

is leaking in and out, for example, and how much carbon dioxide is being scrubbed from the atmosphere. Broecker says he's convinced that managers are now running the facility as advertised. "If they had big sins to cover up, they would never have let us in," he argues.

Still, he and his collaborators, like other scientists doing work at Biosphere 2, were shaken by the advisory committee's resignation last month. "Originally, we thought it was a very bad omen," says Jeff Severinghaus, a graduate student of Broecker's. Now that he and Broecker have spoken to a committee member and learned some of the background, says Severinghaus, "we think it's not such a big deal."

But the committee's rocky tenure shows that Biosphere 2's management is still a long way from being a model of openness. Committee members and scientists say that SBV, as a private company, has had trouble adapting to the scientific culture and its free-wheeling exchange of information. Collaborating with researchers is "an educational process for

SBV," says Phillip Dustan, a biologist at the University of Charleston who is working as a consultant and doing basic research at Biosphere 2. "They're used to working in secret—[it's] that corporate mentality."

For example, says committee member Gerald Soffen, director of university programs at NASA-Goddard, the committee heard about the oxygen problem only after SBV had decided to relieve it by pumping in fresh oxygen. "They didn't really need us to do more than bless" the decision to add oxygen, Soffen says. In January, SBV even added three new members to the committee without consulting the original eight members. Most upsetting of all, say some committee members, SBV ordered the search firm looking for a scientific director not to talk to Lovejoy and justified the ban as necessary for preserving the search's integrity.

Predictably, some committee members doubt whether Corliss, who had been working on a model of Biosphere 2's biogeochemical cycles while at NASA, is up to the job of

directing research at Biosphere 2 and mediating between scientists and management. Though a respected scientist who helped pioneer the study of life at deep-sea hot springs, Corliss has never held an administrative position. "I just do not see Jack running anything like that," Soffen says.

Corliss, for his part, thinks he'll manage just fine—and he seems unconcerned that he won't have the full committee's advice. "The people who couldn't work with us left," he says, and he's not looking for replacements. Though he will continue to receive advice from a few committee members, "we won't have any more committees. I think we know what we're doing." All decisions, he adds, will be made "within the organization"—including the selection of the scientists who have access to Biosphere 2 data. The many scientists who still see bright possibilities within Biosphere 2's dome can only hope that "the organization" takes their interests to heart.

—Traci Watson

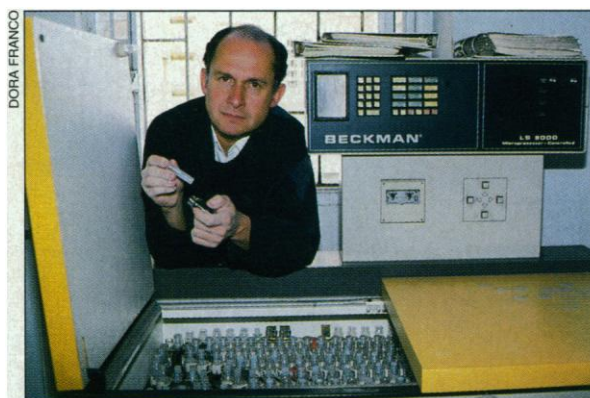
MALARIA

Controversial Vaccine Shows Promise

Manuel Patarroyo is used to marching out of step with the international malaria research community. Ever since the Colombian immunologist burst onto the scene in 1987 with a paper in *Nature* describing a synthetic vaccine that seemed to protect monkeys from the disease, his claim to have produced a new weapon in the war against malaria has been viewed with intense skepticism. Many researchers argued that Patarroyo's vaccine couldn't be all it was cracked up to be—particularly as there seemed to be no correlation between antibody responses to the vaccine and protection against malaria. And when Patarroyo launched straight into a huge program of testing his vaccine in thousands of Colombians, that initial distrust soon turned to open criticism of the design—not to mention the ethics—of Patarroyo's trials. "His initial data and the studies that generated them were obviously flawed," says Ripley Ballou of the Walter Reed Army Institute of Research.

