00;00;06;22 [Jen]: From the California Prevention Training Center in San Francisco, this is Speaking Frankly, the State of Sexual Health. We know good sexual health doesn't just happen, it's created. In this series, we're starting the conversations we should already be having. We'll speak with experts in the field about sex, stigma, and all of the other factors that shape our sexual health and our everyday lives. I'm Jennifer Rogers. On January 21st, 2021, the FDA approved Cabenuva, the first, once monthly

00;00;38;03 injectable HIV treatment for adults. This is a milestone in managing the 40-year-old illness. Today, Dr. Kelly Johnson, a fellow in infectious diseases and in sexually transmitted diseases at the university of California, San Francisco explains the implication of this new treatment and how it affects the 1.2 million Americans living with HIV. Dr. Johnson is a physician focused primarily on HIV prevention, treatment and care. She currently

00;01;09;13 works at San Francisco general hospital in ward 86. Welcome, and I'm so excited to talk to you today. [Kelly]: Yeah, I'm excited to be here. Thanks for having me. [Jen]: The FDA recently announced its approval, like the first injectable HIV treatment on January 21st. So this is a really big deal. It's the first FDA approved injectable, a complete regimen for folks living

00;01;35;02 with HIV to help manage their illness. Can you explain what this means?

00;01;41;27 [Kelly]: Absolutely. And I think, you know, to really talk about the significance of the availability of injectable HIV medications, you have to go like way back to when HIV was kind of like COVID-19 and it was new and there were so many uncertainties and nobody really knew how you got it or how you pass it on or how you treat it. And then, you know, when there started being initial treatment regimens for HIV, they were really challenging. I mean, I have patients who remember taking just handfuls and

00;02;13;02 handfuls and handfuls of pills, many of which had pretty significant side effects. And these people just stuck with it for years and years and things on that front, you know, have gotten better to some extent over time. Many patients can now do quite well with HIV on one pill once a day with, well, not zero side effects, at least less side effects than there used to be with HIV treatment regimens.

00;02;39;27 But all that said, even if you're not talking about pill burden, you're still talking about having to take a medication every day of your life. And if you think about that, even just for yourself, at least I'll speak for myself, like trying to take a prenatal when I was pregnant every day or trying to be on birth control. Like those things are really hard to stick with. You have to be super committed and organized and really feel that it's a priority to take your medication. So I think some patients

00;03;11;23 really struggle with taking a pill every day and that can be just the logistical challenges or it can also be stigma for some patients. They don't feel comfortable telling their friends and family that they're living with HIV and they may not feel comfortable having a pill bottle with them or having a pill bottle that's clearly labeled like readily visible in their medicine cabinet. So I have heard of patients, you know, taking their HIV medications and transferring them into like a vitamin bottle or an

00;03;44;18 unmarked bottle or something just to make it less, less of an advertisement, I guess, about their health status and specifically their HIV status. So for all those reasons, for people who are struggling with the daily pill or for people who have some feelings of either shame or stigma or whatever, for all of those people like having an HIV medication

00;04;07;28 that could be injectable is a really exciting possibility.

00;04;12;07 [Jen]: So is there a difference in efficacy between the injectable treatment and the pills that have been approved to date to manage HIV?

00;04;24;05 [Kelly]: Yeah. So it's a really good question. And I think to get the answer, you have to kind of understand how these trials are designed. So there were two big trials or studies that led to the approval of cabin, new boat as the injectable HIV medication, they're called Atlas and Flair. If you like the names of the trials, but basically in these trials, they go for non-inferiority. So they compare to an oral medication and their goal is to demonstrate non-inferiority, it's not worse than taking an oral

00;04;56;11 medication they're not designed or powered to determine superiority. So it's not designed to say that one, an injectable is better than an oral in general. It's just not how these trials are designed. But rather to say that it's just as good as an oral that's enough to get FDA approval. And that's what happened here, but they are really efficacious. We're talking like over 90% virologic suppression on either injectable or oral HIV

00;05;24;09 medications with adherence.

00;05;26;06 [Jen]: So I know you wanted to talk a little bit about the studies in particular that led to the approval of this injectable. Can you elaborate for us on that?

