Swanson. Presumably, the additional stress caused by the moon's gravitational distortion of Earth's crust can, given nearly but not quite enough pressurization by new magma, touch off an eruption.

If CVO scientists are increasingly familiar with dome-building eruptions, they are considerably more uneasy about large explosive eruptions. There were only five of them at Mount St. Helens during the summer of 1980. They were predicted on the basis of precursory seismic activity, but only hours ahead. Two other volcanoes might serve as analogs—Bezymianny in Kamchatka and Santiaguito in Guatemala. They have been forming domes since 1956 and 1922, respectively, and have produced several large explosions each. Unfortunately, they have not been monitored closely enough to provide any reassuring precursors.

Swanson declines to speculate on when Mount St. Helens might produce its next explosive eruption, but he mentions three possible hazards that may yet arise. A catastrophic landslide might fall off the dome, or a new injection of magma into the plumbing system might lead to an explosive eruption. More likely, he says, congealing magma might cork the throat of the volcano as dome-building eruptions become less frequent. The resulting pressure buildup could produce a major explosion. "It's likely the dome will continue to grow episodically and perhaps it will have some relatively large explosions," says Swanson. "I wouldn't be surprised if we had a large explosion at any time."

The problem is that CVO scientists are not at all sure how to predict large explosive eruptions more than a few hours ahead. That should give little comfort to climbers in the crater this summer. If pressure builds deep within the mountain, the heretofore crucial monitoring of the dome may be of no use. Instead, predictions more than a few hours ahead will probably depend on detecting slow swelling of uncertain magnitude of the whole mountain.

"This worries us very much," says Swanson. "We don't really know what to expect if there would be some pressure increase. I have a nagging fear that we just wouldn't see it." Precursory swelling might be too small to be noticed, monitoring might be interrupted by bad weather, or increased seismicity preceding an explosion could easily be taken as a precursor of dome-building, he notes.

Obviously, the public pressure that led to the reopening of Mount St. Helens and its crater has done more than create new challenges for climbers. It is also pushing the science of volcano prediction near its limit. ■ **Richard A. Kerr**

Broad Issues Debated at AIDS Vaccine Workshop

Both scientific and policy issues, including the effect of an acceptable AIDS vaccine, the utility of certain preclinical tests, and the design of vaccine trials, dominated the discussion

"I think it is virtually certain that there will be initial clinical trials of an AIDS vaccine in the United States this calendar year," Gerald Quinnan of the Food and Drug Administration (FDA) said at a recent workshop on the subject.* In an atmosphere of not wanting to waste time, while striving to maintain high scientific standards for an AIDS vaccine, workshop participants raised many tough issues, few of which met with general consensus. Their comments will help to guide FDA officials who must identify quickly what requirements should be met by candidate vaccines as they enter clinical trials and what the designs of those trials should be.

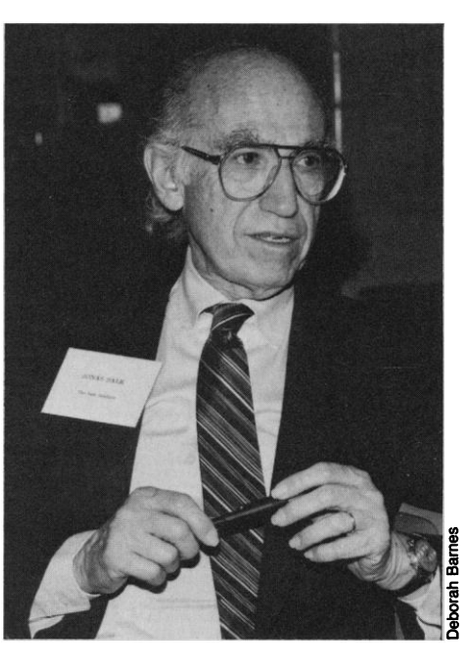
The FDA is now considering at least two proposals from researchers to do initial toxicity tests of candidate vaccines for AIDS in humans and anticipate several more proposals soon. But despite the ability of these and other potential vaccines to stimulate various test animals—mice, rabbits, guinea pigs, and primates—to make antibodies against the AIDS virus, none has induced protective immunity in chimpanzees, which, until very recently, were the only animals that researchers could infect with the AIDS virus.

