

PUBLIC HEALTH

Anthrax Vaccine Begins A New Round of Tests

Almost everybody loves to hate the anthrax vaccine. It's old, inefficient, and the cause of many complaints. Indeed, when the U.S. government recently offered to vaccinate thousands of people who may have been exposed to anthrax spores in spiked mailings, only 130 rolled up their sleeves. Many in the U.S. military have also balked at orders to receive

PLANNED ANTHRAX VACCINE STUDIES

Immunological effects of changes in route of administration and dose reduction (CDC, Emory University, Baylor College of Medicine, Walter Reed Army Institute of Research, Mayo Clinic, University of Alabama, Birmingham)

Effect of different doses on immunogenicity and challenge in nonhuman primates (CDC, Battelle Memorial Institute)

Serological assays and studies of immune correlates of protection (CDC, FDA, NIH, USAMRIID, Battelle Memorial Institute, Emory University)

National survey of knowledge, attitudes, and beliefs regarding the anthrax vaccine among military personnel (CDC, DOD, Research Triangle Institute)

Testing hypotheses for adverse events using military medical database (CDC, DOD)

Survey of health care providers regarding the anthrax vaccine and the reporting of possible adverse events (CDC, FDA, DOD)

Comparative evaluation of the effect of anthrax vaccine on health-related quality of life (CDC, DOD)

Retrospective study of long-term adverse effects among vaccinated mill workers (CDC)

Study of hormonal correlates of adverse events among female clinical trial participants (CDC, DOD)

Studies of vaccine delivery and follow-up of adverse events (CDC, DOD National Vaccine Healthcare Center Network)

six anthrax shots plus annual boosters.

Approved 32 years ago, this vaccine made from a laboratory bacterial culture was designed to protect textile mill workers against skin infections. Now it is being used against inhaled anthrax, and the government is reexamining its safety and efficacy. Since 1999, Congress has given the Centers for Disease Control and Prevention (CDC) in Atlanta \$36 million for such studies, responding to complaints from service members and problems at the sole manufacturing plant—owned by BioPort Corp. in Lansing, Michigan. BioPort has been compelled to suspend production since 1998 for safety

checks. Researchers planning the CDC studies briefed an oversight panel at the Institute of Medicine (IOM) in Washington, D.C., last week—and got a mixed review.

Dennis Kasper, a molecular geneticist at Harvard Medical School in Boston, for example, saw “good progress.” But clinical microbiologist Patricia Ferrieri of the University of Minnesota Medical School in Minneapolis said to CDC scientists: “Forgive the plain language, but you need to get your act together.” It is “urgent,” she said, to move faster on this complex set of studies.

One of the most urgent CDC studies is a clinical trial of 1300 volunteers to test the effectiveness of fewer shots (four or five rather than the standard six) and a gentler route of injection (intramuscular rather than subcutaneous). This trial is on hold until the government permits BioPort to resume vaccine production. CDC's Nina Marano said she hopes that CDC can begin enrolling subjects this month.

Jairam Lingappa of CDC's special pathogens branch described a complementary study in macaques that's designed to reveal precisely how much vaccine is needed—and at what intervals—to protect against lethal infections. Researchers have tentatively defined an antibody test to measure the immune response in blood. If CDC finds a way to bridge animal and human data, this could become important for testing future anthrax vaccines. Sixty of a planned 108 monkeys have already received shots, but the trial is now being restructured.

While these groups examine efficacy, others are checking on safety and side effects. The CDC's Michael McNeil, for example, reported on an ambitious epidemiological study that will look for long-term effects by focusing on a textile mill “in the U.S. Southeast” that for 30 years required all employees to get anthrax shots. “Even the man who filled the Coke machine got vaccinated,” McNeil said. CDC hopes to get information on more than 1300 of the estimated 2778 people who received nine or more shots, looking at everything from cause of death to self-reported current “energy level” and “cognitive function.”

CDC is also planning a survey of military personnel to learn about their attitudes and experiences. It will mine data in military medical records, searching for problems and testing theories. U.S. Army clinical teams will conduct studies of vaccine procedures and adverse events.

