

**South African AIDS Conference
Plenary 1: “HIV Prevention”
Dr. Rod Hoff
August 4, 2003**

¹ kaisernetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We apologize for any inaccuracies.

South African AIDS Conference
Plenary 1: "HIV Prevention," Dr. Rod Hoff
August 4, 2003

2

SPEAKER: I think really putting into the context the reason that this conference is taking place and challenging us, and certainly challenging our next speaker to show us the way out of perhaps some of the (unintelligible) of prevention. Let's hope he (unintelligible). We're running slightly to Durbin beach time, but I hope that this room is going to agree with me that perhaps the official (unintelligible) perhaps just a little in place, because I don't want to lose this very important plenary. Let me introduce to you Rod Hoff. Rod is Senior Epidemiologist and Chief of the International Resource Branch at the Division of AIDS at the National Institute of Allergy and Infectious Diseases at NIH based in Bethesda. He has worked on HIV/AIDS for the past eighteen years. He's very well known to many South Africans who have worked closely with him in some of the international initiatives in which he's played a central role. He was very much part of the formation of both the HPTN and the HVTN network, the prevention trials and vaccine trials networks, and most recently he has formed the Comprehensive International Program of Research on AIDS, CIPRA, and there are as many people in Africa, a very large crowds to two collaborative groups working in that program. He came here by way of China where he's been working on the SARS academic, but assures me that he's not contagious. Thank you Rod.

DR. ROD HOFF: Thank you James. Thanks for that introduction, and I want to thank the organizers for inviting me to present at this important meeting. We have a lot of important work to

¹ kaisernetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We apologize for any inaccuracies.

do as shown by Quarisha's presentation that proceeding me. It's not possible in twenty minutes to cover all of prevention as Quarisha mentioned. There are a number of symposia about prevention that will be following this morning's session and also tomorrow morning. I'd like to begin my session with a quick look at the new paradigm that emerged from the international meeting here three years ago, the comprehensive prevention, care and treatment approach. I'll then go into some specific prevention interventions for HIV, spending more time on the mother to child transmission, HIV vaccines and microbicides. I'll then tell you a little bit about the international trial networks that are supported by the US and IH. I'll go into a little bit of a detail about the CIPRA, and then talk about some of the new comprehensive prevention care and treatment initiatives.

It's important to look back to the meeting three years ago and the tension in the discussions that occurred at the meeting on scaling up for HIV prevention programs together with something that had to be done about the growing problem of caring and treating for people with HIV/AIDS. The sessions became very heated during the meeting. The prevention people making the point that the limited resources that were available for HIV/AIDS prevention presented the most cost effective approach. Those who talked regarding the need for care and treatment for the growing number of individuals experiencing AIDS, pointed out that prevention can not be successful without the provision of care and treatment for those affected for the disease. Importantly, the meeting ended with an important speech by President

¹ kaisernetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We apologize for any inaccuracies.

South African AIDS Conference
Plenary 1: "HIV Prevention," Dr. Rod Hoff
August 4, 2003

4

Mandela, who pointed out that we can do both prevention and treatment because it is the right thing to do.

So, this leads to the new paradigm of linking prevention, care and treatment, overlapping in some cases and supporting this through an important research that informs all three of the important activities in controlling the epidemic.

It's important to look in terms of prevention what the people the population involved that are at the highest risk of HIV infection. Most importantly, more than 95% are in developing country. Of the 14,000 new infections per day, about 12,000 are in persons age 15-49 years of age, of whom almost 50% are women and about 50% are about 15-24 year olds. The last is most important because preventions need to start in the adolescence before people reach adulthood. Two thousand of the 14,000 new cases per day are in children, and most of those are infected through peri-natal transmission.

This is a list of the different kinds of preventions that are currently available or in development. Public health education is perhaps the most important. It has some very simple premises. There should be a general awareness of HIV/AIDS, how you become infected with the virus, and most importantly how do you protect yourself against infection, but very discouragingly awareness is still not generally understood. Even with the epidemic in South Africa, there are people who still don't understand the basic principles of how to protect themselves against HIV infection. In China where the epidemic is beginning to take off with a fear of an epidemic that we've just

¹ kaisernetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We apologize for any inaccuracies.

heard about in South Africa taking place, less than 20% of the population have a general appreciation of HIV, how you become infected with HIV infection, and most importantly almost no information on how to protect themselves from infection.

The next more intensive intervention or prevention for HIV is voluntary counseling and testing. The premise of this program that if people will come forward to be tested if they suspect that they had been exposed, the knowledge that they gain from counseling and whether they're learning their HIV sero status, can help them arrange their lives either if they are infected to take precautions not to pass the infection on to other individuals, and if they are negative to change their risk behaviors so that they do not become exposed to HIV infection in the future. Voluntary counseling and testing is the important concept of stigma. Knowledge of HIV status carries an important burden in society, and many people do not come forward to be tested knowing that stigma can change their lives dramatically. The other problem with voluntary counseling and testing that if you test positive until recently, the availability of treatment for your infection also inhibited people from coming forward. In essence, what was the point of being tested if there was nothing for them in terms of treating their infection? There are a number of behavioral interventions that are more intensive than voluntary counseling and testing that are being applied to high risk groups around the world, and various symposiums at this session will be looking at the status of these more intensive intervention.

