Drug combo routs HIV from blood and tissue

Even after drugs have banished HIV from the bloodstream, the virus may still lurk in the lymphoid tissues of the body. A successful AIDS-preventive treatment must therefore destroy HIV hiding in those tissues. If not completely routed, the virus may ultimately rebound.

A new study now demonstrates that a three-drug regimen clears nearly all of the virus from the lymphoid tissue of adults with advanced HIV infection. A second report shows that another three-drug treatment results in a striking reduction of the virus in the bloodstream of some HIV-infected babies.

Some researchers view such results as the first step toward the ultimate goal of a complete cure—for both adults and children. Others remain wary. Even if drug therapy can quash most of the virus in the body, there's still a chance that any remnants will smolder and later ignite a fire of infection, warns virologist Winston Cavert of the University of Minnesota Medical School in Minneapolis.

In the first study, Cavert's team focused on the lymphoid tissue. The researchers wanted to find out whether drug regimens that clear HIV from the blood would also shut down HIV factories in the tonsils and lymph nodes.

They studied 10 HIV-infected people who were being treated with a regimen of ritonavir, AZT, and lamivudine. Ritonavir belongs to a new class of drugs, called protease inhibitors, that has generated considerable optimism in the war on AIDS (SN: 7/13/96, p. 21). The other two drugs inhibit reverse transcriptase, an enzyme crucial to viral infection.

After 6 months, the researchers tested a snip of lymphoid tissue from the tonsils of the patients. In the May 9 SCIENCE, the scientists report that the treatment's triple whammy had eliminated 99.9 percent of HIV—even in the tissues' follicular dendritic cells, which trap and store HIV.

"That [result] tells us that antiviral therapy is having a profound effect, even at the level of lymphoid tissue," comments Anthony S. Fauci, director of the National Institute of Allergy and Infectious Diseases in Bethesda, Md.

The second study, published in the May 8 NEW ENGLAND JOURNAL OF MEDICINE (NEJM), looks at HIV in the bloodstream. Katherine Luzuriaga of the University of Massachusetts Medical School in Worcester and her colleagues worked with eight babies who had been infected with HIV early in life, probably at birth. Typically, doctors give such infants a single antiviral drug. Luzuriaga's team wanted to try a three-pronged attack with AZT and two other drugs that also block reverse transcriptase.

In all but one of the babies, the triple-drug therapy dramatically reduced HIV infection. The team observed a 96 percent or greater drop in the concentrations of viral RNA after the first 4 weeks of treatment. Subsequently, HIV reasserted itself in some of the seven infants, but the treatment maintained at least a 32 percent reduction in viral RNA concentrations throughout the 6-month study. In two babies, HIV was cleared to almost undetectable amounts.

The researchers did not look for HIV sequestered in the lymphoid tissues, Luzuriaga says. However, there's no reason to believe that the drug therapy failed in that quarter, according to Fauci. Luzuriaga hopes to continue the study, perhaps looking at the youngsters' tonsils after they have been on a potent drug regimen for 2 years.

Luzuriaga believes that a three-drug attack which includes a protease inhibitor might prove even more effective at clearing HIV infection in babies, and she has already modified the regimen for some of the infants. Furthermore, she says the results might have been even better if the researchers had administered the drugs in the babies' first month of life rather than starting treatment at 2 to 16 months of age.

A third study, in the same issue of NEJM, underscores the importance of immediate treatment for babies with HIV infection.

William T. Shearer of the Baylor College of Medicine in Houston and his colleagues show that the amount of HIV in the blood peaks 1 to 2 months after birth and declines only slowly during the next 2 years. This finding may explain why babies with HIV tend to get sick and die faster than adults. In adults, the amount of virus peaks and then drops dramatically. *— K.A. Fackelmann*

Chemical drivers for tiny Brownian motors

A microscopic particle suspended in a liquid is continually bombarded by molecules of the solvent. Because these random collisions aren't evenly distributed at all times, the particle gets shoved this way and that and moves about erratically.

Known as Brownian motion, this constant jiggling has attracted the attention of researchers interested in harnessing such movement to create tiny motors and pumps and to develop improved methods of separating different-size particles or transporting various molecules. Systems of this sort could potentially serve as models of cellular ion pumps and biomolecular motors (SN: 3/22/97, p. 173), which drive muscle contraction and other biological processes.

Now, biochemist R. Dean Astumian of the University of Chicago and his coworkers have proposed a scheme in which chemical energy deposited in appropriate locations can bias Brownian motion to push particles and large molecules in a chosen direction. He outlines the method in the May 9 SCIENCE.

In a conventional electric motor, a start-up coil provides the energy that sets the rotor spinning in a particular direction and inertia keeps it going. Continued energy input compensates for friction in the system.

A protein immersed in water faces considerably more resistance to motion. "It's like trying to swim in butter," says Marcelo O. Magnasco of Rockefeller University in New York.

The trick is to keep nudging a molecule or microscopic particle to maintain its motion in a certain direction. That can be done by using the microscopic equivalent of a notched ratchet wheel that can rotate in only one direction.

In recent years, researchers have proposed and investigated several methods of creating the required ratchet configuration and supplying energy to produce fluctuations that the mechanism can rectify into motion in a particular direction. For example, two microscopic, comblike electrodes with interleaved teeth, made of metal deposited on a glass slide, can generate an oscillating electric field that allows a particle immersed in a liquid to move only in a favored direction.

Because particles of different sizes experience different amounts of friction and Brownian motion, it's possible to set up conditions so that larger particles move in a direction opposite to that of smaller particles, researchers have suggested.

Astumian now proposes that chemical reactions, rather than an oscillating electric field, could provide the energy fluctuations needed to drive particle transport. In this case, changes in the electric charge of molecules or ions in a reaction could supply the impetus. For example, the biochemical molecule ATP typically has a negative charge in solution. When it binds to a protein, it changes the protein's net charge. In principle, two proteins that react with ATP at different rates would move differently, allowing them to be separated.

"Several technological hurdles remain, however, before a practical device can be constructed," Astumian cautions. *— I. Peterson*