

## [National AIDS Treatment Advocacy Project](#)

### **CNS Penetration and HIV**

The subject of viral replication in the CNS and brain and treatment of it was briefly addressed by David Ho at the Vancouver Conference. As well, in discussions with Abbott and an oral session, I brought up this subject hoping to learn more about it. In my final report on the Conference I discuss what Ho said about CNS penetration.

He said the CNS was one of a number of "compartments" (including lymph nodes and testes) for which are important to study. With potent therapy that can lower plasma RNA at least two logs or to very low levels, we can lower plasma RNA to "undetectable" levels. In the study of nelfinavir/AZT/3TC in treatment-naive individuals (the first study in this population), described in the [final day's report](#), 11/11 subjects achieved a reduction in their viral load measurement to below 25 copies. A noteworthy achievement with significant implications. However, if we are able to "drain" HIV from plasma, what can we achieve in these other "compartments?"

Ho and Martin Markowitz will soon be initiating lymph node biopsies on these study subjects to detect the therapeutic affect in this widely agreed upon important "compartment."

Ho said the CNS was an important but difficult "compartment" to reach with therapy. He said there aren't enough HIV drugs that penetrate the CNS and, for those that do, they don't penetrate well enough.

Having said that, Glaxo Wellcome says their two new important HIV antiviral drugs (1592U89 and 141W94) both penetrate the CNS well. In fact, based on the early animal studies, the CNS penetration was so high for 141W94 (protease inhibitor), that some researchers have commented to me that the penetration may be so high as to cause complications, such as headaches. Glaxo's 1592U89, a reverse-transcriptase inhibitor whose RNA and CD4 data is impressive, also apparently penetrates the CNS well. In fact, Glaxo will be conducting a study of this drug in individuals with HIV clinically diagnosed dementia (see the article on [1592U89](#)).

At the Vancouver Conference, I discussed the CNS penetration of ritonavir with Abbott officials. They say that, although it seems as though CNS penetration may be minimal by ritonavir, the development of CNS or brain related conditions were reduced by therapy with ritonavir, as was evidenced by the data from their endpoint study #247 in advanced HIV disease. You will be able to check the list of opportunistic infections whose incidence were reduced during that study in the NATAP Protease Inhibitor Report; a booklet now being updated with information and data from Vancouver, available in the near future.