00;05;36;10 [Kelly]: Well, what I wanted to point out was because of how the studies were designed. There's some caveats to how the FDA approval for injectable medications came out. So right now the approval is for patients who have virologic suppression. So they're already undetectable on their oral HIV medications that's who would be approved by the FDA to switch over to injectables. And right now the prescribing information is for an oral

00;06;07;28 lead in phase. And what I mean by that is patients would be prescribed 30 days or one month of the two medications by mouth that subsequently form the injectable regimen. The idea is to make sure that people tolerate the regimen. There's not an allergic reaction. There's not negative side effects to the point of intolerance. So that's how the FDA approval is written right now.

00;06;34;23 [Jen]: So just to be clear, this isn't apples to apples, it’s not the oral medication and what that consisted of and making an equivalent in an injectable form, these are different medications that are being put into the injectables. Is that correct? [Kelly] It's half correct. Um [Jen] okay. Tell me, tell me.

00;06;55;02 [Kelly]: Yeah, so the injectable medicine Cabenuva, it's two medications in one and their names are cabotegravir and rilpivirine. They go together, the shots will have one rilpivirine and in one cabotegravir and rilpivirine is already an available oral medication for HIV treatment. Cabotegravirwill be made available as an oral form specifically for patients who are looking to go on the injectables. But so far it's not a medication

00;07;27;28 that we're using in HIV treatment.

00;07;30;20 [Jen]: That's helpful. Thank you. I know to date folks have had the option. If they're taking an oral medication to treat HIV, they can do that by mail, if it's easier. So you can't mail a shot. So how do you see this impacting accessibility?

00;07;51;16 [Kelly]: It's a really good question right now. The FDA came out with this approval and the first step is insurance formularies have to incorporate injectable medication. So that's where we're at right now. The insurance companies are looking to put this on formularies. That process can take like up to three months or so from approval. So we don't really know yet exactly. Who's going to be permitted to give these medications. I did see a brief from the HIV medical association that they're anticipating

00;08;24;13 that the shots will be primarily available in clinics and maybe some specialty pharmacies, specialty pharmacies associated with the pharmaceutical company that makes these medications. It probably won't be available at like your Walgreens or your CVS, at least anytime soon. And your rights there won't be an option to mail somebody a shot. So, you know, this is something that would be taken into account when patients are

00;08;52;13 considering what's easiest for them and works best with their lifestyle. And like I've said before, it's probably not that every patient will want to switch over to injectables. I think it's just nice to have another option for certain patients, you know, to, to be able to switch over to injectables. And just in case, I didn't make it fully clear before. I do want to spend some time talking about which patients right now per the FDA would qualify to receive injectable meds.

00;09;20;25 [Jen]: Please tell us. [Kelly] The approval

00;09;22;28 right now is for patients who have achieved virologic suppression, meaning they have an undetectable viral load. They don't have a history of treatment failure, so they haven't failed a regimen before

00;09;35;20 [Jen]: and when you say failed, that means you've not adhered to it for a certain period of time. Right?

00;09;41;00 [Kelly]: Good question. More often failure kind of refers to like the medication didn't work because the patient had resistance or potentially adherence issues. That's certainly a concern, but yeah, people can't have been on a regimen and failed in the past and they also can't have resistance to any components of the two medications within the injectable.

00;10;02;22 [Jen]: You made mention earlier that this new injectable is really appropriate for folks who have viral suppression. So they're at undetectable levels, right? So given the number of folks in the United States today who have HIV, who are living with HIV, how many folks are at a suppress level to where it's undetectable?

00;10;27;13 [Kelly]: So there's a report from CDC in 2018, at least right now there's 1.2 million people in the US who are living with HIV. And about 14% of them or one in every seven patients with HIV doesn't know that they have HIV infection. So that's one barrier. People may not know that they're infected, but then of the people who are living with HIV, at least in 2018, 76% have received some HIV care. So that's a significant majority and 65%

00;11;00;16 were virally suppressed, which is the same thing as being undetectable. I wouldn't say that all 65% of those 1.2 million people would qualify for injectable medications, because there are those other caveats of like not having any known or suspected resistance and not having failed a prior treatment regimens. Like what I mean by failed is, is developing a detectable virus while they're on treatment. So the percentage of people

00;11;27;19 who would be eligible for injectable medications by the current FDA prescribing standards is this smaller than the total pool. But that's an overview of, of at least who has been able to achieve virologic suppression in our country. It's 65% of people with HIV.

