Diary of a Doc: Vaccine Update at ICAAC

October 6, 2006 By Lloyd Bailey, MD

Last week's 46th annual Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) in San Francisco included an update on the thorny issue of HIV vaccines. Developing a vaccine to prevent HIV infection has been a significant challenge, and, sadly, traditional vaccines are not expected to reach clinical use for another ten years.

Among the biggest obstacles to vaccine development are the tremendous variability of HIV's structure—not just globally but locally—and HIV's ability to infect and destroy many of the immune cells chiefly responsible for defending the body against HIV infection.

But HIV infection also differs markedly from other viral infections for which successful vaccines have been created—such as measles or hepatitis B infection. During measles infection, for example, the vast majority of infected individuals spontaneously recover, clear the virus from their bodies and develop an immune response to help prevent them from ever becoming infected with the virus again. It's apparent that the body's natural immune defenses are integral in creating the positive outcomes seen with vaccines in these viral infections.

HIV, on the other hand, is never fully cleared from the body, so the immune response that researchers are seeking to spark isn't very effective against HIV to begin with. Even those currently infected with HIV are vulnerable to infection with a second (different) strand of the virus—as seen in HIV superinfection.

Are all HIV immune system responses ineffective? Clearly, the answer is no. Though HIV has never been fully cleared from an individual, many have immune responses capable of keeping viral loads low and greatly slowing the destruction of CD4 cells. These individuals are long-term nonprogressors (LTNPs)—defined here as individuals infected with HIV for ten or more years who remain clinically healthy.

These LTNPs have been extensively studied, and a number of factors have been found to explain their excellent long-term health.

Recent studies have shown, for instance, that up to 70% of the body's total CD4 cells are destroyed in the first 14 days following HIV infection. As a result of this fast and furious destruction of CD4 cells, defenses against many diseases are lost. Even when the CD4 count in peripheral

blood is restored with effective HIV treatment, these defenses are often not restored. Among the defenses lost in these early days following HIV infection are the CD4 cells responsible for fighting HIV itself.

Researchers believe that LTNPs have a smaller proportion of their CD4 cells destroyed during these first few days following HIV infection. This preservation of CD4 cells may be in large part responsible for the greatly improved long-term course of their HIV.

It would be extraordinarily difficult to identify anyone this soon after HIV infection—symptoms of infection don't commonly occur until somewhere around the tenth to 14th day. But what if a vaccine could be developed that would sensitize the body's immune system to respond during this early period of CD4 destruction?

This vaccine would not be effective at blocking HIV infection itself but instead would prime certain immune defenses to begin fighting HIV immediately following infection. The goal of such a vaccine would be to prevent much of the CD4 cell loss in those early days, thus creating a long-term disease course similar to LTNPs.

At ICAAC, research was presented regarding a vaccine of this type that was given to uninfected macaque monkeys. The vaccine was not effective at blocking infection, but it did greatly reduce viral loads in the first few weeks following infection. With less virus present, fewer CD4 cells were destroyed.

This vaccine will eventually be studied in humans. And, if effective, it could end up having a positive effect on HIV infection rates after all. As much as 40% of all new HIV infections are believed to originate from someone newly infected with HIV because the amount of virus in initial infection is much, much higher than at any other point during the disease. It's not uncommon to see viral loads in the millions during this brief period, thus making it much easier to pass on the infection.

Studies are also underway to determine whether this priming of the immune system—to recognize and kill HIV—may also have some benefit for those already infected with HIV.

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