AIDS announcement raises questions

A claim by French researchers that the immune-suppressive drug cyclosporine works well against AIDS, the ultimate manifestation of immune suppression, has met with widespread disapproval from the U.S. scientific community. But the criticism won't stop the drug's clinical trials, one of the French scientists told SCIENCE NEWS this week.

Jean-Marie Andrieu, who with Philippe Even and Alain Venet of Laennec Hospital in Paris held a press conference last week to announce "dramatic" improvement in two of six patients on cyclosporine for up to eight days. Andrieu declined to update the first week's results, saying they are reserving the details for the scientific community.

In a telephone interview, he said "it's going well" and that five other groups around the world have begun trials. Andrieu and his colleagues are pursuing the treatment with "many" new patients at Laennec, a public assistance hospital. It is not connected with the Pasteur Institute, the Paris research facility that first identified the AIDS virus. The Pasteur Institute is withholding judgment on cyclosporine, pending more data.

Several U.S. scientists expressed concern about the short period of time the patients had been treated. Improvement, they said, could have been due to one of the syndrome's periodic remissions. In addition, they criticized the lack of data given and the forum for the presentation.

Martin S. Hirsch of the Massachusetts General Hospital in Boston, who is investigating several AIDS drugs in clinical trials, comments, "At the moment we don't have any evidence cyclosporine has any effect in AIDS. It's extremely hard to fathom how in six days cyclosporine could have such a dramatic effect on the disease."

Hirsch is worried that patients will get cyclosporine — which, unlike other AIDS drugs under investigation, is readily available by prescription — before its value is determined. "We're talking about a drug with a lot of potential risks," he says. Among the risks: kidney toxicity and increased susceptibility to infection.

Responding to criticism from U.S. researchers, Andrieu says, "This is their own problem. Maybe they're right to criticize, maybe they're wrong." His group announced the results in a press conference rather than at a scientific meeting or in a publication in order to get the word out quickly, he says.

If cyclosporine does work, it presents a paradox: How can an immune suppressor reverse a syndrome caused by a suppressed immune system? It does so by slowing or stopping interleukin-2, an immune system modulator, says Andrieu. Interleukin-2 inactivates the T4 cells, which are the cells infected by the AIDS virus. By "resting" these cells, Andrieu says, cyclosporine inhibits the viruses within them from replicating and spreading.

Allan Hess of Johns Hopkins University in Baltimore, who has studied the use of cyclosporine in organ transplants, hypothesizes that the drug could conceivably work by inhibiting the white blood cells that kill virally infected T4 cells. Other AIDS drugs currently under investigation work by inhibiting viral replication, but cyclosporine has not been shown to have this ability, says Hess.

Cyclosporine may share a limitation with other AIDS drugs under study — failure to cross the blood-brain barrier into the central nervous system. Recent studies have shown that the virus can infect brain cells (SN: 1/12/85, p. 22); drugs that don't cross the barrier will miss some of the viruses. Cyclosporine, says Hess, is generally thought not to cross the blood-brain barrier.

The maker of cyclosporine, Sandoz, Ltd. of Basel, Switzerland, is planning to begin U.S. clinical studies after consultation with the Food and Drug Administration.

—J. Silberner

The pill and breast cancer

Two years after birth control pills were linked to breast cancer, women who have avoided oral contraceptives will be reassured by a new federal study exonerating the pill — or will they? On one side, results reported in the Nov. 2 LANCET find no relationship between the pill and development of breast cancer in women under 45. On the other side, skeptics, including LANCET editors, fear the report will prematurely settle a serious debate years before all the evidence is available.

In the recent study, researchers at the Bethesda, Md.-based National Institute of Child Health and Human Development (NICHD) and Centers for Disease Control in Atlanta tested the pill-cancer connection in a case-control study of more than 4,000 women aged 20 to 45. The study was prompted by the "pill scare" that followed two 1983 reports suggesting the use of oral contraceptives by young women increased their risk of developing breast cancer before 45 years of age (SN: 10/29/83, p. 279). Statistics underscored the need for such a study. The pill is the leading reversible method of birth control in the United States, with more than 8 million current users (70 to 80 percent of all U.S. women have used it at some time); and 1 out of every 12 women eventually will develop breast cancer.

As part of the NICHD's larger Cancer and Steroid Hormone Study done between Dec. 1, 1980, and Dec. 1, 1982, interviewers had questioned 2,088 women recently diagnosed with breast cancer and 2,065 controls without the disease and living in the same geographic areas. To prompt the subjects' recall of past pill use, interviewers had used a calendar of important events in each subject's life and pictures of different pill types.

Using these previously gathered data, principal investigator Bruce Stadel of NICHD and others analyzed pill-use habits earlier indicted as possible risk factors. One 1983 report from British scientists at Radcliffe Infirmary in Oxford had found that women who use the pill for longer than four years before having their first child appear to be three times more likely to develop breast cancer before age 45 than are those who do not use it before having their first child. The other 1983 report, from a group at the University of Southern California School of Medicine in Los Angeles (USC), had said that women who use pills with high levels of the hormone progestogen for more than four years prior to age 25 have four times the risk of developing breast cancer before age 37.

Stadel, speaking at an NICHD news conference last week, said the large numbers of women interviewed in the latest study lend statistical stability to conclusions that none of the pill-use factors examined in those two studies contributes to early-onset breast cancer. "[The study's relative risk analysis] constitutes strong evidence [that] pill use in the United States over the past 20 years ...has had no effect on the overall risk of breast cancer," he said. "We are reasonably confident that those earlier reports do not warrant continued concern."

Others are not so sure. Although an editorial in the same issue of LANCET calls the Stadel study "a powerful challenge" to earlier conclusions, it says possible biases in survey methods may account for the differences, meaning "firmer conclusions must perforce await more epidemiological investigation." And Brian Henderson, a coauthor of the 1983 USC study, told SCIENCE NEWS he agrees with the editorial's cautionary statements about geographic differences affecting pill use, as well as with the editors' concern that some cancer cases have not had time to develop since the pill was introduced in 1960.

Henderson, who says he considers the latest study results "less prone to possible error" than his own 1983 conclusions, adds that "[the Stadel study] doesn't necessarily disprove what we found, but shows we need more study." He and his 1983 coauthors are currently doing two more studies of the pill-breast cancer relationship. *—D.D. Edwards*