Being Alive

FROM THE 4TH NATIONAL CONFERENCE ON RETROVIRUSES: Antiretroviral Affects on Blood, Semen, Spinal Fluid, and Lymph Tissue

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The information emerging from this year's conference is mostly a continuation of the good news that first started emerging from last January's 3rd National Conference, where the data for protease inhibitor therapy were first publicly released. There are, however, some significant concerns, which are delineated below.

Some Protease Inhibitor Results At last year's conference, Merck released data for about 20 participants in their now well-known study of individuals who were 3TC and protease-naive but extensively AZT-experienced. These people were treated with AZT, 3TC, and Crixivan. Follow-up data extended only to 24 weeks. About 85% had "undetectable" viral load with CD4 count increases of about 100 cells.

Abbott reported short-term (about 5 months) data indicating clinical benefit in their study of individuals with advanced aids treated with ritonavir (participants on average had about 25 or less CD4 cells prior to study entry). The early results showed that survival was extended and progression of aids was slowed. Since that time, there has been a steady flow of generally positive news. Encouraging data for a new class of drugs-non-nucleoside reverse transcriptase inhibitors (NNRTIs)-have been emerging and is discussed below.

Remaining Concerns However, not all the news is exclusively positive. A number of individuals either did not respond well to the new therapies or initially responded well, but their viral load rebounded either sooner or later. It is difficult to estimate how many individuals have experienced this problem, but you are not pleased if you are one of them.

A factor contributing to this problem is that in many cases doctors and patients were not well prepared to know how to use the drugs properly. In many instances, a potent protease inhibitor was merely added on to therapy one may have been taking for a while. Data from studies indicate clearly that to maximize your benefit from protease inhibitor therapy or any therapeutic regimen, you should begin if possible with at least 2 and preferably 3 drugs that you've never before taken.

Non-compliance is another problematic cause for the development of resistance and failure. In order to benefit from the new therapies, one must be prepared to commit to strict adherence or compliance to the instructions for taking the medications-dosing, hydration, eating, storage, etc. Other factors may be relevant to why some individuals were not able to benefit from protease inhibitor therapy, but at this point they have not been identified.

For those who have responded well to the new therapeutic regimens there is good news emerging from this conference. And, for those of you who have not been able to respond well, there is also hope from some of these newer promising drugs.

Viral Load in Other Body "Compartments" Early in 1996, amidst the realization that we could render viral load in peripheral blood to "undetectable" levels, it was also realized that viral activity in other "compartments" would now become of vital interest. The vast majority of virus in humans is contained in peripheral blood, but it resides in other parts of the body as well. Researchers started studying viral activity in these other compartments and the effect of the new potent antiretroviral regimens. It is crucial to determine whether potent therapy can be effective in reducing viral activity in these other compartments. Can the virus find "sanctuary" in any of these compartments? These other "compartments" include semen, lymph tissue and spinal fluid. Preliminary results from ongoing small studies reported at this conference indicate that reduction of replicating virus in blood to "undetectable" levels was accompanied by similar reductions in viral activity in the cellular compartment (inside the cells) in the semen. This does not by any means imply that these individuals are not fully capable of transmitting hiv through unprotected sex. In fact, provirus dna was detected in all these subjects, but it is uncertain whether it is infectious or noninfectious.

HIV in Lymph Tissue In lymph tissue studies, gut associated lymph tissue and tonsillar lymph tissue were examined with similar results. When blood plasma viral load is rendered "undetectable," the lymph tissue samples display similar reductions in viral activity. But, again, provirus dna was detected. After 6 months of therapy for some individuals from whom lymph tissue samples were taken, there was residual hiv rna virus detectable, but there was a clear reduction in virus.

HIV in the Central Nervous System Research exploring viral activity in the CNS (Central Nervous System) was more mixed and uncertain. Preliminary information was reported from several small studies indicating that the course of disease progression appears to be complicated and not yet well understood. For the participants in one small study, investigators reported hiv rna load in blood plasma correlated with hiv rna in CSF, but they also found no correlation between the degree of neurocognitive decline and hiv rna load in CSF or blood plasma.

Some researchers suggest that there is a distinct course of disease progression in the CNS, separate from that in the peripheral blood. There may be a compartmentalization between the blood and the brain. It appears possible that factors other than viral load in the brain can affect neurocognitive hiv-related disorder. This compartmentalization may be more well-defined in advanced hiv than in earlier disease.

Although it has not been discerned just yet, there is some concern that the brain can be a sanctuary for hiv. There are, however, some suggestions for treatment. Early detection of a neurological concern may be a key. Dr. Justin MacCarther, a prominent neurology researcher at Johns Hopkins University, said there is a reversible phase of impairment, and also an irreversible phase. Therefore, early diagnosis and treatment is imperative. It has also been suggested that if possible, when designing a therapeutic regimen or drug combination, you should consider combination therapy for the brain. That is, you should consider including two drugs that are expected to penetrate the CNS-

these include AZT, d4T and nevirapine.

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