central Illinois. I'm the oldest of five children. Neither my parents nor my grandparents or anybody close to me had ever gone to college, and so I had no real role model for navigating the higher educational system. That made it a little challenging to go through and get started in college.

Higingbotham: Since you didn't have many influences about going to college, what influenced you to wanting to get higher education?

Preston: I think my family always kind of assumed that we would go to college, and in particular, my grandfather, who had been a child during World War I and then actually fought in World War II, was a huge proponent of us going to college. He always said that education was something that they couldn't take away from you, and he always encouraged us to get a profession. His preferred professions were school teaching or nursing. When I was a young woman, those were the professions for women. Of course, thankfully, that has expanded since then, but at least we had that push at the beginning.

Higingbotham: Yeah, definitely. I think a lot of people have that push especially if their parents or grandparents didn't have education. Do you have any significant memories from your childhood that really made you want to pursue science?

Preston: I remember in eighth grade that I decided that I wanted to be a scientist. When I reflect on that, I'm not even sure I knew what scientists did or how one became a scientist, but there was some spark there that happened – that made that my goal.

Higingbotham: From science, you got interested in medicine. Did you have anything later in education that made you want to pursue biomedical sciences?

Preston: Let's see. Well, my undergraduate degree was in pharmacy. I chose pharmacy – to be honest, it came from an encyclopedia that my parents had that listed a lot of different professions. We went through the book and that was the one that appealed to me. I eventually got a job in a pharmacy to see what it was like, and that started me down the medical realm. While I was in pharmacy school, I had a lot of colleagues in the dorm, and we lived with people who were in medical school and nursing school. I hadn't known about graduate school. That just was never something that anybody I knew went to, but one of my friends did. She gave me the idea that I should go on to graduate school after college. Another thing that happened while I was in pharmacy school is that I answered a flyer that was hanging

in an elevator that said, “Would you like to work with monkeys? We have a volunteer opportunity.” I answered that opportunity, and I ended up being an observer of a monkey colony where they were testing amphetamine and phencyclidine as part of substance abuse research. That was a great opportunity. It got me to know people who were scientists and know the professors, and I think ultimately led to my going to graduate school and studying substance abuse.

Higingbotham: Where was this monkey colony? I don't feel like Illinois is very conducive to having a monkey colony.

Preston: Well, it was not a free-ranging monkey colony. They were actually a social group that were housed in a building at the Illinois State Psychiatric Institute.

Higingbotham: Okay. You kind of discussed it a bit, but was there anything else you'd like to talk about with your college education at the University of Illinois Chicago?

Preston: I would say that pharmacy education was an extremely good education. It gave a good science base. We studied histology, microbiology, biochemistry, physiology, pharmacology – I actually got as much pharmacology education in pharmacy school as I did in graduate school, in getting a PhD in Pharmacology. One of the things that was happening at the time is that I was right on the cusp of the PharmD [Doctor of Pharmacy] program. Prior to my going to college, pharmacists were primarily involved in dispensing medication, so you look for drug interactions, but it was more of a mechanical kind of job whereas nowadays the pharmacist plays a much greater role in the medical teams [by] advising doctors and monitoring patients. Some of our instructors had been PharmDs, but there were only, I think at the time, maybe two or three universities where you could get a PharmD degree. When I graduated from pharmacy school and worked in a pharmacy, what I discovered about myself is that it was not a career for me. That's when I decided to go back to graduate school and pursue pharmacology.

Higingbotham: That was at the University of Chicago, and so you switched to pharmacology and psychiatry. Could you talk a bit more about that program?

Preston: The people that I was working with in the monkey colony knew a lot more about substance abuse research than I did, so the professor who wrote my letter of recommendation for graduate school said, “When you get to the University of Chicago, you should work for Dr. Bob Schuster because he's a great scientist and very influential in the research field.” Actually, that's what happened. I was able to get him, Dr. Schuster, as my graduate advisor and ultimately, quite a few years later, Bob Schuster became a director of NIDA. In fact, he was well placed. His appointment was both in Pharmacology and in the Department of Psychiatry at the University of Chicago, and within his lab, we had both psychology students and pharmacology students. The kind of research we did was called behavioral pharmacology. You look at the behavioral effects as well as the pharmacology of drugs, and that's where that pairing up of psychology and pharmacology happened.

Higingbotham: That definitely makes sense. You talked about Bob Schuster – did you have any other influences during your time at college?

