

Dr. Candace Tingen

Behind The Mask

October 22, 2021

Barr: Good afternoon. Today is October 22, 2021. My name is Gabrielle Barr, and I'm the archivist at the Office of NIH History and Stetten Museum. Today I have the pleasure of speaking with Dr. Candace Tingen. Dr. Tingen is a program director with the Gynecologic Health and Disease Branch (GHDB) at the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD). Today she is going to be speaking about the NICHD grants that are looking to see how the COVID-19 vaccines may be affecting menstrual cycles. Thank you very much for being with me.

Tingen: Thank you for having me.

Barr: To begin, have vaccinations in general in the past affected the menstrual cycle?

Tingen: That's a really good question, and the truth is that we really don't know much about how vaccinations affect the menstrual cycle. It's not data that's collected in the pharma trials—so pharmaceutical companies do not collect specific data about menstrual health during the trials—and there haven't been a lot of studies. The one case that we do have some information on is the HPV vaccine. We do know from a very few small studies that they did report some changes in menstrual cycle for just a few cycles following vaccination. For the first three or so cycles after vaccination there were changes, but for flu vaccines and other vaccines, we really don't know that information.

Barr: Do you think that will become something that will be included in trials, and that will be assessed?

Tingen: That would be the hope. NIH has been putting forward a lot of effort in this area over the last decade, saying that women and those with a uterus and those who menstruate are different from the standard white male. You can't have a one size fits all in a trial and so collecting reproductive health information is actually an important indicator. NIH and NICHD have been working in that area for a long time, and we continue to make a call for that research in pharmaceutical trials. In our point of view, there's also a real research opportunity here to look at the basic mechanisms of what might be happening and how to adjust for that in pharmaceutical trials. We would love to see that collected by the companies that produce vaccines and medications themselves throughout the development pipeline.

Barr: When did women begin expressing their concern that COVID vaccines could impact their cycles, and when were actual cases being reported? Some people were concerned before they even got it.

Tingen: Right. There are different levels of concern. I will say that our entire research proposal—all the research that we are funding—is designed to show whether these changes are real changes, and whether they are really linked to the vaccine. We don't know that at this point. When did women start reporting this potential linkage? It really started making the rounds in the April or May time point. That was just because it started hitting some of the larger media outlets. People at a smaller level on their own social media and groups and forums had been linking potential changes to the vaccine earlier than that, but I would say around April or May is when it started really hitting the news cycle.

Barr: What are some characteristics of the situations that women report? Is it missed periods, irregular periods, or heavier periods?

Tingen: It's all the above and other changes. We have seen varying reports in the vaccine side effect reporting system (VAERS) as well as anecdotal individual reports. Many different types of changes have been reported, so it's not just a single change that's being reported by all women. Some people say they are experiencing shorter or longer periods. Some people report experiencing heavier flow than normal. Some people report experiencing spotting or breakthrough bleeding between cycles. Some people have reported perhaps a change in their pain—they're having more cramping than they normally have, for example. Even some people who do not usually currently menstruate—so people who are postmenopausal, are on oral contraceptives, or for other reasons don't menstruate—have been reporting potential breakthrough bleeding. These are some of the things that may be linked that people are reporting, but it really spans the gamut of potential menstrual changes.

Barr: Will you describe the studies that NICHD is funding that are looking at the links between the COVID-19 vaccines and disruptions in women's cycles, including the institutions that were awarded grants, how their studies are being conducted, and what populations are being included in these studies that NICHD is supporting?

Tingen: Sure, yes. I would love to. We, with co-funding from ORWH, awarded five administrative supplements to five different institutions, and they are doing different kinds of projects so that we can really come at these questions from several different angles. We awarded to Dr. Lauren Wise from Boston University, Dr. Laura Payne from Harvard Medical School, Dr. Mostafa Borahay from Johns Hopkins University, Dr. Staci Ann Missmer from Michigan State University, and Dr. Allison Edelman from Oregon Health and Science University. Several of these are using existing cohorts so they had already been tracking women for other reasons. For example, Dr. Wise is tracking them for a fertility study—a time to pregnancy study. She was already tracking menstrual cycles, so she could therefore just ask about COVID vaccination and tie that timing to changes in the menstrual cycle. Dr. Payne is looking

specifically at adolescents because we know that adolescents have different patterns and flow for their cycles, even normally. We think that potentially, if there is an effect for vaccination, they may have different effects than adult populations, so Dr. Payne is specifically looking at adolescents. Dr. Borahay is actually doing a two-part study in that he is going to be looking at app cycle tracking data, so for apps like Glow and Natural Cycles and things like that. They track menstrual health data from millions and millions of women, so Dr. Borahay is going to be looking into that data and also doing a new recruitment study of people who have not yet been vaccinated, so that he can follow them pre- and post-vaccination. Dr. Missmer is one that has existing cohorts. She has two cohorts that have actually been following people for decades in one of her cases. She has an immense amount of data on pain and menstrual cycles, and a lot of different variables. She'll then be tying those variables to the timing of vaccination, again to look at pre- and post-vaccination changes. Dr. Edelman is completely focused on getting this data from the cycle tracking apps, so in her study she's looking at millions of users of these apps. That's one of the ones that will be our first data we see out of this because that data is already existing in the apps, and she can pull it and clean it.

