AIDS drug approved, vaccine tested

Both the treatment and prevention of AIDS took another step forward last week with the announcement of federal approval for sales of an AIDS drug and a report that an experimental vaccine had been injected into humans.

A drug that does not cure AIDS but appears to prolong the lives of some of its victims was approved for prescription use last week by the Food and Drug Administration (FDA). Azidothymidine (AZT) — made under the brand name Retrovir by the Burroughs Wellcome Co. of Research Triangle Park, N.C. — is already being used with FDA's blessing by thousands of AIDS patients in the United States.

When a study begun early last year to test AZT's efficacy showed promising results, the research project was discontinued and the drug was made more widely available (SN: 9/27/86, p. 196). Only days before the AZT decision, the FDA announced it would propose a rule change that would speed approval for drugs that were considered experimental but that caused improvement in terminally ill patients (SN: 3/21/87, p. 189). The FDA approval was preceded this month by similar government action in Great Britain and France.

Treatment with AZT, however, is not expected to be the last word in AIDS drug development. It appears to be effective in a limited group of AIDS patients. Annual costs for the AZT treament have been estimated to be between $7,000 and $10,000 per patient. And, because the drug can cause immune system suppression and anemia in recipients, alternative treatments are being studied. Among those are ribavirin (SN: 1/5/85, p.7) and dideoxycytidine, which appears to inhibit the AIDS virus's ability to infect cells. The latter drug is in preliminary clinical trials, with results expected within a few months.

A combination of drugs eventually may be required to treat AIDS, but even that prospect is complicated. A report in the March 13 SCIENCE suggests that ribavirin hampers activity of AZT.

Despite its disadvantages, AZT is significant as the first approved treatment of the fatal disease. According to Robert E. Windom, an assistant secretary in the Department of Health and Human Services, most AIDS patients are expected to qualify for AZT use under the FDA-approved indications accompanying the approval.

And in the first reported experimental trial of an AIDS vaccine in humans, a French scientist has injected himself with a vaccine made by inserting a gene for the AIDS virus envelope into vaccinia virus. Daniel Zagury of the Pierre and Marie Curie Institute in Paris and his co-workers say in a letter in the March 19 NATURE that after the injection, they combined a sample of Zagury's blood *in vitro* with the AIDS virus and found that the vaccine had activated his immune system against AIDS.

His immune response (both antibody production and cell-mediated immunity) was measured for nine weeks following the primary immunization. The scientists detected not only antibodies against the strain of AIDS virus used, but also heightened blood lymphocyte responses when using Zagury's blood in subsequent tests. The cellular response also was mounted against a very different strain of AIDS virus — an important aspect, given the virus's ability to mutate rapidly. No adverse affects, such as body temperature changes, were observed after injection, say the scientists.

According to the report, booster shots of the vaccine have been given to Zagury and some of a "small group" of volunteers immunized in Zaire, where the work is being done. The results of this study do not show that the vaccine could actually prevent AIDS, but they do suggest that the two-pronged immune system may be enticed to subdue the lethal virus.

Clinical trials of AIDS vaccines in the United States could begin this year, according to Anthony Fauci, director of the National Institute of Allergy and Infectious Diseases. Fauci cautions that even if early trials began soon, a widely available vaccine probably would not be reality until the mid-1990s. — *D.D. Edwards*

Thalidomide: Is there a silver lining?

Once exiled from medicine for the severe birth defects it can cause, the drug thalidomide may have found a respectable role in preventing the severe reaction associated with transplanting tissues.

According to Georgia B. Vogelsang of the Johns Hopkins University School of Medicine in Baltimore, thalidomide is being used successfully there to treat graft-versus-host disease (GVHD) in a small group of bone marrow recipients. She reported preliminary results this week in San Diego at the American Cancer Society's annual Science Writers' Seminar.

In the late 1950s, women given thalidomide as a sleep-inducing and anti-morning sickness drug while pregnant ran the risk of giving birth to infants who lacked arms or legs. It is "one of the most notorious drugs ever introduced," says Vogelsang.

Nevertheless, Vogelsang believes thalidomide may redeem itself in the transplantation field. Although bone marrow transplants often are used to treat leukemia, aplastic anemia and certain genetic disorders, there can be serious setbacks. Because bone marrow contains a large number of cells capable of an immune response, clinicians are careful to match a recipient with donor bone marrow through compatibility testing. However, in 40 to 60 percent of these grafts, the donor bone marrow (graft) recognizes the recipient (host) as foreign and "attacks." The potentially fatal GVHD that results may be acute or chronic, with symptoms that include mouth ulcers, skin problems and liver failure. To fight GVHD, the immunosupressant cyclosporine currently is the drug of choice; but its high toxicity and slow-acting effects reduce its usefulness.

In the search for alternatives, studies have shown that cyclosporine and thalidomide influence the same type of immune cell. This, coupled with earlier observations in the 1960s that thalidomide may have caused improvement of leprosy, pointed the way to thalidomide, says Vogelsang.

Encouraged by animal studies, the researchers have recently administered thalidomide to four bone marrow recipients, two with acute GVHD and two with the chronic form. In the present scheme, cyclosporine is being given in tandem with the thalidomide, but in lower doses and for shorter periods of time than usual. "Our real hope is that [thalidomide] will be complementary to cyclosporine," explains Vogelsang, who says three of the four patients have "responded beautifully."

One of those patients, who had suffered from GVHD for three years, is regaining normal hair and skin growth, as well as limb mobility lost through thickening of the skin. Vogelsang adds that concurrent studies in England and France are showing similar overall positive results.

Vogelsang and her co-workers are planning studies of thalidomide's effects on solid-organ transplants, but two problems arise with extended use of the drug. First, while the bone marrow recipients have been made sterile by previous treatment, other organ recipients may still be capable of pregnancy. Second, given the huge liability risk, no U.S. drug company has been willing to manufacture the compound. Therefore, Vogelsang is trading skin-disease drugs for thalidomide "on a pill for pill basis" with a dermatologist in Brazil, where the drug is made for treatment of leprosy.

Whether thalidomide becomes the prodigal son that is warmly welcomed home remains a question to be answered by further research. But, says Charles A. Coltman of the Cancer Therapy and Research Center in San Antonio, Tex., the use of thalidomide "may well be one of the most important advances in bone marrow transplantation." — *D.D. Edwards*