Mathematical model stirs AIDS controversy

"Provocative" seems an understatement for a speculative new report suggesting that early treatment with zidovudine (AZT) or similar antiviral agents, while benefiting infected individuals, might indirectly increase both the number of infections and the daily death toll from AIDS in certain population groups.

Yet the report's authors – three British biologists who base their conclusions on a mathematical model chock-full of controversial assumptions – emphasize that they do not recommend stopping early drug treatment for people infected with the AIDS-causing virus, or HIV.

"Not for an instant are we suggesting that one should modify current practices in giving [zidovudine]," says Robert M. May of Oxford University. "But [we are] saying that the drug should be accompanied by intensive counseling and that more thought should be given to the possibility of [HIV-infected individuals] infecting others, as well as to simply keeping people alive."

May and his collaborators, Roy M. Anderson and Sunetra Gupta of the University of London, say their model offers only a crude assessment of the effects of zidovudine therapy on the spread of HIV by infected people who have not developed symptoms of AIDS. Zidovudine has been shown to delay disease progression in these individuals (SN: 8/26/89, p.135).

However, the researchers contend, the new analysis indicates that among populations in which HIV transmission proceeds relatively slowly – such as certain groups of heterosexuals – early treatment can promote transmission and lead to a higher death rate. In contrast, they say, among groups that generally transmit the virus rapidly – such as intravenous drug users and some populations of male homosexuals – both the patients and their communities benefit from early treatment of HIV infection.

May and his co-workers, who describe the study in the March 28 NATURE, based their model on two widely disputed assumptions. They postulated that zidovudine can only temporarily lower the amount of HIV in blood and semen, and they assumed that people receiving early anti-AIDS treatment are no more likely to avoid disease-spreading behaviors than are people who test HIV-positive but do not receive treatment.

Under such circumstances, early zidovudine therapy may enable asymptomatic individuals to stay healthier or even live longer, but this reprieve would also increase the possibility that they will infect many others, according to the researchers' model. For certain populations, the model indicates that deaths resulting from an increased infection rate would statistically outweigh the extra months or years of survival potentially gained from early treatment, and would thus lead to higher overall mortality from AIDS.

Paul Volberding of the University of California, San Francisco, argues that the researchers relied on data from patients with advanced cases of AIDS in assuming that zidovudine reduces blood concentrations of HIV for only a year or less. More recent studies hint that the drug can lower viral concentrations for two years or more in asymptomatic patients, notes Volberding, who heads a multicenter clinical trial of zidovudine.

He also questions the "cynical" assumption that asymptomatic HIV-positives who seek treatment don't change their behavior. "By the time an infected person has started [drug] therapy, he has come to grips with the nature of his disease, and that will certainly translate into a change in behavior," he says.

"Right now it's just very difficult to get good numbers for a model like this," adds David D. Ho, an AIDS researcher at the New York University Medical Center in New York City. "If you put garbage in, you get garbage out."

Martin Delaney, a spokesman for Project Inform, an AIDS information center in San Francisco, worries about the report's social impact. "To make a lot of assumptions and present this kind of modeling just contributes to hysteria, and I frankly think it's irresponsible," he asserts.

"I can see why people find it [our report] worrying," says May. "God knows that these [HIV-infected] people have enough on their plate without the thought that somebody is suggesting that now there's an additional problem with a drug that seems to be offering some help. We're just saying that what is unequivocally to the benefit of an individual can become more complicated when you look at it from the level of an entire population."

– R. Cowen

Cracking open the center of a temblor

Like expectant fathers of yesteryear, confined to pacing in the waiting room, seismologists cannot actually witness the birth of an earthquake. Instead, they must rely on information gathered by listening devices placed on the ground surface, far from where the action occurs.

Despite this handicap, a new generation of instruments monitoring northern California's Loma Prieta quake has given researchers their best glimpse yet of a fault beginning to rupture.

The instruments, called broadband seismometers, can record both long- and short-period waves created by earthquakes. Unlike other monitoring devices, which become overwhelmed almost instantly by intense shaking, they can continue to record seismic waves when a quake hits nearby. California scientists have deployed these seismometers for several years, but the Loma Prieta temblor of October 1989 was the first large quake to hit an area equipped with them.

The devices that recorded Loma Prieta are among the simpler broadband instruments available today, and they caught only the first few seconds of the seismic waves before succumbing to the shaking. But even that short span of data has provided unprecedented information, says David Wald of the California Institute of Technology in Pasadena. He and his colleagues presented their findings in San Francisco this week at a meeting of the Seismological Society of America.

The researchers report that Loma Prieta started with a perplexing prologue of weak, long-period vibrations. Wald describes the quake as beginning with a low groan that eventually turned into a loud chorus of both long- and short-period shaking.

Scientists are still debating what happened at the beginning of the quake, says study coauthor Thomas H. Heaton, a seismologist with the U.S. Geological Survey in Pasadena. At first, the researchers thought the weak initial waves might represent a small shock preceding the magnitude 7.1 main shock. But the long-period trembling doesn't resemble a normal small earthquake, which has many more short-period vibrations, Heaton says.

Loma Prieta's type of preliminary shaking may not be so unusual. Other large California earthquakes have started off with small precursor shocks immediately before the violent shaking. But because these occurred before the use of broadband instruments, it's not clear whether they had similar long-period vibrations, says Heaton.

The kind of information collected by broadband instruments "is very important for understanding how the rupture starts," says Hiroo Kanamori, a seismologist at Caltech.

The predominance of long-period waves during the first 2 seconds suggests that the fracture initially spread smoothly and slowly from the earthquake hypocenter, located about 18 kilometers below the surface. Then, Wald proposes, the rupture grew more erratically, stopping and starting in a motion that produced many more short-period vibrations.

– R. Monastersky

News of the week continued on p.203