Preston: I think that having that opportunity to work with the scientists doing the research was a very great opportunity, and I highly recommend that students try to get that kind of opportunity. We even went to the Society for Neuroscience meeting in New York. That was a quite an experience – going to that as an undergraduate and going on the train and just getting exposed to all kinds of science that I

didn't even know existed. I remember watching one about circadian rhythm in birds; it was fascinating. I think that just sort of fueled that idea that I wanted to pursue science.

Higingbotham: Yeah, hands-on research – you can't really top that. Going to your post-doctoral fellowship could you talk a bit about your time at Johns Hopkins University School of Medicine and your fellowship there?

Preston: I had done behavioral pharmacology with Dr. Schuster's lab, and I had the background in pharmacy so I kind of had that the medical part there. When I was looking for a postdoctoral program, I needed to move to the Washington/Baltimore area because that's where my husband was working. I applied for a postdoctoral fellowship at Johns Hopkins, and the group that I worked with was called the Behavioral Pharmacology Research Unit. It was still behavioral pharmacology, but this time, instead of being in rats and monkeys, which is what I did with graduate school, it was with people. It was a great opportunity; they were a great research group. I didn't really know it at the time, but Bob Schuster was a very good friend of Dr. Joseph Brady, who's one of the pioneers of behavioral pharmacology and he's at Johns Hopkins. That's kind of how I ended up there, at Johns Hopkins. I did a two-year post-doc, and then they offered me the opportunity to stay on as faculty. Altogether, I was at Hopkins for nine years.

Higingbotham: What a great opportunity. Since you were at Hopkins for nine years, what really brought you to NIDA?

Preston: I was recruited by the scientific director at the NIDA intramural research program. I was a friend of his wife's, and we started carpooling to Baltimore, and it was on the same campus. That's really how it happened.

Higingbotham: Early in your time at NIDA, the institute was part of the Alcohol Drug Abuse and Mental Health Administration [ADAMHA] instead of the NIH. How was it different back then than how it is now as part of NIH proper?

Preston: We just had a different set of rules. Of course, we all worked for the Federal government, so we had those sort of overarching rules, but one of the big differences that affected me was that our IRB [Institutional Review Board] that we use for our clinical research was actually the Hopkins IRB. Once we became part of NIH, that wasn't acceptable to NIH. We had to develop our own IRB. That was a major change. There were a lot of changes. When we first joined NIH, for example, they always listed on the website the institutes alphabetically, but we ended up at the bottom of the list. It took a while to really get incorporated into NIH. Of course, our leadership wasn't part of the committees of NIH, and so that took a while. I think it was not a real hard transition, but I think it took us a while to really get into the whole NIH way of life.

Higingbotham: Definitely. Going towards your research specifically, not just your affiliation, I guess I should say, with different institutes, much of your research is based around developing and testing the efficacy and safety of new treatments for substance use along with understanding the individual and environmental factors that affect substance taking and relapse. What interested you in this specific part of substance use research?

Preston: I started off at Hopkins doing abuse liability assessments. That was one of the main things that they did. While I was there, I also developed a human methodology for using a technique called drug discrimination. That was an animal technique that really lent itself to being studied in humans so we

could tease apart more of the receptor effects of different kinds of opioids. I also wrote a grant to test medications in a behavioral pharmacology lab or medications that might be effective in treating cocaine. We had that idea of treatments, and I did mostly those laboratory type studies when I was at Hopkins. When I moved to NIDA, they offered me two choices: I could continue doing the same kind of lab studies I'd been doing before, or I could take over a new program that they had funded to have an outpatient substance abuse treatment program treatment research program. I thought, "I want to try this new opportunity," so I chose the substance abuse treatment program. That meant learning a whole lot about doing clinical trials and treatment. In that, we did clinical trials of behavioral treatments of medication treatments, and we were very interested in seeing if we could combine behavioral and pharmacologic treatments to get a better outcome. We did a series of studies on contingency management and combining that with different doses or dose increases of methadone, which is an effective treatment for opioid dependence that doesn't entirely reduce all of the bad or adverse things of using opioids. We combined it with cognitive behavioral therapy and contingency management and methadone. That's how we kind of moved into the treatment realm. Then over time, we had the opportunity to use electronic diaries to do ecological momentary assessment [EMA] which is monitoring people's mood and behaviors and activities as they go about their daily lives. We've kind of transitioned over time in that way.

Higingbotham: Yeah, I saw that in a lot of your studies after, I think it was, 2005 you started to use the ecological momentary assessments. That became a tool that you used fairly often. What really made you decide to use the EMA?