¹ kaisernetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We apologize for any inaccuracies.

The most important biomedical intervention that we have are the male condom. This is universally available, but not universally used. Topical microbicides, that is substances that kill the HIV virus that can be used by women to protect themselves against HIV infection is an important, would be an important intervention to add to the armamentarium of preventions. These are in various stages of testing and I'll describe this in more detail later.

It has been known for sometime that those people who are infected by STDs are both more able to transmit the infection and are more susceptible to infection, and treating of the STDs theoretically then can lower the rates of HIV infection.

I won't be covering intravenous drug transmission, but clean needles, drug abuse treatment, can certainly lower transmission in these cases.

Mother to child transmission has been the most affective in terms of developing new biomedical interventions, and I will explain later that in this area alone even in South Africa, transmissions could be reduced to very lower levels, perhaps lower then two to three percent.

The great hope for interventions are HIV vaccines. These are in various stages of development, but at this time we do not have an effective HIV vaccine.

Specifically into mother to child transmission, the virus can be passed on from mother to child during the intrauterine phase of gestation, during the birth process, and through breast milk. In

¹ kaisernetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We apologize for any inaccuracies.

the United States - we're having a pointer problem here - without any intervention, about 25% of the offspring of HIV positive women become infected with the virus. In the United States, this was about 25% without breast feeding. When the 0-7-6 regimen with AZT given to the mother for several weeks and to the baby for another six weeks, transmission was reduced down to four to eight percent, and then with the advent of heart therapy, a three drug combination, the incidents of infection in HIV positive mothers has dropped to one to two percent and many centers in the United States have, although many HIV positive women are giving birth, less than one percent are born infected. In the United States, it is 1,200 peri-natal infections are prevented alone annually in the United States. Now, in developing countries there are more than 2,000 infected offspring born of sero-positive mothers per day. And, the approach in developing countries where you not only have the intrauterine and peri-natal transmission phase leading to 20-25% of infection because of the need for breastfeeding for nutritional purposes and for prevention of disease, nevertheless another 5-15% become infected with HIV during the breastfeeding phase. To prevent infection under developing country conditions, several courses of antiretroviral therapy have been devised to greatly reduce at least by half the rate of peri-natal transmission. These regimens include AZT, Nevirapine and combinations of AZT with 3TC.

The most important development over the past few weeks is that postnatally if you prophylax the infant postnatally during

¹ kaisernetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We apologize for any inaccuracies.

breastfeeding, you can prevent the majority of breastfeeding transmission, and this was reported a few weeks ago at the Paris pathogenesis (misspelled?) meeting and it described a clinical trial done in Uganda and then Rwanda where the mothers in the study received perinatally AZT and dDI, the infant for one week after infection, and then postnatally during the breast feeding period, one group was given the Nevirapine and another group given 3TC. The important finding from the study is although there was some uterine infection leading to a six percent transmission, the prophylaxis with Nevirapine or 3TC greatly reduced the rate of breast milk transmission. This was done together with exclusive breast feeding, with no other food supplement than breast milk, but it showed that the important breast milk transmission could be done by relatively simple prophylaxis of the infant for six months.

Now, moving to HIV vaccine development, there will be a symposium tomorrow at this conference on the status of HIV vaccine development, and here I just point out a few of the most recent development. A phase three trial of the VaxGen GP120 product was tested in an efficacy trial in the United States, and the results were announced in January. Disappointingly, the vaccine failed to protect individuals in this case, mostly gay men in the trial against HIV infection. Another trial with the VaxGen product is ongoing in Thailand in intravenous drug users. So, with this disappointing results, there's new interest in new concepts that induce cell needed immunity that are concepts that are now moving into phase three

¹ kaisernetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We apologize for any inaccuracies.

trials, namely one in Thailand where the AV pox (misspelled?) combination with GP120 are going to be used in a phase three trials.

There's also growing interest with an expanding number of new vaccine constructs that are in the pipeline and I'll show you a few of those in a bit, but the important change in paradigm in vaccine development are the realization that vaccines might not protect against infection but may protect against disease. Infection may be at low levels at which the progression of HIV/AIDS does not take place.

This is a summary then of the various HIV vaccines in various phases of testing and evaluation. The VaxGen trial which I mentioned earlier was negative, the ongoing trial in Thailand, and the AV Pox GP120 trial that will get underway in Thailand this fall. A number of products are now in phase one testing, some of them here in South Africa, and there are 17 products that are now entering into pre-phase one or phase one studies around the world. The new development is that international sites are now participating in these trials based on the realization that efficacy trials of almost all HIV vaccines will have to be done in the international setting.

Moving on to the topic of microbicides, again, disappointments presented here at the meeting three years ago. Monoxodil (misspelled?) phase three trial showed no efficacy, and importantly showed some safety concerns that the use of the product actually may have enhanced HIV infection. Over the past three years there has been a renewed global effort to develop protection that

¹ kaisernetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We apologize for any inaccuracies.

women can use and know that microbicides are the leading candidates to do this. There will be a session on microbicides right after this session.