00;11;43;03 [Jen]: So not of the people who know they have HIV.

00;11;47;18 [Kelly]: So we combined those two numbers for this 2018 CDC report. It's people with HIV, both diagnosed and undiagnosed.

00;11;56;12 [Jen]: Interesting. Okay. Thank you for clearing that up. When your patients heard about this injectable, what's the response that you've been hearing?

00;12;05;16 [Kelly]: I would say like everything new, it's really mixed. Some patients that I have, are already asking me, like, when is this available? Am I eligible? Could I be in a clinical trial of this? Some people are really excited about this possibility. And again, this is probably people who are really finding it challenging to take a pill every day, or just, don't like the idea of having to take a pill every day and want that freedom that comes with injections. Then other people are more like, you know, I'm fine. I've been doing this for a long time. I don't really mind

00;12;38;22 taking my pill every day. And it would be more convenient for me to keep doing what I'm doing. As you know, right now, the prescribing information is for injectables to be given every month. And there's like a seven day wiggle room on either side the injection, but still that means the way that it's prescribed right now. People have to have really good followup and be coming into the clinic at a specific date on a really regular basis. And

00;13;09;05 that may be something, again, that's more a personal preference for some patients that may be great, no problem. And for others, that may be also kind of a challenge.

00;13;18;01 And I would say there are basically two groups of people who might want and or benefit from injectable medications. Some are patients who are really adherent to their HIV medications, who would qualify by the FDA prescribing information to go on injectable medication. And that would be great. It's convenient for them. They don't mind coming into clinic likely to work in terms of virologic, suppression, et cetera. But there's this other group of people who are really struggling to take their medications. And that may be because of stigma or because of unstable housing or because of substance

00;13;54;21 use disorder or whatever their particular challenges are. And this is where the current approval is a little bit tricky because right now you have to have this oral lead in phase. You have to try the oral components of the injectables first, before you can switch over to the injectables. And technically you're supposed to already be virologically suppressed before you switch over. And this may be really a challenge for some people who are already really

00;14;20;23 struggling to take oral medications. They may not have achieved that virologic suppression, and they may not want or be able to be on pills for 30 days before they go to injectables. So I think there is some controversy and some challenge there in terms of how individual clinics will roll this out and whether they might stick with the FDA prescribing information, which of course is how the medication is prescribed right now, approved to be prescribed, or if they'll go off label and kind of change it up, and say,

00;14;51;13 okay, you tolerated these pills for a week and maybe you're not virologically suppressed, but we'll still feel comfortable giving this to you. I don't know the answer to that. I think a lot of clinics will be grappling with those questions.

00;15;05;09 [Jen]: You said 1.2 million people in the United States are currently living with HIV. One in seven don't know that they're positive. Can you give us an overview of who's living with this illness and what are some barriers to treatment that folks are facing? Because I know, I mean, Black and Brown communities have been hit really, really hard and even geographically specific, I know the Southern States in particular have seen

00;15;41;01 much higher rates of HIV than other parts of the country. And I'd love to hear from you on that.

00;15;46;08 [Kelly]: Yeah. I think you really hit the nail on the head, especially black and Latinx persons of color have higher rates of HIV compared with the rest of the population. And you're totally right about the geographic component where the South and Southeast has been disproportionately affected by the HIV epidemic.

00;16;04;27 [Jen]: Can you speak to what's driving that either anecdotally or, or otherwise?

00;16;10;21 [Kelly]: I think this would be all anecdotal. Some of it is pre-exposure prophylaxis or PrEP for HIV has not had the same uptake in the South, as it has say in other regions of the country, like the West and the Northeast. So that's definitely one thing that's driving it. There's insurance and economic and financial factors that play into why PrEP isn't widely available to patients in the South. I think as a person from the South originally that there's also some cultural differences that make it

00;16;41;25 perhaps even more challenging for people to feel comfortable talking about their sex lives, talking about wanting to protect themselves from HIV acquisition sharing with their partners, sharing with their clinicians, what types of sex they're having and what types of partners are having. I think there's, well, everybody, you know, stigma is real for everybody universally. I think the South has even more cultural barriers to talking

00;17;07;04 about sex and its sequala compared with other parts of the country.