Preston: It was a very exciting opportunity. Prior to using that, we would ask people to fill out questionnaires once a month or every week. The problem with doing that is it's a lot of retrospective, and you get what they call recall bias. It happens to everybody. You remember the most salient thing or intervening time softens the effect. People have done studies showing that in fact how you feel in the moment and reporting how you feel is different than you would feel a week later. We are very interested in the influences on drug use and craving, which many people report is a big problem for them in drug use. How did that actually relate to their opportunity of ending up using drugs in spite of trying not to use drugs? That was one of the exciting things; you'd have a much finer temporal change across the day in mood say compared to just average for the week.

Higingbotham: You later combined EMA with GPS tracking which is referred to in your studies as geographical momentary assessment or GMA. Was this something you wanted to do early on when you started using it or did you want to add this element as results came in on other studies?

Preston: There's a big tradition in animal studies where they monitor activity levels and movements within a cage, and I sort of thought about that in terms of our participants. Also, one of the people we hired had been involved in migration studies of animals. It seemed like it could be of interest because people might believe or think they know what triggers drug use, but in fact it occurred to us that it could be environmental influences that they weren't aware of. There's been a huge movement showing that, in fact, environment affects health, so that's how we got interested. Now fortunately for us, the NIH put out a request for proposals for development of environmental monitoring tools. That was the Genes and Environment Initiative [Genes, Environment, and Health Initiative]. We put in a proposal in partnership with another colleague at Hopkins, and we actually got awarded that. It gave us opportunity to work with other scientists who were developing technology to monitor environmental influences. We worked with people who were developing ways of monitoring exposure to light and activity and also just biosensors in general. That's how we actually got started doing that.

Higingbotham: How did the GPS element really enrich your findings?

Preston: We were able to show that there were some environmental influences on people's craving. Not so much their drug use really, but it varied a lot by people. It actually turned out to be much more complicated than we anticipated, and also even just analyzing the GPS data turned out to be much more complicated than we anticipated.

Higingbotham: I can see that. You mentioned working with people that use biosensors. The next evolution it seemed in the studies was adding biosensors for people to wear, I believe. How did this help to give a more holistic image of the factors that might affect substance use?

Preston: Yeah. One of the things that we found is that craving did precede drug use fairly reliably, and we were asking people to report on their craving like five times a day, four times a day, three times a day. But the truth is that you can't keep asking people 25 times a day about their craving; it's annoying. It could even have adverse effects if it triggered people. A possible alternative would be to monitor physiological responses and perhaps in combination with the GPS, to develop a signature or identify a signature that could replace the self-report. That's the idea behind that. Again, that turns out to be very complicated, because, for example, heart rate goes up both when you're stressed and when you're craving, so to be able to tease those two apart can be pretty hard. The other thing is that collecting heart rate, at least back when we were doing it, by putting ECG electrodes on the chest gave you the best heart rate data. Even though the Fitbits and those sorts of devices can measure your heart rate, they're not necessarily at the level of accuracy that you need. There needed to be a lot greater technology development to perfect that. I think it's a way to go; it's possible, but in the time that I was working on it, it was really tough.

Higingbotham: Speaking of that, can you talk a bit about the development of the mHealth platform and your role in its creation?

Preston: One of our goals was to develop a just-in-time treatment for substance abuse. If we could predict when people were going to be craving—which predicted when they would use drugs—and we could send them a message—perhaps a part of a mindfulness message or a cognitive behavioral message—then we might be able to intervene to prevent them [from] going on to use drugs. That was the idea behind our work, and we did write a patent application and submitted it. It ultimately wasn't approved, but it was our first attempt at doing it. I believe that people are continuing to work on that.

Higingbotham: You mentioned the technology really wasn't where it needed to be while you were working on this. Can you talk a bit about how the quickly changing technology affected your development of the platform—both helped it or made it harder?

Preston: When we initially started EMA, we used what was called personal digital assistants [PDAs], at the time it was Palm Pilots, and we were so fortunate that we had a group of IT professionals at the NIDA intramural research program who we collaborated with and programmed those for us. They were quite reliable, and they were inexpensive. The downside was that they're not wireless, so people had to come in. It wasn't much of a problem for us because we were doing our studies and had people who were receiving methadone and who actually came to our clinic seven days a week, so we could download the data. Ideally, we wanted to move to a smartphone platform. That became complicated, because early in the Android development, they were changing the operating systems very frequently

which would break the program to have our program on the device itself. Then the other issue with that is that the lifespan of any device was about six months, and so you could start with one device but by the time you needed to replace devices that had been broken or lost, that device wasn't available anymore and you had to get a different device. That created problems. It was less of a problem with the PDAs because we could buy a bunch of them. and they lasted fine. But I think people have found that as a real barrier to putting an app on a phone. Now some groups have gotten around it by having a link to a website which makes it so they can control it, but it's still a bit of an issue. And of course, with our study population, they didn't necessarily have smartphones or know how to use smartphones. Teaching them to use them, on the other hand, was a benefit to them, because when we switched to using smartphones, they had an access to a cell phone which they might not otherwise have had.

