BIOMEDICAL RESEARCH

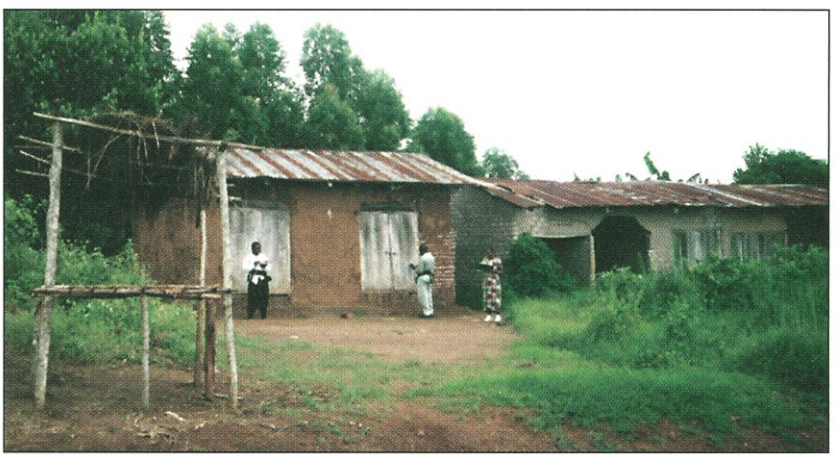
Study of HIV Transmission Sparks Ethics Debate

A study on AIDS transmission in Uganda has reignited a smoldering debate on the ethics of research in developing countries. Last week, *The New England Journal of Medicine* published a paper reporting that HIV-infected individuals are much less likely to pass their infection on to a sex partner if they carry a low number of viral particles in their blood. But in an unusual move, the journal also published a strongly worded editorial questioning the study's ethics.

The journal's editor, Marcia Angell, objected to the fact that the study did not offer participants treatment for HIV infection and uninfected individuals were not told that their partners were HIV-positive. The study's authors counter that the ethical requirements Angell advocates would make research impossible in the developing world, where 90% of HIV-infected people live.

Such debates are not new. Scientists have struggled for several years with the ethics of HIV studies in countries where expensive and complex therapy is unavailable. The United Nations Programme on HIV/AIDS (UNAIDS) issued a so-called guidance document on conducting AIDS vaccine trials in late February without reaching a clear consensus despite months of debate (*Science*, 3 July 1998, p. 22). The document recommends that participants in trials receive care and treatment for HIV and its complications, "with the ideal being to provide the best proven therapy, and the minimum to provide the highest level of care attainable in the host country." The U.S. National Bioethics Advisory Commission (NBAC) is also trying to come up with recommendations for U.S.-sponsored studies.

The paper published last week is a retrospective analysis of a study, conducted from 1994 to 1998, designed to determine whether intensive treatment of sexually transmitted diseases (STDs) such as syphilis and chlamydia might help to prevent HIV transmission. A research team led by public health physician Maria Wawer of Columbia University, with colleagues from the United States and Uganda, tested more than 15,000 adults in 10 rural communities for infection with HIV and other STDs. The team then mass-treated study participants in five communities with antibiotics, whether or not they showed STD symptoms. Participants in five control communities were told of their test results and were referred to free clinics, which the researchers stocked with antibiotics. But they did not automatically receive doses of drugs. When a preliminary analysis of the data showed that mass treatment with antibiotics lowered the rate of other STDs but did not influence HIV transmission, the researchers ended the study and gave all participants the antibiotic therapy. The team reported the initial results last year in *The Lancet*.



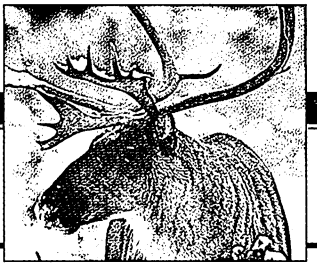
Door to door. Researchers gather information on HIV and other sexually transmitted diseases in a village in rural Uganda.