00;17;11;24 [Jen]: And that's hard because it's not simply behavior change. You're really looking at how do you disentangle and kind of undo very deeply ingrained social norms and beliefs that have taken centuries to build. Right?

00;17;30;04 [Kelly]: Yeah. I have no idea what the answer is to that, but I would just say there's just such a difference. I think so I live in San Francisco right now, which is definitely on one end of the spectrum where yeah, I mean, which is great, but I feel that many folks are actually fairly comfortable discussing their sex lives and seeking sexual health services and feeling at least maybe less shame around sexual practices. Whereas I wouldn't say that's the same in the South where I think there's just some really deeply ingrained ideas about what's proper and appropriate

00;18;01;00 and what's not, and it's really hard to figure out a way around that. One, one example that comes to mind is actually about, you know, you asked me at the top of this program, like what are my pronouns? And I've gotten used to hearing that question like, Oh, they’re she, her hers, those are my pronouns and people are gonna ask me about them. But if I mentioned that to friends and family back back, I'm from Southeast Virginia and I love Virginia. I do not wish anything ill in saying this, but I would just imagine that folks are not as, they would be suppressed.

00;18;31;03 They're not as, as open or used to hearing people talk about gender and talk about sex and have it be a, just like an opening to a conversation that would be really foreign to people where I'm originally from. On the topic of gender, which I realize is slightly off topic for this. And you can decide if you want to cut it out, but [Jen] no, I love it. Go for it. [Kelly] But we've been talking a lot at some of the lectures I've been in recently about how you should address your patients, you know, because you might walk into a room and see a patient and they appear to you to be male or to be female.

00;19;04;09 And it's very ingrained, at least in me as a person raised in the South to be like Mr. John Smith or Mrs. Jane Smith, like, hello, how are you? I'm Dr. So-and-so. What I'm learning is that I should really focus on trying to reprogram that because we haven't talked about how they identify in terms of their gender. I don't know if they want to be addressed as Mr. as to use he/him pronouns or feminine or non-binary, you know, like we just haven't had the conversation yet. So that's been

00;19;37;08 something I've been thinking about a lot in terms of how to, how to reprogram my own thinking.

00;19;44;27 [Jen] Thanks for sharing that. I want to talk a little bit about U equals U can you tell us about what it means if somebody's virally suppressed? So they have HIV, they have an undetectable viral load. What does that mean in terms of the potential for passing it to another sexual partner? For instance.

00;20;03;29 [Kelly]: It's a really great question. It's really important to talk about it because it's such a significant and important change in thinking that's occurred over the last, I don't know, five, 10 years maybe, but there've been some really significant studies published in big journals. The really, really good data that if you are a person living with HIV, but you have an undetectable viral load, you cannot transmit the virus to a sexual partner. Even if you're not using condoms, even if you're not being super cautious in what kind of sexual acts you're participating in.

00;20;35;03 It doesn't matter. The virus cannot transmit. What do I mean by undetectable? I mean then if we take a milliliter of your blood, we cannot find the HIV virus. And we know that our medications that we have today are strong enough, powerful enough. If we can partner with our patients to achieve that adherence, if it is an oral pill or the monthly clinic visits, if it is an injectable medication, like we can get to undetectable.

00;21;02;19 And that means untransmissable. I have found for some of my patients that can really be a motivating factor. Even when, you know, for themselves taking a daily pill, it's such a hassle and maybe they don't really have any symptoms of HIV. So they may not feel like it's important for me and my health that I must take this pill every day. They just don't feel that. But if you start introducing well, you could also, you know, your sexual partners could also be protected from HIV. And that means that

00;21;33;23 you can free up the sexual activities that you can allow yourself to participate in. That can be something that people are really motivated by. So I think it's another tool in the toolbox when talking about reasons to be on HIV treatment, if you are a person living with HIV.