The increased enthusiasm that this will be possible is an improved line of products that work on a number of different of mechanisms, and in order to test these just like vaccines there has been an expansion of the international clinical trial capacity to test these microbicides products. Two products, buffer gel and PRO-2000 (misspelled?) will be tested in an international trial by the HPTM under the leadership of Slim (misspelled?) Karim who is the chair of the protocol and South Africa will be participating in this trial. Four other products - Cellulose Acetate, C31G, Dextrin Sulfate and Caraguard will be started in efficacy trials sometime next year.

There's also increasing interest in the use of anti-repral (misspelled?) -viral drugs for prevention. There have been studies in the United States, in Europe using post-exposure prophylaxis for high risk, occupational and more recently on non-occupational exposures to HIV. There's also a - two trials being designed using pre-exposure prophylaxis of high risk groups. This is using the drug Chanoprevere (misspelled?) in studies that will be starting soon in Cameroon and Cambodia. There has also been an attempt to use heart therapy to reduce sexual transmission among discordant couples. In this case, the infected person treated with heart, with the goal of reducing viral load and thereby reducing the risk of transmission from the

¹ kaisernetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We apologize for any inaccuracies.

infected partner to the uninfected partner. HPTN 052 which will take place in many sites in Africa will test this concept.

The international clinical trial mechanisms that will be testing these mechanisms will be supported through the US NIH as described here, as well as other clinical support structures supported by the NARS in France, and the MRC in the UK. For the US NIH, both the prevention and trial vaccine networks are depicted in this slide. South Africa has sites participating in both of these networks. The movement to the international trials sites again is a realization that many of the prevention interventions can only be tested that in the setting of developing countries where the incidence of HIV is greater than much of the industrialized world. With it goes along an important ethical considerations in doing trials in these countries, issues of the healthcare infrastructure that must be on the ground before such trials can be conducted, and in most cases the provision of anti-retro viral drugs for those who become infected in these trials.

I'd like to now move into the movement of the NIH to make available opportunities for international research investigators to develop their own research agenda to address the HIV epidemic in their setting. The goals of this program called the Comprehensive International Program of Research on AIDS or CIPRA is to develop long-term support for developing countries to plan and implement a comprehensive HIV prevention and treatment research agenda relevant to their populations, and to do this enhance their infrastructure

¹ kaisernetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We apologize for any inaccuracies.

necessary to conduct such research. The map here shows the number of new sites that are now participating in this program. The red dots indicate a small planning grant of 50,000 dollars per year to enable a country to pull together a research team to propose a research program in the future. The purple dots, which we have one in Senegal, is a grant program that provides research funding for one focused research grant plus resources for further developing the infrastructure that is necessary to conduct the research, and finally, the U19 grant is a comprehensive, multi-project grant that enables most countries to take on a sophisticated multi-disciplinary comprehensive research program to address their research needs. There are three of these currently funded - one in China and two in South Africa, and Dr. MacIntyre is one of the PIs in Johannesburg, and Dr. Salim Karim in Durbin. We will continue to expand opportunities with this epidemic for those of you who are interested in applying for this program. There will be a workshop in hall 2C from 18:00 to 20:00. There will be people there that can explain the grant writing process and the overall structure of the program. There will be another session tomorrow morning, again describing the program and the mechanisms for applying for NIH grants.

Finally, with the paradigm of moving to a comprehensive prevention care and treatment paradigm, there are important global fund projects that have been funded around the world, and the US emergency initiative - the fourteen countries, ten in Africa, and two in the Caribbean that are participating in this program are listed

¹ kaisernetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We apologize for any inaccuracies.

here. I indicate these for the important reason that as we now combine prevention care and treatment into one, we're going to have to be innovated in designing the research that will inform the prevention, care and treatment programs. The availability of resources for these programs really presents a challenge and an opportunity to design the relevant research for these countries.

Now, looking to the challenges for prevention in the future, we will need more effective prevention strategies. We need access to anti-retroviral treatments around the world to compliment prevention programs. We need to do a lot to develop the healthcare infrastructure of therapy and for prevention. An HIV vaccine would be crucial to help us in preventing of spreading epidemic. We need female control protections to compliment the male condom in preventing transmission among sexual partners. The estimated cost for the combined prevention, care and treatment programs needed internationally is somewhere between three and five billion per year. We are partially there in meeting this goal. Much more money will need to be raised in order to compliment these programs.

So, finally our conclusions, the HIV/AIDS epidemic continues to expand especially in developing countries, control of the epidemic requires a comprehensive effort, as Quarisha mentioned these epidemics will not go away. We have to plan long-term into the future and make sure that the resources are there, and lastly, mostly and most important, prevention care and treatment must be integrated. Thank you.

¹ kaisernetwork.org makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We apologize for any inaccuracies.

South African AIDS Conference
Plenary 1: "HIV Prevention," Dr. Rod Hoff
August 4, 2003

14

SPEAKER: Thank you, Rod.