Any new vaccine has to be judged both safe and effective by the FDA, and officials must determine that an AIDS vaccine meets these standards as well as passing requirements that are unique to the AIDS virus and the immune deficiency disease it causes. Workshop participants focused on three issues in particular. First, what is an acceptable end point for an AIDS vaccine trial—protection against infection or protection against viral transmission or disease? Second, how well do the results of preclinical tests predict vaccine efficacy in humans? And third, which human populations should receive test vaccines?

Nearly all researchers agree that an ideal AIDS vaccine should protect an immunized person from infection by the virus, but some doubt that such a vaccine will ever exist. To prevent infection, a vaccine must stimulate a spectrum of immune responses including production of antibodies directed against specific viral proteins and cell-mediated immune responses that are antibody-independent, says Anthony Fauci of the National Institute of Allergy and Infectious Diseases.

However, researchers are finding that the theoretical efficacy of an ideal vaccine is difficult to translate into reality because of two major obstacles. Dani Bolognesi of Duke University Medical Center in Durham, North Carolina notes that one is the high mutation rate of the AIDS virus. This results in many different viral strains against which a single vaccine may not be effective. The other is the necessity to protect against both free virus particles and cells infected with the virus. Bolognesi notes that, to date, none of the potential vaccines meet these criteria completely.

Some researchers question whether it may be unrealistic to require an AIDS vaccine to



Deborah Barnes

Jonas Salk *advocates identifying the in vivo immune responses that protect against the AIDS virus.*

*The "Scientific Workshop on AIDS Vaccines," held 25 to 27 March at NIH, was sponsored by the U.S. Public Health Service AIDS Task Force Subgroup on Vaccine Development and the U.S. Army Medical Research and Development Command.

protect against infection. For example, Donald Burke of Walter Reed Army Medical Center in Washington, D.C., says that an end point other than prevention of infection may be possible with an AIDS vaccine. "A vaccine may block transmissibility of the virus or disease progression," he says.

King Holmes of Harborview Medical Center in Seattle reported new data indicating that, by modifying certain immune reponses in an infected person—perhaps by preventing the decrease in T4 cells—an appropriately designed vaccine might reduce transmissibility of the virus. Citing other examples of abnormal regulation of immune responses in AIDS patients, Quinnan suggests that vaccines targeted toward promoting normal immune response regulation might reduce viral transmission.

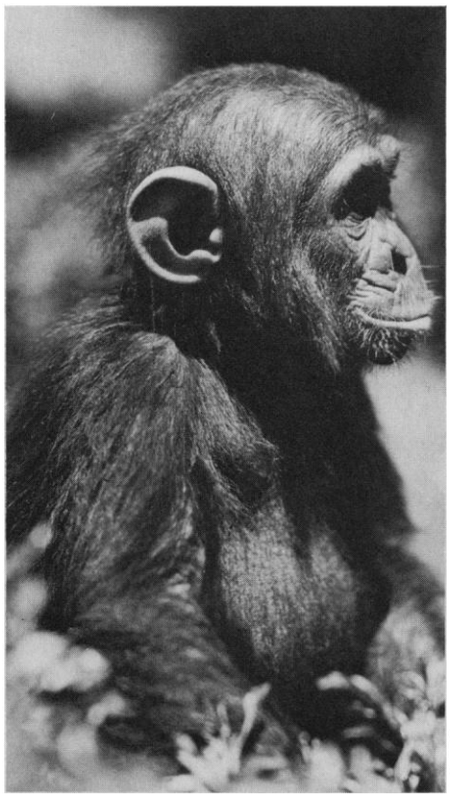
But Robert Gallo of the National Cancer Institute says that, in order for a vaccine to be effective it must prevent infection by the AIDS virus. He indicates that his laboratory is developing a "cocktail of immunogens," a collection of antigens in the vaccine preparation that he hopes will stimulate a multiplicity of immune responses and protect against many different strains of the AIDS virus.

Addressing a second issue, workshop participants challenged how well certain preclinical tests—done in vitro and in animals—predict a candidate vaccine's safety and efficacy in humans.

