nevertheless lead by extrapolation to a virtually complete destruction by the year 2135, which more or less coincides with the time at which the World Bank estimates that global population will plateau at 11 billion. With the forests vanished or largely disrupted, up to half the world's species of animals, plants, and insects would disappear too.

Ariel Lugo of the USDA Forest Service in Puerto Rico dissented from this generally supported view. He suggested that many species would survive in the secondary forests that sometimes replace the rain forests, and that extrapolation of current trends might be misleading. "By changing the rate of deforestation only slightly you can get a species loss that is only 9% rather than 50% over the next few decades," said Lugo. Wilson argued that, on the contrary, simple extrapolation might be too conservative. "Population pressures in the Third World will certainly continue to accelerate deforestation during the coming decades."

According to David Raup, of the University of Chicago, a figure of 50% extinction would be closely comparable with the mass extinction of 65 million years ago, during which the dinosaurs finally disappeared together with 60 to 80% of the rest of the world's species. The difference between natural mass extinctions and the current extinction spasm, if indeed that is what it is, is twofold. First, unlike previous events, current losses involve large numbers of plant species. Second, the agent that is causing extinction—namely, human intervention—will persist, therefore potentially preventing the diversity rebound that typically occurs after natural events.

The degree of ignorance about fundamental processes underlying diversity and its response to disturbance is profound. For instance, Wilson notes that "the study of extinction remains one of the most neglected subjects in ecology." He added that "the magnitude and control of biological diversity is not just a central problem of evolutionary biology; it is one of the key problems of science as a whole."

One reason for the ignorance, and a measure of the value placed on this branch of biology, is the relatively modest funding that tropical biology currently receives: the figure stands at some $30 million a year in the United States, compared with at least $5 billion spent on molecular and cellular biology, including biomedicine. "It is a pity congressmen don't die of species extinction," quipped one participant.

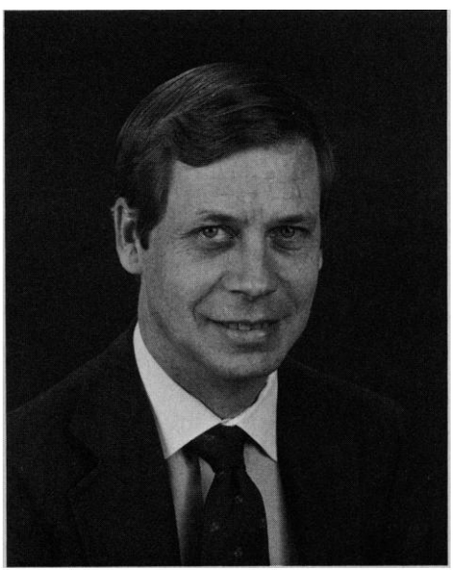
Ehrlich blames an understandable insensitivity rather than indifference. "Human beings have great difficulty in reacting to changes that occur on a scale of decades," he concluded. ■ ROGER LEWIN

Promising Results Halt Trial of Anti-AIDS Drug

Although not a cure for AIDS and in spite of some toxic side effects, AZT appears to increase the survival of a subset of AIDS patients who participated in clinical trials

OFFICIALS from the Public Health Service (PHS) and the Burroughs Wellcome Company have announced that AZT, an AIDS drug tested in clinical trials, prolongs the survival of some AIDS patients. The company has terminated its clinical trials prematurely and will make AZT available to additional AIDS patients who meet certain clinical criteria.

"AZT (3′-azido-3′-deoxythymidine) is not a cure for AIDS," said Robert Windom, assistant secretary for health, who spoke at a news conference announcing the recent decision. "Although the study results we are announcing today hold great promise for prolonging life for certain patients with AIDS, uncertainties remain: uncertainties about possible toxic effects, uncertainties about long-term benefits, or ill effects."



David Barry. *Overseeing development and testing of AZT for Burroughs Wellcome.*

Windom also indicated that he will help facilitate the process by which AZT is approved for commercial distribution.* First, Burroughs Wellcome must file an application for a new drug. Then, Harry Meyer of the Food and Drug Administration will oversee the approval process, which may be completed by January 1987. After the drug is commercially available, physicians will be able to dispense it by prescription. As a result, future clinical trials will probably include AZT alone or in combination with other drugs.