The IOM panel's main critique of the CDC's large agenda last week was that it had not gelled. Some parts—such as the clinical trial—have been put on hold because of the vaccine shortage. Others were delayed by the terrorist and anthrax attacks, as Randy Louchart of CDC's National Immunization Program explained. Other CDC

that can convert hydrogen into electrical energy, with water as the only byproduct.

But the panels warned that the 2004 deadline for rolling out affordable supercars was unrealistic. And air-quality advocates complained that the power plant deemed the best bet by PNGV engineers, a hybrid diesel-electric engine, wouldn't meet clean air rules. Such problems led the panel last year to call for a serious rethink of the program's structure and goals.

Abraham's answer, announced on 9 January at Detroit's annual auto show, is Freedom CAR. It drops the emphasis on diesel hybrids in favor of PNGV's fuel cell effort, a shift welcomed by many environmentalists. But Abraham drew darts for failing to set deadlines for what he promised would be a decades-long “fundamental research and development” effort. “It remains to be seen how substantive the changes will be, but I'm concerned that we'll give up some important near-term work for benefits that we may not see for decades,” says Dan Reicher, a former Clinton Administration energy official now with the World Resources Institute in Washington, D.C.

The reaction of fuel cell advocates is decidedly more upbeat. “It makes sense,” says Vernon Roan, who heads the University of Florida's fuel cell laboratory in Gainesville and served on PNGV peer-review panels. “The government ought to support high-risk/high-payoff research that is in the national interest.” John Turner, a hydrogen fuel cell expert at the National Renewable Energy Laboratory in Golden, Colorado, agrees: “It's where we ought to be headed.”

Roan and other experts note, however, that the change in name from the unpronounceable to the patriotic (PNGV to Freedom CAR) may be the most noticeable immediate change. Much of PNGV's research agenda is expected to continue under the new program, because fuel cell cars will also need improved materials and better electrical systems, for example. Department of Energy (DOE) officials say the agency spends about \$100 million a year on fuel cell research, with about half of that going to polymer exchange membrane cells, the type most likely to be used in cars and trucks. DOE spends another \$30 million on hydrogen research, principally looking for efficient ways to generate and store the gas.

Turner calls this budget a start but says it's “small potatoes” compared to what will be needed to get fuel cell cars to market. One major challenge will be replacing the trillion-dollar, gasoline-based infrastructure with a network of hydrogen fuel stations. The cost of a hydrogen future won't be known until 4 February, when the president sends Congress his request for the 2003 budget.

—DAVID MALAKOFF AND ROBERT F. SERVICE

staffers noted that researchers have been struggling to modify their plans to include suggestions from expert advisers, as the IOM group had urged them to do earlier.

During last week's meeting, IOM panel members said they were not sure how they can evaluate CDC's plans—and produce a peer-reviewed report—before the end of the year, as Congress has requested. They urged the CDC scientists to nail down their research agenda before this group meets to put its views in writing at a closed meeting in March.

—ELIOT MARSHALL

JAPAN

Libraries Seek Ways to Hold Down Costs

TOKYO—Japan's university libraries are losing the battle to keep scientific journals on their shelves. Soaring subscription prices, an unfavorable exchange rate, and a decentralized approach to collections have led to a dramatic reduction in the number of available titles at the country's 99 national universities. But library officials haven't given up the fight. Last week they met here to discuss taking advantage of cheaper online access and using their joint bargaining power to bring down subscription costs.

Japan's library crisis parallels the problems facing U.S. and European institutions (*Science*, 30 October 1998, p. 853). Although the government has steadily boosted spending on science and technology throughout the 1990s, most of the money has gone into competitive grants. The country's two 5-year science plans, for example, contained "no mention of scientific and scholarly communication," says Syun Tutiya, a professor of information sciences and director of the library at Chiba University, east of Tokyo, who helped organize the 9 January symposium. The problem has been exacerbated by a steady decline in the value of the yen against the dollar and most European currencies, making foreign periodicals ever more expensive. As a result, the number of titles received by the national libraries has dropped by half since peaking at 40,000 in 1989.