Burke reflected the frustration felt by many about the usefulness of in vitro screening of potential vaccines. "I have yet to see any convincing data that the ability of antibodies to neutralize the AIDS virus in vitro confers on them an ability to neutralize virus in vivo. It brings into question whether what you are measuring in vitro in any way represents what is happening in vivo."

Nevertheless, many researchers have built upon in vitro results to justify the next level of vaccine testing, namely, screening for protective immunity in chimpanzees. Chimpanzees do not develop an immune deficiency disease like AIDS, although they are susceptible to infection by the virus. About 20 chimpanzees have been given various prototype vaccines and some have been challenged by injecting virus, but the results so far indicate that no vaccines have prevented infection, according to data from Larry Arthur of NCI in Frederick, Maryland, and George Todaro of Oncogen in Seattle.

Jonas Salk of the Salk Institute in La Jolla, California, cautions against using chimpanzees for vaccine screening, suggesting that they be used instead to study what components of an immunological response would protect them from infection and what parts of the AIDS virus induce that response. "I would use chimpanzees to determine which immunogens of the virus are required for inducing immunity to infection," he says.



Jatti/FPG

Chimpanzees *are in short supply for vaccine screening.*

Fauci thinks that animals should be used primarily for safety testing rather than extensive vaccine screening. "The development of a good animal model for AIDS is very important, but the chimpanzee model is not strictly analogous to human infection," he says. "If a vaccine protects the chimpanzee, it doesn't tell you what will happen in humans. And if it doesn't protect, it still doesn't tell you what will happen."

But Gordon Dreesman of Southwest Foundation for Biomedical Research in San Antonio, Texas, has a different perspective. "It is too early to say that the chimpanzee is not a good model for AIDS," he says. Dreesman, Jorg Eichberg, also of Southwest Foundation, and their colleagues are currently doing studies to determine if other viruses that commonly infect human AIDS patients may act as cofactors and alter a chimpanzee's response to the AIDS virus, thus making it more similar to the human response.

The debate about relying solely on chimpanzees for vaccine screening may soon be a moot one, however. New data from Patricia Fultz of the Centers for Disease Control (CDC) in Atlanta indicate that rhesus macaque monkeys can be persistently infected with a different virus that may cause AIDS, called LAV-2 for lymphadenopathy-associated virus type 2. Luc Montagnier of the Pasteur Institute in Paris and his colleagues have reported that LAV-2 causes AIDS in some West African patients. The potential for using LAV-2 infections in macaques as a model for human AIDS is hailed by other researchers, including Salk as a " . . . very good idea. It will give us a tremendously useful research tool for evaluating in vivo responses to a vaccine," he says.

Throughout the workshop, participants raised a third area of concern, namely, what groups of people should receive test vaccines and how clinical trials should be designed. Complicating these decisions are ethical and legal issues—product liability, in particular—as well as the debate about whether a vaccine should prevent infection or disease.

A central question in identifying who should be given a candidate AIDS vaccine, is whether to include people already infected with the virus. A year ago, at a meeting sponsored by the Public Health Service at Coolfont, West Virginia, virtually no one seriously considered vaccinating someone who is already infected. But now, these ideas are changing.

Salk is among those who think that it may be possible to design a vaccine that will protect a person already infected with the AIDS virus from developing disease. And Wade Parks of the University of Miami School of Medicine in Miami notes that, most of the 1000 or more children in the United States with AIDS are born infected with the virus, making them a population that would be necessary to immunize "post infection."

"If a vaccine were available and the mother were seropositive, I would vaccinate children at birth," says Parks. In order to be able to determine which children should be vaccinated, he says, pregnant women would need to be tested on a medical basis to determine if they carry the AIDS virus. But vaccinating children against AIDS may differ from vaccinating adults and Parks suggests that researchers plan a series of vaccine trials to be conducted specifically in children.