The gulf between Patarroyo and the malaria research establishment may be about to narrow, however, with a paper scheduled for publication in the 20 March *Lancet* that Patarroyo believes will silence his critics. The paper describes a new Colombian trial—designed in consultation with a former skeptic—involving more than 1500 people. It shows the vaccine reduced the risk of malaria by 39% in immunized volunteers. Indeed, with a Walter Reed group now planning a clinical trial in Thailand using a U.S.-made version of Patarroyo's vaccine, and an international trial in Tanzanian children already under way (*Science*, 9 October 1992, p. 207),

1993 could be the year in which the maverick Colombian scientist—and his controversial vaccine—finally come out of the cold. "There's no question about it," says malaria vaccine pioneer Ruth Nussenzweig of New



In from the cold. Manuel Patarroyo hopes to gain credibility by publishing his results in the *Lancet*.

York University School of Medicine. "He's coming back into the mainstream."

For Patarroyo, the skepticism he's encountered until now is easy to explain: "I knew it would not be easy for people to swallow the fact that I had made the first...vaccine against a parasitic disease," he says. But to most malaria researchers, it has been Patarroyo's consistently unorthodox approach that has posed the greatest barrier to acceptance. The conventional wisdom is that to be effective, a malaria vaccine would have to mobilize the cellular component of the immune system in addition to generating antibodies.

Yet Patarroyo made his vaccine from peptides more likely to produce an antibody response. What's more, many researchers in the mid-1980s were pinning their hopes on a vaccine to attack the parasite in its sporozoite stage, the form in which the organism is injected into the bloodstream by a biting mosquito. But Patarroyo targeted mainly the merozoite form, which develops from the sporozoite and causes the fevers and chills typical of the disease. Although his initial attempts to find a merozoite peptide that would completely protect monkeys from malaria were unsuccessful, he eventually came up with a cocktail of three peptides that showed promise, and then by a deft stroke of chemical legerdemain used two sporozoite peptides to link them in a stable form.

What really drove a wedge between Patarroyo and the malaria research establishment, however, was the speed with which he then rushed into the field. Even at the time of his second *Nature* paper, in 1988, describing a preliminary trial showing the vaccine to protect two out of five immunized human volunteers, questions were being asked about the ethics of Patarroyo's research. In an accompanying article, malariologist Louis Miller of the National Institute of Allergy and Infectious Diseases in Bethesda wrote that Patarroyo's "failure strictly to follow the protocol [of his study] placed some volunteers at excessive risk" of a dangerously high parasite load. And concerns were voiced more and more loudly as the numbers of people

Patarroyo treated with his vaccine rapidly escalated into the tens of thousands—particularly as Patarroyo had, by then, almost totally divorced himself from the usual scientific process. “He said he didn’t have time to come to international meetings,” recalls New York’s Nussenzweig. And as Patarroyo knew he could rely on funding from his friend the Colombian president, he never had to submit his work for peer review. “Nobody saw the data,” says Nussenzweig. “That caused ill will on the part of the scientific community.”

Those feelings seemed justified, when two groups—one from the Centers for Disease Control and Prevention in Atlanta, the other from del Valle University in Cali, Colombia—in a trial sponsored by the World Health Organization (WHO) in 1990 to repeat Patarroyo’s original monkey experiments, failed to replicate his results. And when a WHO-mandated expert group visited Patarroyo’s lab and concluded that none of his trials fulfilled all the conditions for randomization, double-blind, and placebo control, the vaccine was relegated to the fringes of international malaria research. Britain’s Medical Research Council, for instance, has twice turned down a proposal to test the vaccine in the Gambia.

So what explains Patarroyo’s sudden re-

habilitation? One reason is that it’s now apparent that the two WHO-sponsored studies may not have accurately repeated Patarroyo’s methods. Walter Reed’s Ballou says the correct formulation of the vaccine is extremely difficult to achieve. “The first time I mixed [it],” he says, “I ended up with a completely nonimmunogenic vaccine.” But now that he’s worked extensively with the vaccine, Ballou says he’s getting results identical to Patarroyo’s. The second reason is that Patarroyo has finally started attending international meetings and listening to his detractors. Indeed, in designing the trial reported in the *Lancet*, he enlisted the help of epidemiologist Pedro Alonso of Spain’s National Research Council, who—although he’s friendly with Patarroyo—has criticized his previous trials.

