STOCKHOLM--Preliminary results on use of two antiviral AIDS drugs--dideoxycytidine (ddC) and azidothymidine (AZT)--given alternately to patients with AIDS and AIDS-related complex (ARC) suggest that the combination may be better tolerated than AZT alone. There is evidence of an antiviral effect against the AIDS virus, indicating that the drug combination merits further study.

The study is small, and final conclusions are not possible.

The findings were reported today by Robert Yarchoan, M.D., of the U.S. National Cancer Institute (NCI), Bethesda, Md., at the 4th International Conference on AIDS in Stockholm. The research was performed in the NCI's Clinical Oncology Program, headed by Samuel Broder, M.D.

The treatment is still in very early patient testing. In this study, only 17 patients have received the therapy.
"Each of the drugs has some potentially dose-limiting complications," Dr. Yarchoan said. "Giving the patient rest periods from each drug lessens the toxicities that would occur if either agent was given continuously."

ddC can cause peripheral neuropathy, a reversible nervous system disorder leading to pain in the feet and hands. But Dr. Yarchoan and his NCI colleagues found that the neuropathy could be delayed or may not even occur if the drug is given in a dosing regimen with "rest periods" built in. AZT can cause bone marrow damage, a side effect limiting its use in some patients.

"Some patients have received the drug combination of AZT for one week alternating with ddC for one week for as long as 48 weeks," Dr. Yarchoan said, "which means we now know the therapy can be tolerated for long enough to be useful in treating AIDS."

In the study, patients who received the therapy had increases in the numbers and functioning of their T cells, important measures of immune system repair. T cells are immune system white blood cells that are crucial to protecting the body from infection and are severely depleted in patients with AIDS and advanced ARC.

In addition, the amount of AIDS virus in the blood of patients receiving the therapy was decreased. Their appetites improved, and they gained weight.

The patients have been receiving ddC and AZT intravenously in an alternating weekly regimen. Of the 17 patients treated, 12 patients have received the therapy for 12 to 48 weeks. Of the remaining five patients, three developed AIDS-related complications, and one of the three patients died. Two patients had to discontinue therapy because of toxicities—one of them developed arthritis, and the other developed neuropathy and died of AIDS.

These findings update a report published in January 1988 on the first 6 patients entered on the study at nine weeks of therapy. At that time, the

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scientists reported that the drug combination appeared to be well tolerated. Data were not yet available suggesting that the combination may be better tolerated than AZT alone, or that the AIDS viral load in the patients' blood was decreased.

These earlier findings were reported in the British journal The Lancet* by NCI scientists in collaboration with scientists from Abbott Laboratories, Abbott Park, Ill.; Hoffmann-La Roche Inc., Nutley, N.J.; University of Miami, Miami, Fla.; U.S. National Institute of Neurological and Communicative Disorders and Stroke, Bethesda, Md.; and Memorial Sloan-Kettering Cancer Center, N.Y.

It is still not known, Dr. Yarchoan said, if alternating ddC/AZT will be better than AZT alone or than intermittent AZT (administered every other week), which has not been tested yet. Also, the contribution of ddC to this regimen still has to be evaluated.

The therapeutic effectiveness of ddC alone still needs to be defined. One NCI study has shown that ddC alone may decrease the amount of AIDS virus in patients. However, the drug (at high doses) could only be tolerated on a short-term basis when given continuously because of its side effects. Studies of ddC alone and in combination with AZT are being conducted or planned by NCI and other U.S. research centers. Investigators at Stanford University Medical School, Palo Alto, Calif., are presently leading a multicenter test of ddC in combination with AZT.

These drugs are the two most developed candidates among the nucleoside analogs (a class of antiviral agents) studied thus far. The drugs act

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similarly to inhibit the AIDS virus, but they are activated by different sets of enzymes in the body's cells. Because they have dissimilar toxicities, they might be used alternately without causing additive toxic effects.

Both AZT and ddC were first synthesized as anticancer agents under NCI grants in the 1960s. The drugs failed to work in cancer chemotherapy and were not studied for nearly two decades. The drugs' individual antiviral activities against the AIDS virus, or human immunodeficiency virus (HIV), were discovered by NCI scientists shortly after HIV was identified as the cause of AIDS.

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