Determining which adults should be included in vaccine trials is also a complex issue. In people at "high risk" for AIDS, including gay and bisexual men, intravenous drug users, spouses of infected persons, and prostitutes, it may be very difficult to distinguish whether certain immune responses, including antibody production, are due to the vacccine or to infection with the virus. Some researchers advocate the use of a marker in the vaccine preparation to make the distinction possible. Another complicating factor is that the people at high risk for

AIDS often carry other infections as well and may respond to immunization against the AIDS virus differently than people who are not multiply infected. Finally, some argue that it might be unethical to withhold even a candidate vaccine from people at high risk for AIDS.

Outside the United States, Daniel Zagury of the Pierre and Marie Curie University in Paris and his colleagues have already begun to test a candidate vaccine for AIDS by injecting himself and 12 Zairian volunteers with a vaccinia virus that contains a protein from the AIDS virus. But within the United States, clinical trials of any new drug or vaccine, including those for AIDS, will occur in three phases—testing for toxicity (phase I), determining proper doses and timing between doses (phase II), and evaluating efficacy (phase III).

Existing prototype vaccines for AIDS include other components that may by themselves elicit side effects—sometimes another virus, which is genetically engineered to express a protein from the AIDS virus, or an adjuvant, a large molecule that is chemically linked to a protein from the AIDS virus to boost the immune response. Samuel Katz of Duke University Medical Center stresses that careful controls are needed at all stages of clinical testing to determine which components of the vaccine preparation may be responsible for any side effects that might occur.

The initial toxicity tests should last between 3 months and 1 year, according to Fauci, but determining whether or not a vaccine is effective will make phase III trials last much longer. The duration of a phase III trial will also be extended if the end point is prevention of disease rather than prevention of infection.

James Curran of the CDC raises a related issue. "Because of the long lag period between infection and serious disease, we will also need to enlarge the sample size to compensate for the small number of people who will get disease in a short period of time," he says.

June Osborn of the University of Michigan School of Public Health in Ann Arbor emphasizes that all volunteers who receive test vaccines need to be counseled about how to avoid becoming infected with the AIDS virus. All researchers agree that counseling is essential and that volunteers must be followed for very long periods of time. But they also recognize that the net result of encouraging people to reduce their risk of getting AIDS, which may lower the rate of new infections, will be to increase the amount of time needed to determine whether a vaccine is effective and prolong the process. ■ **DEBORAH M. BARNES**

Report Urges Funds for Conservation Biology

A report by the Office of Technology Assessment outlines the accelerating rate of species extinction caused by human activity and suggests options that Congress should consider

DURING the past year the issue of conservation biology—and specifically biological diversity—has been in the news to an unprecedented degree, with major international conferences sponsored by the Smithsonian Institution and the National Academy of Sciences in Washington and the New York Zoological Society in New York. Perhaps the prime reason for this quickened pace of activity is the relatively recent realization of the very high rate of extinction of species caused by human activity, both by megadevelopment projects and by creeping environmental destruction and fragmentation. Completing this sharpened focus on the deteriorating state of the biological world is the recent publication of a report by the Office of Technology Assessment (OTA), entitled "Technologies to maintain biological diversity."*

"The report is more comprehensive than anything that has gone before," says David Ehrenfeld of Rutgers University and a member of OTA's advisory panel. "It represents a unique compilation of information on the threat to biological diversity and the approaches by which species can be protected." Representative James H. Scheuer (D–NY), who is chairman of the House Subcommittee on Natural Resources, Agricultural Research and Environment, says "I am very pleased with the thoroughness of OTA's analysis of this urgent global problem. However, the time for describing the problem is passed. It is necessary that we act immediately to remedy the loss of biological diversity." Scheuer's office is currently considering a number of legislative options that could be introduced via his subcommittee. Hearings are to be held in May or June.

Baboons under threat. *The home range of these baboons in Kenya is being fragmented by development for farming land. Effective conservation in the end demands that large portions of natural ecosystems are kept intact.*

The OTA study, which was initiated a little over 2 years ago, was requested by several congressional committees, including the House Committee on Science, Space, and Technology and the Senate Committee on Foreign Relations. Representative Gus Yatron (D–PA), who is chairman of the

*"Technologies to maintain biological diversity," published by the Office of Technology Assessment, 31 March 1987, U.S. Government Printing Office, Washington, D.C. 20402, $15.