00;21;51;02 [Jen]: So I want to shift a little bit and make a comparison to COVID-19. I mean, as you well know, we've, fast-tracked several vaccines worldwide to treat COVID, which we didn't even know existed 13 or 14 months ago. We've been grappling with HIV since 1980, 81. Why has it taken 40 some odd years to have an injectable?

00;22;18;19 [Kelly] There's a lot of reasons why the HIV virus is different and why developing a vaccine for HIV is so much more challenging. One is that HIV has a lot of genetic diversities. There's a lot of different strains of HIV and it replicates really, really fast. So it finds ways to evade our immune system really quickly. It also is sort of smart from a virus standpoint and that it can establish these reservoirs of

00;22;49;17 latent infection. It can hide in the body really soon after infection. And it's really hard for us from a science and medicine perspective to find, and to eradicate or get rid of those latent collections of HIV infection. And then the final piece, or at least a final piece is that we don't have a way that people become naturally immune to HIV. Most vaccines sort of rely

00;23;19;05 on figuring out how the body responds to a particular infection, how the body generates antibodies that neutralize or get rid of an infection.

00;23;29;05 Like that's what happens with COVID. Our body can form antibodies against COVID naturally. That is something that has really evaded us with HIV because the body doesn't form, for the most part, our body doesn't fight off HIV infection, or at least we don't know how that happens, so there's not like a similar known concept of how the immune system could fight off HIV and what we could leverage for a vaccine for HIV. That research is definitely underway. It's not my personal area of focus, but it

00;24;00;16 does exist and people are trying, but I would just point to all those sort of complications with HIV that make it a different virus than COVID-19 and harder to come up with a vaccine.

00;24;13;12 [Jen]: Why has having an injectable form of treatment for HIV taken, you know, certainly decades after oral pills were available for antiretroviral treatment?

00;24;27;21 [Kelly]: It's a really good question. I think I don't fully know the answer of like why the timeline has been, what it's been, but if you go back in time and think about, well, first it was like so many pills and they were all together. And then over time we've been able to simplify and simplify. And for many patients, we're now at one pill once a day, and we're realizing that that may still not be the right answer for every patient all the time. So now there has been sort of renewed or new interest in other formulations of how to deliver HIV medications. So I would sort of

00;25;01;07 postulate that the process has been well first we had to come up with regimens that are relatively simple and relatively easy to tolerate. And then we would start thinking about other forms to deliver HIV medications.

00;25;15;08 [Jen]: How are we going to publicize this to make sure that folks know that this injectable treatment is available? I look at like when PrEP first came out, pre-exposure prophylaxis, you know, in San Francisco, it was all over the buses in certain areas and all over billboards. What is the plan for publicizing this new injectable?

00;25;38;01 [Kelly]: I think a lot of that being on buses, that's really the pharmaceutical companies that drive that. So that wouldn't be a piece that an individual provider and individual clinic is really putting out there. But I do know some clinics are already considering enrolling patients in real world trials of how these things work. So there may be patients who are asking about injectable medications, who even now, if your clinic is a site, you could think about being in a trial and then more broadly, I imagine some patients will hear about it on the news or from other

00;26;11;08 patients, or maybe people [Jen] on our podcast, [Kelly] they'll probably bring it to their providers or the reverse may happen where providers might be in clinic with a patient and be like, Hey, we have this new option available. Is this something you're interested in? We're like you pointed out, we're not really there yet. The medication's not physically in clinics yet. So we can't offer it to people outside of trials yet, but it is coming. But I think there will be a

00;26;40;00 variety of patients bringing it up of providers, bringing it, and then working with patients to figure out who's the right candidate. How will the clinics roll it out? Will we stick with the FDA prescribing information or potentially use it as a trial in patients where we're really struggling with adherence? Those questions haven't been answered yet, but certainly important things to think about as we move into the era of injectable HIV medications,

00;27;07;15 [Jen]: What is the earliest that it could start get into people's arms?

00;27;13;05 [Kelly]: I think, three months for the insurance formulary would put it at, let's see January, February, March, and April, and then I'd give it another, at least say month or two. Optimistically, I'd say by late spring or summer, but that's really just my personal theory, not something I have a specific line into.

00;27;32;27 [Jen]: So to end, I would love to ask you what more do we need to be talking about collectively when it comes to HIV treatment?