Higingbotham: When you were creating this app were you all having the help of programmers in conjunction with scientists?

Preston: Yes.

Higingbotham: And were they NIH programmers or were they a third party?

Preston: These were NIH employees. That was part of their research program—to work with us. We tried using third parties. One of the difficulties at the time was that there are very serious privacy concerns for medical research and in particular substance abuse research. I'm not a computer scientist myself, but it turns out that using the cloud—and some of the links between collecting the data and storing the data wirelessly involved going to cloud storage—may or may not meet the requirements for security and privacy that are required for the Federal government. Making sure that every single step of where those data went met the privacy and security requirements was a bit difficult.

Higingbotham: Yeah, that makes sense. When this was a smartphone app, did you have other monitoring equipment that people had to use like a smart watch or a chest band? Anything like that?

Preston: We've experimented with several of those. We worked with a group that was developing a device that they wore around their chest, a chest band, and it monitored respiration and heart rate. Based on that, we were able to use their data to develop an algorithm to detect cocaine use. That was pretty exciting because we typically would use urine drug screens to monitor cocaine use but the temporal relationship for that was not great. We might collect urine every three days, and it could stay positive in all of the time, but that doesn't mean people were using every day – it just meant that the drug didn't leave their body long enough. You just never really knew when people used. Whereas, if you could monitor their heart rate and use an algorithm to tell, you could tell more closely exactly when they used and then look at what happened before that, to look the antecedents to their drug use to more more precisely identify the factors that were associated with that use. They've since moved on to develop a wristwatch type monitor which would be much more convenient. Having patients wear these ECG leads constantly – it's just not a practical solution at all, whereas wearing a watch certainly would be. But it turns out there are many technological issues with that. The skin color made a difference, the level of activity made a difference, the size of the wrist made a difference. It’s a challenge to do that. We also worked with the group that measured exposure to light, and based on that, we were able to monitor sleep and to look at the relationship between drug use and sleep. There were kind of complicated relationships, and it appears that using opioids and cocaine had differential effects on how early people got up, how late they stayed out or out of bed, and also the quality and the duration of their sleep. Those have major effects on health separate perhaps from the actual drug use itself.

Higingbotham: When you stepped back from working on this project, where were they at with it? I know you said they're still working on trying to figure out how to make some kind of app.

Preston: I know people are still working on it, and they also have developed, and in fact getting approved by the FDA, a mobile app to deliver counseling type interventions, which is great. It's quite a burden to go in and see a counselor all the time, and generally treatment is time limited, whereas if you could have that treatment delivered by a smartphone or even through the web, it would extend the availability of treatment for people both in locale as well as in time. I haven't kept up with people's ability to incorporate physiological monitoring, but definitely there's a lot of work. There's a contingency management app now that's apparently quite effective.

Higingbotham: That's good to hear. I feel like we've talked about that quite a bit. The last question about your research really is how often were you involved in studies which test therapeutics themselves? It seemed like most of your career from 2005 onward was more about this platform or monitoring activities.

Preston: We did quite a few clinical trials over the course. One of the last ones we did was looking at clonidine as a possible relapse prevention medication. That was based on some animal work. Now that was an exciting study because we incorporated the EMA in the randomized clinical trial. What we were able to show with that was that not only was there an increase in time-to-lapse in the patients who are randomized to receive clonidine, but also that—we'd shown in earlier research that when stress increased, craving increased. What clonidine did is it decoupled that craving and stress. People who had moderate levels of stress, if they were receiving clonidine, didn't also have an increase in craving. It decoupled that and that gave us, in addition to knowing that it would be effective, perhaps the mechanism of how clonidine might be helping patients.

Higingbotham: That's very interesting. We'll start moving into the more concluding or overarching questions. You've been involved in the field monitoring opioid use since the beginning of the opioid epidemic. Could you give your perspective as someone studying substance use disorders and treatments on how the health care crisis has evolved and how it might be solved or go on in the future?

