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Oral Session III
Antiviral Approaches to HIV Infection

AIDS Encephalopathy: An AZT Derivative Which May Become "Locked" In The Central Nervous System.

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The recent finding of HIV in brain macrophages coupled with the presence of neurologic symptoms associated with AIDS underscore the need for an anti-HIV agent that would be effective in the CNS. Generally, polar molecules such as nucleosides have difficulty passing the hydrophobic blood-brain barrier. Although AZT has been shown to cross the blood-brain barrier, it may fail to reach an optimal concentration since it can move across the barrier in both directions with equal facility. One approach to this problem would be a progenitor drug which, upon crossing the blood-brain barrier, could be locked in the CNS by a normal biochemical reaction to a second progenitor which would then release active drug. We have capitalized upon the approach of Bodor and colleagues to prepare such a latentiated form of AZT; specifically 5'-[(1,4-dihydro-1-methyl-3-pyridinylcarbonyl)oxy]-3'-azido-3'-deoxythymidine(HPAZT). This was obtained via a sodium dithionite reduction of 5'-[(1-methyl-3-pyridiniumcarbonyl)-3'-azido-3'-deoxythymidine, which in turn could be prepared by esterification of AZT with nicotinoyl chloride in pyridine. This latentiated form of AZT (HPAZT) is currently being evaluated for its behavior in serum and brain extracts as well as in vitro antiviral activity.