Barr: How are these studies taking into account all the different vaccines that are available and the different combinations that are now possible such as people not taking both doses or a person who took Johnson & Johnson now being able to take an mRNA vaccine as their booster?

Tingen: They were specifically looking at first vaccinations, but clearly as we are moving towards boosters, there's going to be the ability to collect that data. Each of them collects the timing, the date of vaccination, and the manufacturer so they can therefore disaggregate those who receive different patterns timing of vaccinations. They will be able to analyze based on those questions as well.

Barr: How do these studies take into account other factors that can affect periods, like stress, that have been very common in this pandemic?

Tingen: The ones that are moving forward with new recruitment, so Dr. Borahay's and Dr. Payne's, are already planning to look at perceived stress scales, sleep patterns, and even diet, so they can factor in some of those. The other studies, that have already been collecting data, take into account a lot of those; stress and pain are normal things they were already looking at. For most of those we'll be able to at least look at those characteristics. You're exactly right; there are differences in the way that we eat and sleep and our mental health during the pandemic. All these things can affect periods.

Barr: What do you hope to learn from these studies, and what do you hope its effect will be in the long-term?

Tingen: The first question we hope to be able to answer for the public is whether there is a risk of menstrual cycle changes that is tied to vaccination. Then it would be lovely to be able to answer whether that risk is different based on, for example, manufacturer, timing, or characteristics of the person receiving the vaccine. For example, do older or younger women, women with endometriosis, etc. have different risk factors for those menstrual changes and what is the term of these changes? How long do they last? What's the duration? Is it a cycle or two that are perhaps a little different, or is it several cycles? That would be incredibly useful information, and that's what the studies are designed to answer. Much like when you take a medication and it says on the bottle "may cause drowsiness", you know not to take that medication in the morning, but to take it in the evening and that helps prepare you—so when you feel drowsy, you're not concerned because you know that it's been studied. That's the kind of reassurance we want to give to women. If there are minor changes in a menstrual cycle—if you might have a longer cycle or a slightly heavier flow—we want them to know that going in, so they can take that into account and so that it's not a fear factor for them. The fear is really accumulating because of a lack of information, so we want to provide the information to make sure that women know what they're getting into.

Barr: In some cases, it's been reported that these vaccines have stopped people's periods. Can you talk a little bit about that and the length of time? That must be really disconcerting for women.

Tingen: Most of the reports that we are seeing—and most of the thoughts have been—mostly minor changes that have been in the short term, but people's bodies react differently. I would confirm again that we do not yet know if these changes are due to vaccination. Obviously, people's cycles can stop for different reasons that are not just due to vaccination. We know that COVID-19 itself changes the menstrual cycle so at least a quarter to a half of people who are hospitalized with COVID-19 experience menstrual cycle changes.

Barr: That's more than I would have thought.

Tingen: It's really common amongst people who get severe COVID-19 to experience these menstrual cycle changes. The biological rationale here is that menstruation is an inflammatory process. It involves the immune system, it involves immune cells in the uterus itself, and there is immune system overlap from the brain to the ovaries all the way to the uterus in the menstrual cycle process. If the immune system is changing a little bit in the short-term then it makes sense that perhaps menstruation is showing signs of that change.

Barr: The current grants are for a year, but I'm guessing you would love to extend it to see if there is a connection—and why there is a connection on a chemical and biological level.

Tingen: This is just the starting point. If all these five studies are showing us there is a link, then certainly there is a bigger dive into the mechanism. We do have some small studies into that. Several of the studies are taking either saliva samples, menstrual effluent—which is period blood and tissue—or peripheral blood—so a blood sample, or an endometrial biopsy—a biopsy of the lining of the uterus. They will be looking for immune cell changes and hormone changes in those tissues. That's our beginning step in looking at the mechanism, but certainly if there is a link found, then I think this is just the starting point for some of those deeper dives. We would want to learn more about them in totality, not just about COVID-19 vaccinations, but whether this is true for other vaccinations and if this is something we should think of as a kind of global change to expect when the immune system is geared up in response to vaccination.

Barr: Do you worry at all that some women will choose not to get vaccinated and put themselves at risk for a deadly disease in order to not incur issues with disruption of their menstrual cycle? It's a very hard choice for a lot of women.

Tingen: Right. Well, first, it's important to note that many women are afraid of menstrual changes due to a perceived link to fertility, but we already have good data that fertility is not affected by COVID 19 vaccination. I think the women or people who are not getting vaccinated at this point in time may already be afraid of some of these questions, so giving them information is actually helpful to answer their questions and address the fear that they're bringing into this. If you think you might have menstrual changes because of the vaccine, you're also very likely to have them if you get COVID-19 infection itself, if the mechanism is tied to immune system activation. I would say, if I was trying to prevent those menstrual changes, I would still go with the vaccine over the very high rates you have for COVID-19.