CREDIT: M. Z. CHEN AND M. WAWER/THE JOHNS HOPKINS SCHOOL OF PUBLIC HEALTH

In an attempt to find out if other factors besides antibiotics made a difference in transmission, the researchers went back to their records and matched up sexual partners, something they had not done during the study period. They identified 415 long-term couples in which, at the beginning of the study, one partner was infected and the other was not. Ninety of the uninfected partners became infected during the study. After analyzing a variety of factors, including age, the presence of other diseases, travel history, and the number of sexual partners, the researchers concluded that the most significant factor was the amount of virus in the infected partner's blood. The chance of transmission doubled with every 10-fold increase in viral load.

Angell was especially troubled that the researchers left it up to HIV-infected participants to inform their at-risk spouses or partners. The fact that the researchers identified the discordant couples only after the study ended does not mitigate their responsibility, Angell says. The team had the data, and "if you have an identifiable partner, you owe it to that partner to see that they are informed," she says. However, co-author Ronald Gray of The Johns Hopkins University says Ugandan national policy prohibits a health worker from telling a third party about an individual's HIV status. All HIV-positive participants were encouraged to tell their partners, he says. The team also provided free condoms and conducted HIV awareness and prevention campaigns in all the villages. In addition, personal and couples counseling was freely available, Gray says.

Angell and Peter Lurie of the consumer-advocate group Public Citizen in Washington, D.C., are both troubled that study participants with HIV were left untreated. They argue that researchers should provide the best available treatment to their subjects even if such care is not usually obtainable where the research is conducted. But Wawer and her team say that the cocktail of antiretroviral agents in use in wealthy countries would be impossible to distribute in rural Uganda, no matter the cost. The complicated regimen involves taking pills at regular intervals and requires close monitoring by a clinician. That is simply impossible in villages without medical services of any kind, she says. Edward Mbidde, a medical



oncologist at Makerere University in Kampala, Uganda, says that holding all studies in the developing world to the same standard of care available in wealthy countries would make such research impractical.

But Lurie disagrees. "If you're able to pull off the study, you should be able to pull off administering medications to people," he says. Drug companies might have been willing to donate the drugs for free, he says, and a different study design "might have produced useful information about the ability of people in rural Africa to take these drugs."

The debate is unlikely to be resolved soon. NBAC will continue to hear testimony from panels of international researchers, and it plans to issue draft guidelines by early summer. But it faces a tough task: "In seven meetings around the world, we were simply not able to get a consensus" on what treatment should be provided for HIV-infected participants in poor countries, says Barry Bloom of Harvard University, who headed the UNAIDS Vaccine Advisory Committee that drew up the recently issued guidelines. He says researchers attempting to design ethical trials need to ask themselves, "Even if you can't provide antiretrovirals, can you do better than nothing?" It's a question that all parties agree desperately needs an answer.

–GRETCHEN VOGEL

ECOLOGY

Five Researchers Die In Boating Accident

A spring-break research trip ended last week in a disaster that left the tight-knit world of professional ecologists mourning the loss of five of its own. The scientists —two Americans from the University of California (UC), Davis, and two Japanese from Kyoto University—died after their boat capsized in high seas off Baja, Mexico. A third Japanese scientist was missing and presumed dead as *Science* went to press.

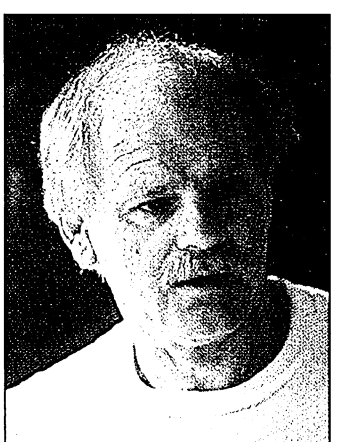
The victims of the changeable weather in the Sea of Cortez were expedition leader Gary Allan Polis, 53, a spider and scorpion expert at UC Davis; Michael Rose, 28, a postgraduate researcher in Polis's lab; termite ecologist Takuya Abe, 55, of the Center for Ecological Research at Kyoto University; and junior colleagues Masahiko Higashi, 45, and Shigeru Nakano, 37.