But Japan's libraries also face a host of institutional challenges. Many journals are ordered not by the library but by individual professors, using research

funds. And those subscriptions may be canceled at any time. The result can be both multiple subscriptions and sudden gaps in a library's collection. In addition, many individual departments have their own libraries, which typically are not accessible by outsiders. All these factors, says Tutiya, means "we really don't know the extent of our journals crisis."

Even so, there is consensus that the biggest challenge is rising subscription prices. Individual universities traditionally have purchased material through subscription agents and have had little or no direct contact with publishers. However, last year a consortium of national university libraries negotiated discounts and package deals with Europe-based Reed Elsevier and several other major academic publishers. Although nondisclosure clauses prevent Tutiya from providing details, he acknowledges that "it is a discount."

Library officials hope to extend the consortium approach to online journal access. An advisory panel to the Ministry of Education, Culture, Sports, Science, and Technology is finalizing recommendations likely to lead to funding later this year for site licenses that provide online access to journals. The idea is to negotiate agreements with journal publishers involving faculty, staff, and students at some 70 national universities, says Jun Adachi, a member of the working group drafting the recommendations and an information scientist at the National Institute for Informatics (NII), which hosted last week's symposium.

Meeting participants also heard from Alison Buckholtz, associate enterprise director for the Scholarly Publishing and Academic Resources Coalition (SPARC), a library advocacy group based in Washington, D.C. "There has been a lot of interest in our ideas for online journals and alternatives to commercial journal publications," says Buckholtz. NII is expected to play a major role in advocating similar reforms, because Japan's national university libraries are not allowed to spend money to join an advocacy organization such as SPARC.

Tutiya sees last week's meeting as the first step in getting libraries to develop a strategy for coping with the changes sweeping through academic publishing. Such a plan, he and others say, would be an essential ingredient in convincing government officials that Japanese academic libraries need help.

—DENNIS NORMILE



Elusive target. "We don't know the extent of our crisis," says Syun Tutiya of Chiba University.

TAIWAN

Frank Shu Named University Head

Frank Shu, an astronomer at the University of California, Berkeley, is coming home—for the first time. Next month Shu becomes president of Taiwan's National Tsinghua University, Hsinchu, adding to the list of prominent ethnic Chinese scientists from abroad who hope to build Taiwan into a scientific and technological powerhouse. "His coming to Taiwan is quite a coup for the academic community here," says K. Y. (Fred) Lo, director of Academia Sinica's Institute of Astronomy and Astrophysics in Taipei.



Impact. Frank Shu hopes to "make a difference" in Taiwan.

Shu, 59, was born in the southern China city of Kunming but as a child moved to the United States with his family. Trained at the Massachusetts Institute of Technology and Harvard University, he joined the Berkeley faculty in 1973 and in 1998 was named one of a handful of University Professors. Although Shu has never lived in Taiwan, he will be following in the footsteps of his father, Shien-siu, who led the university in the early 1970s and later helped create Hsinchu Science Park, Taiwan's "Silicon Valley." He is also emulating Lee Yuan-tseh, a Taiwan native son and 1986 chemistry Nobel laureate who left Berkeley in 1994 to become head of Academia Sinica, and dozens of prominent scientists whom Lee has recruited.

Astronomers praise Shu's theoretical work on the structure of spiral galaxies and, more recently, on star formation. "He has played a leading role in making star formation a major field," says Anneila Sargent, a radio astronomer at the California Institute of Technology in Pasadena and current president of the American Astronomical Society, which Shu headed in 1995.

Shu says he decided to take the job "because I realized I can make a bigger difference in Taiwan than by remaining in the United States." But he admits he faces some significant challenges in raising the quality of Taiwan's universities. In addition to tapping private sources to supplement government funding, Shu also hopes to change a culture in which resources are shared equally to one in which academic stars receive the support they need to shine. "There is a growing understanding [among government officials] that science at the forefront is an elitist affair," he says.

—DENNIS NORMILE