00;27;43;05 [Kelly]: Well, I actually think there is another really important thing to talk about with injectable medication, but it's more about how to prevent acquisition of HIV rather than how to care for folks already living with HIV. And that is that one of these injectable medications, Cabotegravir has been studied for pre-exposure prophylaxis. Nnot approved yet, not available in this country. However, there've been two recent trials called HPTN, 083 and HPTN 084, which have

00;28;17;01 demonstrated that these are effective medications. And in fact for HPTN 083, that trial was stopped early by the data safety monitoring board. And it was in women because it actually appeared that injectable PrEP was more effective than oral Truvada, which is a common medication that's being used for PrEP.

00;28;41;22 [Jen] Really. So what are next steps with that in, I mean, what would a timeline look like in terms of potentially getting an injectable medication for PrEP and just to be clear pre-exposure prophylaxis that can help someone prevent contracting HIV if they were to be exposed to it?

00;29;01;06 [Kelly]: Yea that's correct. Right now, these medications haven't been approved. So I imagine it will be on the order of months to maybe a year, but I don't think it's that far off based on the data that's available, but this will be an option for people for pre-exposure prophylaxis.

00;29;18;26 [Jen]: That's incredibly exciting. And what about for pep for post-exposure prophylaxis?

00;29;25;16 [Kelly]: I'm not aware of any data or plans for injectable post-exposure prophylaxis. Again, I think it's along the lines of just the benefits of increasing options. You know, some people don't mind taking a pill, every some for PrEP, you know, some people might like the event driven or sex driven PrEP where you just take pills around the time that you're having sex. And for other people, perhaps an injectable medication is a sort of set it and forget it strategy. That might be a really good

00;29;55;17 option. One sort of caveat about injectable PrEP. So that should be mentioned in any conversation about it is that the injectable Cabotegravir has a really long tail. And what I mean by that is that it's detectable in the plasma or the blood for up to a year after a person stops taking it. So there is some concern that if a patient was getting their injectable PrEP and then they stopped and they didn't go on Truvada or any other PrEP

00;30;27;26 medication, but they kept having sexual exposures that not only could they acquire HIV, but that they could acquire HIV that had resistance mutations because they would still have some level of an HIV medication in their blood at the time they acquired HIV.

00;30;45;21 [Jen]: So if there's a tail of prep, injectable, for instance, if I were to take it and then I stopped taking it after a few months, it's still going to exist in my system for up to a year. Is that correct?

00;30;58;15 [Kelly]: That's correct. But at decreasing and decreasing, decreasing, totally. So not at a therapeutic level or a level needed to really prevent HIV, but just trace amounts that if you acquired HIV by sex or, or whatever else you, you got HIV, while you still had a trace amount of this HIV medicine in your body, there's at least a theoretical risk that that would promote the development of resistance because the virus would see just a little bit of a, of an antiviral medication and could respond to

00;31;30;07 that by generating resistance mutations.

00;31;32;27 [Jen]: That's what I wanted to understand. That was really helpful. Is there anything else you'd like to share about your work or about this recently approved injectable treatment?

00;31;43;12 [Kelly]: Say, just to understand, you know, that there are trials ongoing about whether it will be possible to space out injections from every month to every other month and whether it might be possible to go direct, to inject, like not necessarily do the 30 day or a lead in there is work underway in those areas. And so I think we may see some changes or additions to the FDA approval as it's currently written. Cause right now it feels like it's great, but it's exclusive of a lot of people who might

00;32;15;20 benefit from injectable medications. So I would just be on the lookout for potential changes down the line.

00;32;23;27 [Jen]: Well, thank you so, so much for taking time. It was lovely to talk with you today.

00;32;28;17 [Kelly]: Of course, it was really great to be here.

00;32;32;03 [Jen]: Thank you to our guest, Dr. Kelly Johnson, a fellow in infectious diseases and in sexually transmitted diseases at the University of California, San Francisco.

00;32;40;02 Speaking Frankly, is a production of the California Prevention Training Center in San Francisco, California. It's produced by me, Jennifer Rogers and Laura Marie Lazar. And it's edited by Nils Myers at 152 West Productions. Mm.