Transcript: PrEP - Preparing for Success?

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At the XVII International AIDS Conference in Mexico City, David Evans talks with Ian McGowan, MD, PhD, from the University of Pittsburgh in Pennsylvania, about the promise of pre-exposure prophylaxis to prevent HIV transmission and how we should prepare for the possibility that current PrEP trials will prove it to be successful. Click here for the video.

David Evans: Welcome. With me today is Dr. Ian McGowan, professor of medicine at the University of Pittsburg Medical Center. Welcome Dr. McGowan

Ian McGowan: Hi

DE: In terms of prevention tools, one of the most hopeful tools on the horizon is Pre-Exposure Prophylaxis (PrEP. I'm wondering if you could just tell our viewers about the science that makes it so hopeful or exciting that's occurred in the last several years.

IM: I think the whole basis of PrEP as you know, is to give individuals who are HIV negative antiretroviral drugs. Either a single dose such as Viread or a combination drug such as Truvada, they are the two drugs which are being evaluated at the moment. And the hope is that by these individuals taking these drugs on a regular basis they will obviously have a certain level of the drug distributed throughout their body so should a situation arise where potentially they have contact with a HIV infected individual and the possibility of transmission occurs, its hoped that the virus will be unable to replicate in that environment. The hope of PrEP is really based partly on the observations, mother to child transmission studies, where we've shown that if you decrease viral load very significantly, you prevent transmission. There were also, as you may be aware, some animal models, both looking at vaginal challenge and rectal challenge in the face of PrEP regimens, showing variable, but generally good levels of protection. So I think those put together give us a lot of hope that this intervention may actually work.

DE: In terms of the trials that are currently ongoing, when would be the soonest that we might learn something?

IM: I think the expectation is that the first trial to report out would probably be the Thai study, actually looking at the role of PrEP in intravenous drug users. And the hope is that we'll have some news in 2009. So you know, perhaps in a year's time or a little less. These studies are notoriously

hard to predict because you start the study, and perhaps the expected levels of new infection are much lower than you anticipated or recruitment into the study takes longer, and so it can effect when you actually reach the mile stones that you need to to declare whether or not the study is working.

DE: In terms of refinement of PrEP, something that has been discussed at least is, perhaps we may be able to use the drugs intermittently, as opposed to continuously. But there were data presented just in the last several days I think, in monkeys that suggest that that might not work quite as well.

IM: Well you know this all comes down to what we call pharmacokinetics It's really how the drugs are distributed in the body's compartments, what the half-life is with it in different compartments. Whenever we take antibiotics you have to take them on a certain regiment for it to work and that's because the level of drug in your body falls below the level of the drug needed, and it's the same with PrEP. I think its critical that we have a sort of proof of efficacy that if you take it once a day where we know you are going to have the optimal pharmacokinetics, and it works, great, then you could probably back off. But I think it would be a little pre-mature to start rolling out intermittent dosing type regiments before we know actually how the once daily generic approach works.

DE: A lot of the discussion at the conference so far around PrEP has been the notion that it's not too early to start Preparing. Can you tell me a little bit about what that Preparation might look like?

IM: I think whenever you have a public health intervention that needs to be rolled out, generally speaking it's a complex and expensive and logistically challenging exercise. If you think of things like polio vaccination, mother to child transmission is an excellent example, and so it just takes a long time. In this situation you have to imagine who the target group is going to be. I mean in theory it could be anyone who has significant risk of acquisition of HIV, and if we were in Sub-Saharan Africa that would be most of the adult population. Within North America, Latin America you might be able to be more specific. There is a logistical issue there of scale up, of having the right amount of drugs in the right place at the right time. More important and above and beyond that is funding. You know, who is going to fund this? And you know, this is a question which is under debate. There were various likely suspects, but I think all of those agencies will be watching very closely to see what the effectiveness of this intervention is. And as you probably know, we're all hoping we might if not 100 percent we'd be hoping 60, 70, 80 percent. I think if these studies report 20, 30, 40, there's going to be questions at an operational level of is that an appropriate level of protection to roll out. So first this is lets see how strong the evidence is that this invention works, then I think agencies such as UNA, WHO, World Bank, IMF, all of these kind of funding organizations, will be and in fact are looking at scenario casting. And then rolling it out.

DE: One of the things as a treatment educator and treatment activist in 1996-97 when combination treatment really came to the fore, we spent a lot of time doing adherence support and training in people living with HIV and I'm wondering are we going to need to do the same thing for HIV negative people possibly?

IM: I think that's true. I think there's a lot of questions that haven't really been answered or

perhaps even asked at the moment. Everyone thinks PrEP is a good idea, but actually there is this sort of psychological/cultural milieu surrounding it. You're going to take very healthy people and in the case of Truvada, ask them to take duel therapy potentially for the rest of their sexual life. That is a huge change in people's lives. I think people are thinking "Oh it's just like taking the pill," but it's not really like taking the pill. And I think it was instructive, to me at least, that in the CDC study of PrEP in MSM, the safety study, they had a lot of trouble enrolling MSMs into, there's only a 400 participants/patient study, and they had to add another site. Well that said to me something very interesting about willingness to actually take up the technology. So I think that we shouldn't just assume that is going to be a home run, here it is, have everyone use it. So yea, I think you're right, there are issues around adherence, there are issues around testing associated, I mean you can't really give this kind of intervention to people who are HIV positive. That wouldn't work. So there are going to be issues around that.

DE: So last question, so much of the epidemic around the world is in young people, in teens, in early teens even, Viread is not recommended currently for people under 18 because of bone problems. Are there any other possible PrEP treatments waiting in the wings once we know that Truvada or Viread works?

IM: I think if we show proof of principle that antiretroviral given in the right does can help prevent transmission then clearly there are other options out there. Interestingly, Viread was a very good choice. It had a very long half-life. It generally was extremely well tolerated. It had, if you like, a high genetic barrier to resistance, if resistance occurs the cases of mutation, it's not the worse by any stretch of the imagination. So other drugs, people have talked about 3TC, lamivudine. Clearly the genetic barrier there is somewhat lower. I think we'll see. I think another topic we haven't really discussed, and maybe we won't have time today is, PrEP is clearly a critical prevention technology.

The question still remains of whether should you give it orally or topically. And one of my jobs as a co-principal investigator of the microbicides trial network we are going to launch the V.O.I.C.E. study which is Vaginal and Oral Interventions Control the Epidemic. And we'll be asking the questions about the differential safety and the effectiveness of those two roots. Because given orally, you're given a lot of drug, which then distributes hopefully to the right level. But given topically, you're giving a huge amount of drug, but in a very local fashion. And there may be differential patterns of safety, of acceptability, I think the jury is still out. So in part of that study we are doing some very detailed pharmacokinetics, and multi-compartment pharmacokinetics studies. So we are giving people oral or topical drug and then looking at blood, genital biopsies, how it secretes, everything to track how drugs are distributing when given in both modalities.

DE: Well I look forward to hearing the results of those studies in coming years. Are there any closing remarks or thoughts about PrEP?

IM: No. I think we're all hopeful, clinical trials can deliver unexpected results and we just have to uhh, the rationale is that we just have to do the studies the best we can and wait for the results to unfold.