FDA broadens use of unproven AIDS drug

The Food and Drug Administration and the National Institutes of Health last week agreed to an unprecedented widespread distribution of an unapproved AIDS drug, dideoxyinosine (DDI). At the same time, researchers sounded the death knell for dextran sulfate, a once-promising AIDS treatment, and cautioned against bypassing standard procedures for drug approval.

DDI's manufacturer, Bristol-Myers Co. of New York City, plans to distribute the drug free to thousands of AIDS patients who don't respond to or can't tolerate zidovudine (AZT) and who don't qualify for clinical studies of DDI. AZT is the only AIDS drug approved in the United States.

Normally, drug testing for safety and efficacy takes about seven years, says FDA spokesman Brad W. Stone. AIDS patients have lobbied strongly for greater access to experimental therapies outside of drug trials (SN: 7/1/89, p.6).

In a pilot study of 56 patients, DDI showed promise of shoring up immune function by blocking replication of the AIDS virus, thereby boosting patients' CD4-positive T-lymphocytes — the infection-fighting white blood cells destroyed by the virus (SN: 7/29/89, p.69). Researchers at the National Cancer Institute will now compare the drug's efficacy against that of AZT in clinical trials with 2,610 patients.

DDI is not risk-free. Some patients given high doses in the pilot study experienced limb pain and pancreatic swelling. But Robert Yarchoan of the National Cancer Institute, who helped develop DDI, told SCIENCE NEWS these conditions improved after patients stopped taking the drug. A daily dose of 500 to 750 milligrams appears effective and relatively nontoxic, Yarchoan says. The properties that make both DDI and AZT effective against the AIDS virus probably contribute to adverse reactions in patients, he adds. Both drugs are "chain terminators," binding to molecules in a growing chain of viral DNA and terminating the chain, preventing the virus from replicating.

Personal physicians will monitor patients who get DDI outside of clinical trials, reporting the results to researchers leading the clinical trials. It's too early to tell whether DDI will prove less toxic than AZT, which can cause anemia, Yarchoan says.

"There are people out there who seem to be failing on AZT or can't tolerate AZT and now have no therapy available to them. So to those people, death from AIDS is a very severe risk," he says.

The list of promising AIDS drugs got smaller after researchers reported in the Oct. 1 ANNALS OF INTERNAL MEDICINE that dextran sulfate was very poorly absorbed into the blood when administered orally during a clinical trial. Study coauthor Paul S. Lietman of the Johns Hopkins University School of Medicine in Baltimore says the large size and negative charge of dextran sulfate molecules might prevent them from crossing membranes and reaching into the brain and other tissues infected by the AIDS virus. Lietman and his colleagues are now studying the drug's efficacy when given intravenously.

In Japan, dextran sulfate is used as an anticoagulant and cholesterol-lowering agent. Although the drug isn't approved in the United States, FDA allows its importation for personal use. Many AIDS patients began importing oral doses of dextran sulfate after hearing it protected cultured T-lymphocytes from the AIDS-causing virus.

"I don't think it's compassionate to give greater access to unproven drugs," Lietman says. "More patients having access to [dextran sulfate] for the last year wouldn't have helped those patients or society or clinical research."

"Dextran sulfate is dead in most people's minds," agrees Donald I. Abrams of San Francisco General Hospital, who led an earlier clinical trial that revealed toxic side effects of the drug. Abrams says dextran sulfate "underscores the need for careful clinical trials." *— D.E. Loupe*

Listening for hints of the sun's heliopause

Spacecraft visiting other planets have often encountered shock waves formed where the solar wind — the stream of charged particles from the sun — runs at supersonic speeds into the planets' magnetic fields. Many scientists believe that such a shock wave exists on a vastly larger scale in a region called the heliopause, where a similar "wind" from other stars meets the distant limits of the sun's own magnetic field, or magnetosphere.

For more than 30 years, researchers have wondered how far away the heliopause lies. Their estimates have ranged from about five times Earth's distance from the sun (5 astronomical units, or 750 million kilometers) to perhaps 40 times that distance.

Radio emissions detected in 1983 by the Voyager 1 and 2 spacecraft prompted William S. Kurth of the University of Iowa in Iowa City to suggest these signals were associated with the heliopause. Now a scientist suggests the Voyagers may confirm that association by again picking up radio emissions as early as the end of this year.

The two Voyagers, as well as Pioneers 10 and 11, are heading away from the sun in various directions, but so far none has found any identifiable clues to the heliopause's location. Ralph L. McNutt Jr. of the Massachusetts Institute of Technology in Cambridge estimated about a year ago that the 1983 radio emissions could have been triggered just inside the heliopause by the sudden arrival of high-speed streams of the solar wind. The Voyagers had detected the solar-wind streams, too, and McNutt proposed that the "trigger" for the radio emissions could have been the arrival of the streams at the "terminal shock," formed where the solar wind bunches up just inside the heliopause.

Noting the time elapsed between the spacecraft's encounter with the streams and the subsequent radio emissions, he concluded that the shock region lies about 70 to 140 astronomical units (AU) from the sun. He says he now favors a distance of about 120 AU.

Early this past June, Voyager 2, then on the way to Neptune, detected the sudden, dramatic passage of a particularly rapid solar-wind stream, moving at about 550 kilometers per second instead of the usual 400. This week, McNutt told SCIENCE NEWS that a stream moving at this faster rate could reach the terminal shock region by late December.

The sign that such a thing has happened, McNutt says, would be radio signals from the shock wave, triggered by processes that he admits remain poorly understood. And the craft most likely capable of detecting the emissions' expected radio frequencies, he says, would again be the Voyagers.

In McNutt's model, the December date for detecting the terminal shock wave reflects the assumption that a stream of the solar wind is traveling toward the heliopause at 550 kilometers per second and does not slow down on the way. If the heliopause lies at a distance of 120 AU, or about 18 billion km out from the sun, the solar-wind stream that passed Voyager 2 would arrive at the shock wave around the end of this year.

McNutt says the arrival of this fast stream at the terminal shock may "flip the switch" or "turn on the transmitter," triggering radio emissions from the shock wave, which would then head back toward the sun. The emissions would be traveling at the speed of light, which would mean only about half a day would pass before instruments aboard the Voyagers picked them up. (The Pioneers lack instruments to detect the predicted frequencies, McNutt says.)

At a symposium in May, the consensus on the shock wave's distance from the sun was 61 AU, but estimates ranged from 1,000 AU down to no shock at all. Just as uncertain is the distance from any such shock wave to the heliopause, the edge of the sun's influence. *— J. Eberhart*