Preston: One of the very first things I did when I entered my postdoctoral fellowship was to go to a conference on the development of opioids with lower abuse potential. This has been a problem, the opioid crisis, for a long time, and people have been working on different solutions. In fact, they did come up with medications with lower abuse potential. At the same time though, there's so many factors that influence drug use. There was a movement to increase the availability of pain medications because there was concern that because doctors were so concerned about addiction that they were withholding pain medication from patients who really needed it and who weren't at risk for becoming dependent. That pendulum ended up swinging very far and opioids were available in large quantities to a vast number of people. That's outside the range of medicine and science really; that’s public policy. As a consequence, opioid overdoses went way up. At the same time, fentanyl became more widely available, and it replaced heroin in the drug supply. Fentanyl is a much more potent drug, and people were even more likely to overdose so that pushed the number of overdoses up. Now we're kind of swinging in that opposite direction of not giving patients pain medications to try to reduce the amount out there. While people who were using heroin initially were very concerned about getting fentanyl, now it's much more acceptable. I guess the answer to your question is that part of it is medicine and developing better treatments, but the other aspect of it are these other public health policies that scientists don't have

much influence over. I think we're not really going to solve the problem until we can kind of bring all the parties that have influence over both the availability and the treatment together and increase the availability and acceptability of drug treatment.

Higingbotham: That kind of goes into one of my next questions. A large aspect of working with those suffering from substance use disorder involves fighting against stigma associated with substance use. How has this also evolved over the course of your career?

Preston: I think stigma perhaps has gone down a bit, but it's still there. People don't want to admit they've used drugs, and when the health care system discovers that they are, then they are less welcoming to patients who use drugs. Even some treatments are withheld from people who use drugs for, I think, both moralistic and some practical reasons. Like the treatments for hepatitis C. We now have effective treatments but they're fairly expensive and some people don't want to give them to people who are continuing to drink or to use drugs. That has an adverse effect on people's health. It even affects the funding of research. In the genes and environment initiative that I talked about, when we tried to get some additional funding to do the light exposure study, one of the reviewers said, “Well, why would you try this in people who use cocaine because they're not gonna wear the device.” This was a study that was funded by NIDA, so it's just those big things and those little things can all contribute to failure to solve our problem.

Higingbotham: Going back to early in the interview, you mentioned how when you were going to school, some of the careers expected of women were a teacher or nurse, and you're happy how things have changed now. How do you feel the role of women in the medical field has changed?

Preston: Well, there's certainly a lot more. When I was in pharmacy school, one of my dorm mates was in the dental school. She was only one of two women in the class of dentistry. I think that is not the case now. There are lots of women, and I think in numbers there's power and influence to try to you even the playing field. It's a good thing, and I personally was influenced by Bernadette Healy. She was the director of NIH when I decided to go to NIDA, so you know it can make a difference when you have those role models.

Higingbotham: Definitely. I have two more questions. Now that you are retired, you work with the NIDA Clinical Trials Network to review studies. How does this compare to designing or conducting studies, and how has your research experience helped with this?

Preston: I think one of the good things that NIDA has done is try to move the research out of the academic areas and more into the community, and that's what the Clinical Trials Network does. It also opens up the kind of research that can be done. When we do research or identify treatments in academia, it doesn't necessarily go out into the community providers, especially if it's not a medication. Drug companies have mechanisms for promoting their products and to get them used in the community, whereas behavioral treatments, for example, there's nobody advocating and promoting those out there. I mean NIDA does it to a certain extent, but their reach is somewhat limited. The Clinical Trials Network is designed to not only do research but also to help get the research that's available out into the community, and so it's exposed me to different kinds of research that I didn't do. Because I've had a lot of experience of doing research, I can weigh in on study design and practicality a lot of times. It keeps me in touch, otherwise with being retired, I don't go to all those seminars all the time. It keeps my brain in touch with substance abuse research, and hopefully I'm contributing to the field.

Higingbotham: The final question is: Do you have any last words you want to say about your career or any words of wisdom you would like to give to someone just starting their career in the medical field?

Preston: I think the big thing is that you should expect change and really embrace it and maybe even plan for it. If you hit a wall, then you move on. A lot of times, the big questions kind of remain the same. We were still interested in craving and drug use, but the tools to answer those questions are constantly changing and improving. I have good faith that the mobile health platforms will be effective in the future, but we had to start somewhere, and we did it. You need to just push forward and embrace change.

Higingbotham: Thank you so much for joining me today. I really appreciate our talk, and it was very interesting.

Preston: Thank you for this opportunity.