Conspiracy beliefs can affect treatment of people with HIV

Antiretroviral therapy has dramatically improved the quality and quantity of life for people living with HIV; yet some patients still view these medications with suspicion. "You can have the most effective medicines, but if the person doesn't take them, they're not going to work," notes Dr. Lydia Temoshok, Director of the Behavioral Medicine Program at the Institute of Human Virology (IHV) and Professor of Medicine at the University of Maryland School of Medicine (UMSOM). In the course of conducting clinical research over the past 10 years with almost 1000 HIV-infected outpatients and inpatients, she and her colleagues have reached some conclusions about factors that contribute—and don't contribute--to HIV drug treatment adherence. So-called 'common sense' factors like forgetting to take medications, pill burden (taking multiple medications), knowledge of HIV-related information, and understanding the consequences of not taking one's medicines as prescribed did not predict adherence, Temoshok explained. The factors that did predict more optimal adherence, she added, were underlying, chronic attitudes and ways of perceiving, thinking about, and dealing with the world.

Lydia Temoshok, PhD

"What we were finding, again and again, was that it wasn't so much that people forget to take their medicines, it's that they don't want to take their medicines," says Dr. Rebecca Wald, Assistant Professor at the IHV and UMSOM. Wald started to look systematically at the reasons for this. "She decided to focus on conspiracy beliefs,

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Director's Message, *Continued from page 1*

that most of us believed was the main mechanism induced by the vaccine used in the Thai trial, but this was not the case. Among infected people both placebo and vaccinees had the same levels of HIV. However, it is the second point that was most unexpected and important. For the first year, and especially the first six months, there were significantly more infected persons in the placebo group. In other words, there seemed to be complete protection against infection that lasted for a while, but in time the vaccine became ineffective. The rate of infection of the placebo treated groups and the vaccine treated groups became virtually identical.

Protection against infection almost certainly requires a humoral (antibody response) or an innate immune response that quickly produces killer cells that destroy infected cells or a barrage of chemokines that block HIV infection. There was indeed an antibody response, and the final vaccine used in the Thai trials was really not chiefly a CMI-based vaccine as I thought but one that included a significant stimulation of antibody production against the HIV gp120 envelope. Nonetheless, we all know that antibodies to a typical gp120 envelope does not protect except in a type specific manner. So then how could we get a broader affect that would give protection for several months in the vaccinated group? We have to assume one of two possibilities. Either the local population had very specific gp 120 envelopes (Thailand has been dominated by a clade E HIV and the vaccine contained a gp 120 envelope of a clade E HIV), or the expression system used by Sanofi (canary pox viral vector) produced an envelope with a modified form that induced antibodies of the kind we usually do not achieve with conventional gp120. The results have generated much enthusiasm because as such they are historical in that they are the first results of any success in an AIDS vaccine trial. This does not mean there have not been those who argued against the Thai trial results. Some have argued that the apparent positive results could be due to a change in habit when the volunteers knowing they were vaccinated took greater risks. However that does not explain why the vaccinnees did better than the placebo group. There is a second and more recent criticism by some. The trial announcement results were analyzed by what has been called a modified intention to treat evaluation. It is with this analysis that statistical success was seen but not when the analysis was done a second method by what is called a per-protocol analysis. I am not an expert in these kinds of statistical approaches, but from everything I have heard, the analysis that used to report positive results, namely the MITT method, may be the more appropriate for this kind of study. I trust my own instincts. When you look at the curves in those first six months they are clearly quite different from the latter period and to me reveal that something interesting has happened in the early months. In other words, I favor the positive interpretation but with a focus only on a "short-lived" (six months or so) effect.

What to do with these results? Does this mean we go forward with still a larger phase study? That is not the conclusion of the authors of this study nor is it the conclusion of the scientific community. Rather these results should be regarded as an experiment, and we should focus our attention to the events of this early period. What are the things that need to be looked at carefully? Clearly we would like to know everything about the immune response. For instance, we would like to know the levels of beta chemokines in production. We would like to know the type of antibodies produced. Did the antibodies block HIV infection in conventional assays, or were they of other types that simply bound to the virus but didn't really neutralize in the conventional assays but have other effects that block HIV? CMI also needs to be examined, but I bet we are not going to find answers from that direction. In my view the most important cellular experiments to be carried out are to examine the memory B cells during the early period in the vaccinees. As my colleagues, George Lewis and Yongjun Guan, have shown in the last couple of years the memory B cells are good archival records of what antibodies were produced that might not still be found in serum, and the decline in some of those antibodies may be why the vaccine effect was short-lived. I hope our IHV scientists, including myself, can contribute to these analyses. Finally, I congratulate the authors of the work, particularly Jerome Kim, formerly of IHV, and Nelson Michael both of the U.S. Army, Jim Tartaglia of Sanofi-Pasteur, who for so long stayed with his study of ALVAC as a vector including this trial, and the Thai Group.

