AIDS Virus in Bone, Vaccine on Trial

More scientific data flowed into the AIDS research realm this week, as scientists reported encouraging preliminary results from the first U.S. clinical trial of a potential AIDS vaccine and discouraging findings indicating that the virus may infect precursors of cells found in the bone marrow and use them as a reservoir. The bone marrow findings provide more evidence that completely eliminating the virus from the body may be impossible.

In the vaccine trial, roughly one-third of the volunteers have developed antibodies to the AIDS virus (HIV) when given low doses of the potential vaccine, say scientists from the National Institute of Allergy and Infectious Diseases (NIAID) in Bethesda, Md. The federal facility is coordinating the preliminary study, designed to assess side effects and basic immune responses. Made by inserting genes for an HIV-envelope protein (gp160) into baculoviruses, the vaccine was developed by the West Haven, Conn.-based MicroGeneSys, Inc. (SN: 8/22/87, p.116). Further trials, however, would be needed to determine whether the vaccine will actually protect against infection. The vaccine uses only part of the virus' coat to stimulate an immune response, and cannot itself infect cells.

During a joint meeting of the Association of American Physicians, the American Society for Clinical Investigation and the American Federation for Clinical Research held this week in Washington, D.C., NIAID scientists released early results from the ongoing gp160 trial. Thus far, the scientists have injected 59 volunteers with varying amounts of the vaccine, and will add more subjects as they increase the gp160 dose in step-wise fashion, says NIAID Director Anthony S. Fauci.

Of the 15 people receiving 40 micrograms of gp160, six showed an antibody response to gp160 within two months after injection, as detected by blood tests for HIV antibodies. Fauci says he suspects that "a considerably larger percentage will respond to the 80 micrograms" and that four times that amount may eventually be used. Some of those responding received booster shots one month after the initial dose. Side effects, which included local tenderness and fever, were minimal, Fauci says.

Begun last September, the study had a slow start, hampered by volunteers' fears of discrimination by prospective employers and others if they did develop HIV antibodies. The researchers have eliminated those concerns, says Fauci, by giving participants a certificate stating their antibody status is due to participation in a federal study. Although the injection schedule should be completed within about six months, volunteers will be followed for at least one year. The scientists have not yet evaluated the cell-mediated immune response in the volunteers, nor whether their antibodies can neutralize HIV *in vitro*.

"This is *not* a breakthrough," Fauci emphasizes. "This is a successful point in a long, long, arduous journey." Even as he repeatedly cautions that any AIDS vaccine would not be available until the mid-1990s, the disease continues to march slowly through the U.S. population. Doctors have diagnosed the disease in nearly 60,000 U.S. residents since 1981; more than half have died. Although U.S. estimates of the number infected with HIV are sketchy, public health officials currently say between 1.5 and 2 million harbor the virus. (A federal reevaluation of those estimates is scheduled for later this year.)

These infected patients are "in a very real sense time bombs," says San Francisco General Hospital's Paul A. Volberding. Speaking on AIDS public policy at this week's meeting, he said accumulating evidence shows that once an HIV-infected person begins to show symptoms associated with the condition called AIDS-related complex (ARC), eventual death from AIDS appears certain.

Knowing where the AIDS virus hides in the body and what turns it into an immune-cell killer could help explain why an antibody-positive patient begins to show symptoms. A majority of AIDS patients develop neurologic abnormalities, sometimes as their first symptom. Fauci and his co-workers had previously shown that cells called blood monocytes and tissue macrophages can carry HIV into the brain, where the virus infects nerve cells. Now they report HIV apparently can infect the bone marrow cells from which monocytes and macrophages are produced. The scientists used a new technique to isolate the monocyte/macrophage ancestors, which, unlike T lymphocytes, are not killed during HIV infection.

"[The finding] will explain some of the puzzles of HIV infection," says Fauci, who calls it "one of the most exciting things we've come across in the past year." The discovery, which the scientists expected, shows that latent viruses probably maintain a powerful reservoir in the bone marrow, and thus can send infected cells through the body. It also indicates that an effective drug must be able to reach bone marrow cells. On the basis of such results, Fauci says, "It's going to be very difficult to eliminate each and every virus particle from the body."

Rather than eliminating the AIDS virus, some researchers want to prevent the reactivation of latent, or resting, viruses. Fauci reported this week that NIAID researchers have found that substances called cytokines – produced by cells during the normal immune response to infections – can in fact *induce* HIV replication. Among these are tumor necrosis factors, which are produced in large amounts by monocyte/macrophage cells during infections. Researchers at NIAID and elsewhere are looking for drugs to block cytokine release, Fauci says. *– D.D. Edwards*

Repairing blood pressure damage

In patients with uncontrolled high blood pressure, the excessive force of their pumping blood can enlarge the heart and thicken vessel walls, eventually causing heart and kidney disease. Although many drugs lower blood pressure itself, scientists have long remained uncertain whether these drugs also reverse hypertension-induced structural damage. Now, new findings "strongly indicate" that long-term antihypertensive treatment can indeed improve a damaged circulatory system, say Swedish scientists.

Seven years of antihypertensive drug therapy significantly improved heart, blood vessel and kidney functions in patients at Sahlgrenska Hospital in Gothenburg, researchers report in the May 6 JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION. They studied 13 men with high blood pressure and 37 with normal blood pressure, using a variety of techniques to measure pressure and volume of blood in the heart, as well as blood flow in the arms and kidneys.

The hypertensive men and many of the normal controls were first tested at age 49 – when those with high blood pressure began beta blocker drug treatment – and again seven years later. The difference in average blood pressure between the two groups dropped from 51 percent to 7 percent during the study period. Although they did not shrink to normal size, the enlarged left ventricles of the hypertensives' hearts did become significantly smaller over the seven-year period, say the authors. Protein excretion, a sign of kidney malfunction, also dropped dramatically in the treated patients. *– D.D. Edwards*