Clearly, the *Lancet* study goes out of its way to achieve scientific respectability: The 1548 volunteers were individually randomized into vaccine and placebo groups; and Alonso was on hand in the field to ensure correct double-blind procedure. “This is the first trial of Patarroyo’s vaccine that seems to have been conducted rigorously,” confirms epidemiologist Peter Smith of the London School of Hygiene and Tropical Medicine: “It does give evidence of protection.”

One study by itself doesn’t remove all of

the questions surrounding Patarroyo’s vaccine, however. For one thing, it’s still unclear why the vaccine works. And for another, the protective efficacy rate of 39% reported in the *Lancet* paper is much lower than the 70% to 80% that Patarroyo claims to have achieved in his earlier trials. Typically unfazed, Patarroyo says that the low rate is a temporary blip, due to a pH problem with the batch of vaccine used in the latest study. But in countries where malaria is an endemic killer, even a vaccine that reduces the risk of malaria by one-third in the people to whom it’s given would be a huge step forward.

Most malaria researchers are now looking to the planned Walter Reed trial in 1000 Thai children, and the WHO-sponsored international trial in 600 Tanzanians, to provide a more definitive test. But if these trials indicate that Patarroyo’s vaccine does work, he’s hoping that it will do more than just bring him back into the scientific mainstream. Indeed, he’s looking to rehabilitate his entire country’s tarnished image: “I want the world to see that Colombia is not just drug trafficking, that it has another side to it, and that side is good science.”

—John Maurice

John Maurice is a science writer based in Geneva.

DEFENSE CONVERSION

Swords-to-Plowshares Plan Boosts R&D

Using as his backdrop a Westinghouse factory that converted its military radars into tools of drug enforcement, President Clinton last week announced that he is releasing \$1.7 billion immediately to help other companies make the same kind of swords-to-plowshares switch. The money—which will come primarily from the Pentagon’s budget, though many agencies will help spend it—is just the first installment in what the White House intends to be a

\$20 billion “defense conversion” program over the next 4 years, according to Eugene Sperling, an economic adviser to the president. But this downpayment on defense conversion already shows how broadly the Administration is construing the term: It includes a large chunk of funds for R&D and a \$48 million boost for engineering education.

Funding for the new technology push comes from two sources: a \$1.4 billion defense appropriation earmarked by Congress for defense conversion last fall—unused by the Bush Administration—and \$300 million “redirected” from other areas of the 1993 budget. The money will be used to support a hodge-

podge of civilian technology projects, community aid, and retraining of technical workers. About \$500 million will be spent on innovative commercial R&D projects, nonprofit collaborations, and universities, with grants

awarded through a “merit review” process.

About \$500 million will go to commercial R&D, nonprofit collaborations, and universities.

Overseeing the whole effort is a newly formed coordinating panel called the Defense Technology Conversion Council led by the Advanced Research Projects Agency (ARPA). It includes

the National Science Foundation (NSF), the National Aeronautics and Space Administration, the Department of Energy, and the National Institute of Standards and Technology. Those agencies moved rapidly behind the scenes to put the package together. By the time Clinton went before the cameras to make his announcement, ARPA had already assembled a massive guide for grant-seekers, complete with a dial-in information number—(800) DualUse. According to ARPA’s guidebook, this “technology reinvestment project” will make awards on a 50-50 cost basis in the following areas:

■ \$81.9 million for research and develop-

ment on “dual use” technologies that have military and commercial potential.

■ \$42.1 million for carrying new ideas forward into the marketplace or to military uses.

■ \$90.5 million to support regional alliances aimed at commercializing technologies.

■ \$23.5 million for development of advanced manufacturing methods.

■ \$87.4 million for extension services, modeled on the agricultural extension service and aimed at helping small manufacturers upgrade their capabilities.

■ \$90.8 million to help companies that now depend heavily on defense funding find a niche in the nondefense market.

■ \$43.6 million for manufacturing engineering education at colleges and universities.

■ \$4.6 million to support teaching by “manufacturing experts with practical experience” at colleges and universities.

■ \$7.2 million for the small business innovative research program.

The interagency team that put the package together tried to make it as flexible as possible, says Joseph Bordogna, head of the engineering directorate at NSF. Universities can make proposals under many of the headings, he says. The council plans to send a team around the country to drum up interest later this spring, Bordogna says. Proposals should be submitted by July and the awards will be announced in September.

—Eliot Marshall