Polis's 17-member team set out around noon on 27 March in two small boats for a 6-kilometer return voyage from a study site on the island of Cabeza de Caballo to the isolated Mexican port of Bahía de los Angeles. The vessels became separated in windswept seas during a sudden storm. Polis's boat, which carried nine people, capsized about 500 meters offshore, survivors say. Polis apparently died of a heart attack after clinging to the swamped craft for several hours, while the other victims drowned attempting to swim to shore.

Occupants of the second boat—which carried members of a science tourism group from the Earthwatch Institute of Maynard, Massachusetts—returned to search for Polis's boat after it failed to appear. At 10:30 p.m., they reported the disappearance to Mexican authorities, who began an extensive search that eventually led to the recovery of the bodies.

The accident claimed the lives of both prominent practitioners and younger academics just beginning to make their mark. Polis, whose work on insects had been highlighted in popular magazines and even a children's book, had won the Ecological Society of America's Aldo Leopold Award and more than $500,000 in grants from the National Science Foundation (NSF) over the last decade. Abe presented a lower profile, but he was well known in his field for studies of the complex cooperative relationships between termites and plants. NSF director Rita Colwell issued a statement praising all five scientists as "examples of courage" who "put their commitment to knowledge before their comfort and personal security."

–DAVID MALAKOFF



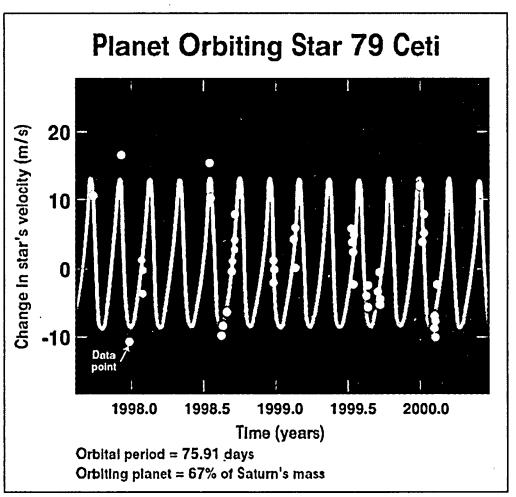
Tragedy. Gary Polis, above, and Takuya Abe were leaders on the trip.

CREDITS: (LEFT TO RIGHT) D. BARRON; G. MARCY/UC BERKELEY

ASTROPHYSICS

New Extrasolar Planets Hint at More to Come

The planet hunters have done it again. On 29 March, NASA announced that astronomers at the University of California, Berkeley, and the Carnegie Institution of Washington had bagged two new planets that circle other stars. Less massive than Saturn, the objects are the smallest extrasolar planets yet found—proof that astronomical techniques are now sensitive enough that scientists could spot our own solar system from afar. The discovery has sparked hopes that glimpses of even smaller planets, Uranus-sized and under, are soon to come.



Cosmic dance. Back-and-forth motion of stars points to ever smaller planetary companions.

"They're pushing and pushing and pushing," says Heidi Hammel, an astrophysicist at the Space Science Institute in Boulder, Colorado. "They'll probably be able to push down to Uranus's mass," she says—possibly within a year.

Over the past half-decade, the discoverers —Geoff Marcy at Berkeley and Paul Butler at Carnegie—have found roughly two-thirds of the 30 or so planets known to orbit distant suns. Because the light coming from those gassy planets is feeble compared to their parent stars' brilliance, they are nearly impossible to see with a telescope. Instead, Marcy and Butler detect them indirectly, by studying how they affect the stars they orbit.

Thanks to gravity, a planet and a star tug on each other with an equal and opposite force. As the planet pulls on the much more