The impetus for the recent decision came from an independent data safety monitoring board (DSMB), which reviewed preliminary data from clinical trials that were designed to test the effectiveness of AZT in a carefully defined group of patients. Burroughs Wellcome enrolled "only AIDS patients who were within 4 months of their first episode of *Pneumocystis carinii* pneumonia," according to Dannie King of Burroughs Wellcome. "Patients with AIDS-related complex (ARC) and significant disease progression such as weight loss, thrush, fever, and herpes zoster, were also eligible for treatment on this protocol." Because of significantly lower death rates in patients receiving AZT, the DSMB concluded that it would be unethical to continue to withhold the drug from patients participating in the trial who were receiving an inactive placebo compound instead of the drug.

A total of 282 patients participated in the AZT clinical trials at 12 different testing centers in the United States. Only one patient died out of the 145 receiving AZT, but 16 of the 137 patients in the placebo group died—11 with AIDS, and five with ARC. The first patient entered the trial in February 1986 and the last patient was enrolled at the end of June. The trial was originally designed to last until December and premature termination admittedly compromises its full research value.

In addition to decreasing the mortality rate of AIDS patients with pneumocystis pneumonia, at least over the short term, AZT also seems to improve their quality of life. To varying degrees, AZT recipients had fewer serious medical complications, showed an increase in the number of circulating T4 lymphocytes, could respond to a

*Burroughs Wellcome will supply AZT free of charge to qualifying patients until the drug is available for sale. The patient's physician must be licensed to practice medicine in the United States and apply for the drug on behalf of an AIDS patient. The PHS and Burroughs Wellcome have established a toll-free information line (1-800-843-9388), open every day from 8 a.m. to midnight, for AIDS patients and their physicians.

mild immune stimulus in a skin test, and had an improved sense of well-being.

One of the advantages of AZT is that it crosses the blood brain barrier and can enter the brain and spinal cord. This property is likely to be of increasing importance as researchers continue to review clinical data, because as many as 60% of AIDS patients have neurological symptoms. These range from mild confusion to global dementia and can also include an impaired ability to move. According to Margaret Fischl of the University of Miami, AZT seems to improve the neurological symptoms of a small number of AIDS patients, but it is still too early to draw conclusions about its full effect on nervous system disease.

To date, the most serious toxic effect of AZT is that it inhibits the normal production of blood cells by the bone marrow. Forty patients who received AZT required transfusions for their anemia, compared to 11 patients from the placebo group who needed transfusions. Another common side effect of AZT was headache.

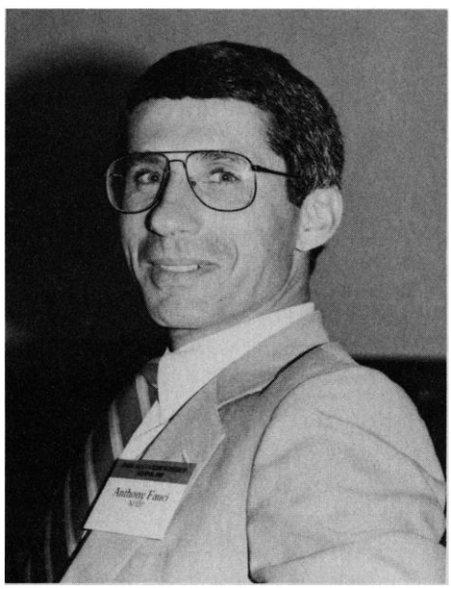
In addition to giving AZT to all of the AIDS patients participating in the Burroughs Wellcome clinical trial, the drug will also be made available to a much larger number of AIDS patients who meet certain clinical criteria. "The minimum criteria for treatment with AZT will be that AIDS patients have *Pneumocystis carinii* pneumonia, or PCP," according to David Barry of Burroughs Wellcome. PCP is the most common opportunistic infection in AIDS patients and about 60%, or over 6000 people, have the lung infection and may be eligible for AZT. AIDS patients with PCP usually live about 30 to 40 weeks, a time that seems to be extended by treatment with AZT.