July 2009 IHV Promotions

Mayurika Ghosh, M.B.B.S.

Mayurika Ghosh, M.B.B.S. of the Institute of Human Virology was promoted to Assistant Professor, non-tenure track, in the University of Maryland School of Medicine, Department of Medicine Division of Infectious Diseases.

Yongjun Guan, Ph.D.

Yongjun Guan, Ph.D. of the Institute of Human Virology was promoted to Assistant Professor, non-tenure track, in the University of Maryland School of Medicine, Department of Microbiology and Immunology.

Wuyuan Lu, Ph.D

Wuyuan Lu, Ph.D. of the Institute of Human Virology was promoted to Professor, with tenure, in the University of Maryland School of Medicine, Department of Biochemistry and Molecular Biology.

Gregory Melikian, Ph.D.

Gregory Melikian, Ph.D. of the Institute of Human Virology was promoted to Professor, with tenure, in the University of Maryland School of Medicine, Department of Microbiology and Immunology.

Marzena E. Pazgier, Ph.D.

Marzena E. Pazgier, Ph.D. of the Institute of Human Virology was promoted to Assistant Professor, non-tenure track, in the University of Maryland School of Medicine, Department of Biochemistry and Molecular Biology.

Lai-Xi Wang, Ph.D.

Lai-Xi Wang, Ph.D. of the Institute of Human Virology was promoted to Professor, with tenure, in the University of Maryland School of Medicine, Department of Biochemistry and Molecular Biology.

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because our research showed that participants in our studies held a number of irrational or semi-rational beliefs that prevented them from taking their medicines correctly or at all," says Temoshok.

Rebecca Wald, PhD

Wald was awarded a two-year NIH grant to study conspiracy beliefs among HIV positive African Americans at the Evelyn Jordan Center, the out-patient HIV clinic affiliated with the IHV and UMMS. Before this, little was known about conspiracy beliefs among people with HIV. She looked specifically at African Americans, since previous studies had found that belief in conspiracy theories tended to be higher within this group, and also that African-American men who believed conspiracy theories were less likely to use condoms. Her research indicated that conspiracy beliefs were common among HIV-positive African Americans. "About 40% of the participants in the study think that there's a secret cure for HIV that only rich people get access to," says Wald. "And about 40% believe that the U.S. government created HIV in the first place." An overlapping 20% of the participants reported their belief that HIV was "deliberately created to get rid of undesirable minorities."

Wald says her study is also one of the first to look at how conspiracy beliefs affect treatment. Her research showed that patients who were not taking antiretroviral therapy (ART) were more likely to endorse conspiracy beliefs. Preliminary results from a follow-up study also suggested that conspiracy beliefs, as well as poor communication with medical providers, reduced patients' willingness to initiate ART over time.

According to Temoshok, IHV behavioral medicine research has revealed some of the underlying and fundamental reasons patients don't take their prescribed medications correctly, including maladaptive coping with stress, depression, and poor relationships with treatment providers. "Trust is a critical factor," she emphasized, adding that if patients felt that their providers cared about them, they were more apt to take their medications correctly, even if they experienced side effects. Many HIV-positive patients "don't have a good background in trusting authority," says Temoshok, and have "decades of mistrust of the medical establishment," adds Wald. Because of this, they may be unwilling to take their doctor's word for the safety and effectiveness of medications for HIV.

Wald says that the most surprising finding from her study was that even patients receiving the best treatment, education and resources available tended to believe in conspiracy theories. "The people who are coming to the clinic here are the best-case scenario," she says; "I think if you looked at people who had HIV but who are not in care, that you would find that these issues are more extreme."

Wald is currently applying for a grant to develop an intervention to reduce mistrust and increase patients' comfort with ART. The first step will be to modify existing intervention techniques to deal with conspiracy beliefs, and then to conduct a series of studies testing the feasibility, acceptability, and effectiveness of this approach. Eventually, this work should lead to a large randomized controlled trial of these innovative, targeted interventions.

Reaching the people who are not coming in for care and have given up on getting treatment is a larger problem, notes Temoshok. But she believes there are creative ways to tackle the problem, starting with wider and increased communication by trusted, credible sources. No matter how much trust exists, however, you can't just lecture patients into taking their medicines, she says. Most of us, including people living with HIV, generally know what we should be doing or not doing to avoid getting ill or more ill. Our research and intervention focus, explains Temoshok, is to tackle the conundrum of why we don't do what is good for us, and then to help people choose what is right—at least more often. Real and lasting behavioral change in terms of optimal HIV medication adherence can only come from helping people find the motivation to change. They will need to not only change what isn't working for them, but also work with trusted medical providers to choose the treatment that is right for them, while the providers recognize that patients are not merely complying with what someone is telling them they should do.