

land's at Irvine, agrees that there could be a place for large-scale "geo-engineering."

But Cicerone knows from experience how easily promising schemes for tinkering with stratospheric chemistry can go bust. Three years ago, he and his colleagues proposed in *Science* that judicious injections of small hydrocarbon molecules such as propane—delivered by a fleet of high-flying tanker airplanes—could shift the complex chemical balance in the stratosphere away from ozone destruction. More recently, however, they reanalyzed the chemistry of this "cure" and found that it would almost certainly exacerbate ozone depletion. Cicerone, along with Rowland and other atmospheric

chemists *Science* contacted, believes Wong would be similarly blind-sided.

For one thing, notes Cicerone, Wong and his colleagues had to inject 20 times as many charges into the chamber as there were chlorine species to deactivate. Other molecules must have sopped up the charges, a process Cicerone says "would be an enormous problem" in the real atmosphere. Even if the charges did reach the chlorine and inactivate it, adds Molina, the resulting chloride ions could combine into chlorine molecules; solar radiation could then blast the molecules apart into a brand-new pair of ozone-eating chlorine atoms. "My bottom line," says Cicerone, "is that you could do this [cause ozone

recovery] in a few cubic meters of air in a laboratory, but you cannot scale it up" to the real stratosphere.

Wong admits that "a lot more needs to be done" to make his scheme workable—but he stands by it. He is convinced that enough of the charges would have the intended effect to warrant testing the technique in the real world. "I have come up with a concept and proved it in principle," he contends doggedly. But to Rowland, planetary engineers like Wong still have a long way to go. "So far," he says, "no one who has talked about remediation has come anywhere close to having a process that can actually do it."

—Ivan Amato

AIDS VACCINES

Immune Response Corp.—Take Two

Scientific data are difficult to evaluate at huge conferences, especially when the presentation attracts standing-room-only crowds, the klieg-light glare of TV cameras, and stock analysts chattering into cellular phones. That was the scene last July at the international AIDS conference in Berlin when results were unveiled from the first double-blind, placebo-controlled trial of a vaccine designed to treat people already infected with HIV—a "therapeutic" rather than a preventive vaccine.

In that highly charged setting, the data took a beating, as did Immune Response Corp. (IRC), the company developing the vaccine in collaboration with Rhone-Poulenc Rorer Inc. Now, however, an extensive analysis of the trial has been published in the June issue of the *Journal of Infectious Diseases*, and while no one is claiming the vaccine works, many researchers agree with the paper's conclusion: The vaccine's effects appear encouraging—albeit modest—and the studies should be expanded. "It's enticing," says Duke University's Dani Bolognesi. "It's not a wash."

That's a significant turnaround from the reception IRC's therapeutic AIDS vaccine received in Berlin—and before. From the beginning, the project was subject to intense scrutiny, partly because it was launched by IRC board member Jonas Salk, of polio vaccine fame. When Salk proposed the idea in a 1987 *Nature* article, many researchers doubted injecting a vaccine into an infected person would have any effect. "The concept that you could give more antigen [a substance that triggers an immune response] to someone who already has a lot of that antigen and expect biological impact is stretching it," says

James Kahn, associate director of the AIDS program at San Francisco General Hospital.

As the paper explains, the study did not evaluate whether the vaccine, an inactivated form of HIV minus the surface protein gp120, can slow the progression of disease and extend the lives of those infected with HIV. Instead, the 1-year trial in 103 healthy, HIV-infected people at nine U.S. sites assessed "surrogate markers" of disease progression such as the decline of CD4s, key white blood cells, and the increase in levels of HIV. "We got consistent [positive] results on all the markers," says Richard Trauger, IRC's chief immunologist on the study and the paper's first author.

Central to the study was a test that measures levels of HIV DNA, or "viral load," in patients' blood cells. This test, which relies on the polymerase chain reaction (PCR),

showed that after 1 year, HIV in treated patients increased an average of only 14%, while the amount in controls increased 56%. IRC's François Ferre, who developed this PCR assay, adds that he was particularly impressed that for the first 6 months

after the vaccinations, HIV levels in some patients remained stable. The reliability of the assay was criticized in Berlin, but now it has ceased to be a major issue. "I can't find anything particularly wrong with this assay," says Brooks Jackson, who heads the virology committee for the AIDS Clinical Trials Group of the National Institute of Allergy and Infectious Diseases (NIAID).

In addition to viral load data, the paper reports that CD4 cells as a fraction of all T lymphocytes—a measure some researchers believe is more telling than absolute CD4

counts—fell only marginally in treated patients (an average of 0.164%) but underwent a moderate drop in controls (5.03%). And the vaccine, which didn't cause any serious side effects, also seems to have boosted the cell-mediated arm of the immune system, which clears infected cells, and boosted some anti-HIV antibody levels. By and large, however, researchers are more interested in the HIV DNA data, because they assume it provides a better measure of disease progression.

Researchers interviewed by *Science* urged that these results be kept in perspective. "I believe the data, but I'm not all that impressed," says David Ho, who heads the Aaron Diamond AIDS Research Center. Jackson, who works at Case Western Reserve University in Cleveland, is of a similar mind. "It may be statistically significant, but it's modest," Jackson says. Then again, he adds, "I didn't think there'd be this much." Others say the data warrant a larger study. "There's something interesting there going on with viral burden, and we need to find out more," says Steven Schnittman, chief of the medical branch at NIAID's Division of AIDS.

Even skeptics like Kahn are getting on board; he is talking to IRC about leading a large-scale trial of the vaccine. "We don't have a lot more to offer, and there's the potential to gain scientific information to move forward," he says. Other researchers are also taking a different tone. Retrovirologist Don Francis of Genentech, who has long been skeptical about therapeutic HIV vaccines, says that although the IRC vaccine "may not be penicillin," he now believes the approach has merit. "We have to throw away the biases engendered in Berlin," says Francis. "Now we should try to ignore the hype and the past and look at the data." The most significant data, of course, would be those showing improvements in life span, and IRC hopes to launch a trial by the end of the year to find out whether the vaccine can delay AIDS symptoms and lengthen life.

—Jon Cohen

"Now we should try to ignore the hype and the past and look at the data."

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