The recently concluded clinical trials comprised the second phase of testing for AZT. The first phase, conducted by the National Cancer Institute (NCI), Duke University, and Burroughs Wellcome, lasted for only 6 weeks. It was designed to determine the safety of the drug in humans and at what dose level it became toxic. Nineteen patients participated in the early tests, 16 of whom are still living, according to Samuel Broder of NCI.

On 20 September, National Institute of Allergy and Infectious Diseases (NIAID) officials met with the principal investigators of 14 newly established treatment evaluation units "to discuss the impact of the AZT results on the design and implementation of future drug trials," said Anthony Fauci, director of NIAID. The units were funded in July and will test other drugs for AIDS, including dideoxycytidine, ribavirin, HPA-23, foscarnet, and interferon alpha. Fauci says that future clinical trials are likely to include tests of AZT alone or in combination with another drug.

On 24 September, NIH and Burroughs Wellcome officials decided on a more detailed description of the clinical criteria that AIDS patients must meet in order to receive AZT. The best candidates for future clinical trials may be patients that have not developed serious infections or illness. These include persons infected with the AIDS virus who show no symptoms of the disease, patients with early Kaposi's sarcoma affecting only the skin, and patients with chronically swollen lymph nodes. Fauci thinks that even after AZT becomes commercially available, "there will be people who are cautious enough about AZT and its side effects to participate in placebo-controlled clinical trials."

The data safety monitoring board that recommended the premature termination of the AZT trial is a six-member panel composed of clinicians, a biostatistician, and a bioethicist. None are employed by Burroughs Wellcome nor were any of the board's members involved in the clinical trials. The board met on 1 August, 10 September, and 18 September to evaluate preliminary clinical data from the AZT trial.



Anthony Fauci. *"Understanding how this drug works in AIDS patients could be one of the most exciting things right now."*

Even though the study reviewed by the board included ARC patients, "the termination of the study was based upon the results that were seen in a particular group of AIDS patients, those who recently had developed PCP," said Fauci. "But the story isn't over with AZT. AZT will be studied further in other groups and the data that have already been collected will be analyzed in more detail. We expect to learn more about AZT and its effect on a variety of other components of AIDS."

In fact, it is still too early to pinpoint exactly how and why AZT has decreased the mortality rate in patients with AIDS and pneumocystis pneumonia. The drug blocks the ability of the AIDS virus to replicate inside a host cell. It interrupts elongation of chains of DNA, making it impossible for the virus to complete DNA synthesis and thus reproduce itself. But how these molecular events, which were initially deduced by studying the action of AZT on virus-infected cells growing in laboratory culture dishes, translate into the clinical improvement of AIDS patients is still not clear.

"Scientifically, understanding how this drug works in AIDS patients could be one of the most exciting things right now," says Fauci. One clear effect that AZT seems to have in people is that it allows the immune system to restore itself partially, at least for a while. "We know that the number of T4 lymphocytes in patients receiving AZT increases, peaks, and then comes down, but the patients continue to do well," according to Fauci. Presumably, the time-delayed fall in the number of T4 cells occurs with bone marrow suppression.

But scientists have no direct evidence that AZT blocks viral replication in AIDS patients as it does in cultured cells. "There is no difference in our ability to isolate and grow the AIDS virus from patients who receive AZT," says Fauci. Fauci thinks that AZT may block the active replication of the virus in human cells, but that it may not affect virus that has inserted itself into the DNA of a host cell to remain there, perhaps for very long periods of time, in a dormant state.

The AIDS virus is spread by sexual contact with an infected person, by the exchange of blood during intravenous drug use, in contaminated blood or blood products, or from an infected mother to her infant during pregnancy or childbirth. As of 15 September, there were 24,859 reported cases of AIDS in the United States, and 11,170 patients are still alive. An estimated 1.5 to 2 million people are infected with the virus.

All of the health officials, as well as the representatives from Burroughs Wellcome stress that it is still too early to tell how effective AZT will be as a long-term therapy in AIDS. Only a few patients have received the drug for a year, and most have received it for 6 months or less. Thus, the potential effectiveness of AZT, as well as its potential toxicity, are simply unknown over the long term. It remains, however, the only therapy for AIDS that has shown even partial effectiveness. ■ **DEBORAH M. BARNES**