Barr: Have the people's situations been similar with the vaccines or the actual disease or have the changes been more severe with the actual disease?

Tingen: I don't know that we have that data yet to compare severity. We are still comparing the changes and the level of changes and, like I said, since it's really such a smorgasbord right now of reported changes, there's not one thing we can point to in order to compare until we finish these studies.

Barr: What has been your role in managing these studies?

Tingen: I'm actually just part of a team at NICHD. We have a wonderful team. I've been the programmatic lead for writing the NOSI—Notice of Special Interest—and for serving as the contact for that Notice of Special Interest. I would certainly shout out all the others that are on the team: Dr.

Caroline Signore, Dr. Esther Eisenberg, Dr. Guillermina Girardi, and Dr. Nahida Chakhtoura, as well as many other NICHD staff that helped us get these awards out quickly.

Barr: What have been some challenges in getting these studies up and running?

Tingen: Fortunately, the way we designed the study as administrative supplements and the way that we required them to have cohorts or pre-existing data, means that we were able to get them up and running much quicker. For the one study, who has one aim of new recruitment, that's where he's going to probably have some trouble—just because he is, at this point, looking to recruit non-vaccinated people who are going to get vaccinated. It's a hard population to reach at this point in the pandemic. That recruitment will be a challenge, and so fortunately they're doing a national recruitment across the country and it's all online, so that will help reach people all over the country. That'll probably be the biggest challenge. Otherwise, they're really off and running.

Barr: Did you get other candidates that you reviewed? I know you selected these five, but can you give an idea of how many other candidates you all looked at as possibilities to fund, and would they be people who you may fund in the future?

Tingen: We did receive more applications than we funded, which is almost always the case at NIH—that we can only fund the most meritorious or the ones that fit the need most at the moment. We do have others in the hopper that could be funded with future rounds of funding if those are approved.

Barr: In addition to being a scientist at NIH, you're also an individual who's living through this pandemic like everyone else. What have been some personal opportunities and challenges for you that COVID-19 has presented?

Tingen: I'm a scientist and also a mother of two young children, all roles that have been challenging in this pandemic. I have twin four-year-olds.

Barr: Wow. You are busy!

Tingen: Having twin four-year-olds at home during the pandemic—when we've been teleworking for close to two years—has been an opportunity and a challenge I would say. It's been nice to spend more time with my family and see them during the day when they break into the room, but that means they're breaking into the room sometimes during the day! We've learned to work together in very

different ways, but as a person who is extroverted and likes to chat, I do miss my office colleagues. I miss water cooler talk that helped us get to know each other and foster those collaborations.

Barr: Is there any moment that has stood out for you during the pandemic? Are there ways that you've coped or any particular memory?

Tingen: I would say walks outside have been a savior to me. I am trapped in my very small home office. I do have windows so that's lovely but getting outside and feeling fresh air and remembering that the world still exists outside of this office is a good thing.

Barr: Is there anything else you would like to share about either your COVID-19 work or about your experiences during the pandemic?

Tingen: Your questions have been great—I think you covered a lot of this. For NIH history, I would just say that this is just the beginning jumping off point. We will probably have future rounds of funding, specifically on this topic and then hopefully a broader interrogation of the topic in general—vaccinations and menstruation.

Barr: Have you been interested in this topic for a long time?

Tingen: Thank you for that question. In 2018 NICHD held a conference called "Menstruation: Science and Society", in which we tried to bring together people who were thinking about menstrual health and menstruation from various aspects—from people who were distributing reusable pads in Africa, to clinicians, to scientists that are looking at the very in-the-weeds nitty gritty information about the endometrium. We were trying to bring together people who speak very different languages but are all interested in menstruation. From that workshop we—Dr. Diana Bianchi, the director of NICHD, Dr. Lisa Halverson, and I—were able to publish an editorial calling for more menstrual health research and more menstruation research and calling for it to be incorporated from the clinical to the pharmaceutical trial to all these levels of interrogation. This is a great next step, and it's a great follow-up for this pathway. I would just say that we are noticing the importance of menstrual health and we are trying to say we don't know everything about menstruation. Even though people may think it's a scientific question that is solved, it really isn't at all settled science; there are so many unknown facets that will require additional research.

Barr: Do you think NICHD will fund a COVID-19 infertility study?

Tingen: There is actually already a NOSI out looking at infectious disease, and they specifically call out COVID-19 and its effect on reproductive health in general, but it's certainly a fertility angle as well. I know they are probably getting applications right now to that, and I imagine they are eager to make awards.

Barr: Definitely. Thank you so much for all that you do, and I wish you and your family continued success and health. Good luck with your four-year-olds!

Tingen: Thank you! Thank you, Gabrielle. This was a great chat.