Problems with bioweapons vaccines

Stockholm bound

502

508 Cholesterol Alzheimer's

has already paid off in another forensic study: Keim's team was the first to identify the strain used in a 1993 anthrax attack by the Aum Shinrikyo cult in Japan. As it turned out, the cult had sprayed a nonvirulent vaccine strain into the Tokyo air, says Keim—which explains why this attack, in contrast to the later release of nerve gas in a subway, was a flop. There's no official word vet on the origins of the strains found in the United States, however.

One of anthrax's most insidious qualities

face of a macrophage and come together to form a doughnut-shaped complex (see figure). Then they bind EF and LF, after which the entire complex is engulfed by the cell membrane and shuttled to a so-called endosome inside the cell. Once there, the PA molecules form a special pore that pierces the endosome's membrane and lets EF and LF out to do their grisly work.

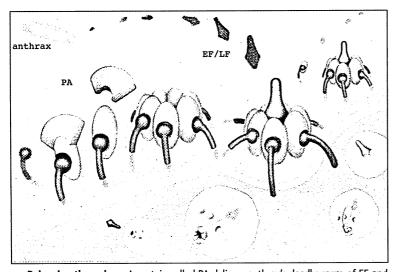
In a paper published in *Science* last spring (27 April, p. 695), Collier showed that a mutated PA molecule could form part

> of the doughnut like normal PA but could also disrupt the membrane pore, preventing the escape of EF and LF. Indeed, he found that rats died quickly from an injection of LF with normal PA, but survived when LF and mutant PA were injected. He hopes to create a drug based on mutant

There could

be a bonus, Collier says. PA is the most important component of the licensed human anthrax vaccine. Because the mutant PA elicits antibodies just as well as the normal form does, it might do double duty: "You would have wrapped into one molecule a therapeutic and a potential vaccine." This would be valuable in a major attack, he says, when thousands of people would need immediate treatment and a vaccine to prevent infection later by lingering spores.

"It's an interesting and very important approach," says Columbia University public health expert Stephen Morse. Harvard biologist Matthew Meselson agrees that Collier's work is "marvelous," but at the same time, he cautions against relying on high-tech solutions to bioterrorism. Developing a new drug often takes years, if not decades, says Meselson. For now, he thinks simple, generic solutions are the best-from installing highly efficient air filters in many buildings to educating the public about do's and don'ts during -MARTIN ENSERINK an outbreak.



Poisoning the poison. A protein called PA delivers anthrax's deadly cargo of EF and LF into cells; adding a mutant PA (purple) can prevent release of EF/LF inside the cells.

is that it produces a toxin aimed at thwarting the immune system that continues to do harm even after the source is eliminated. "You can kill the bug with no effort at all," says Hugh-Jones, "but people will still die, because they're exquisitely sensitive to the toxin." Some researchers have focused on new ways to stop this process. For instance, Harvard University's R. John Collier, who has long been fascinated by the ingenuity of anthrax's aggressive toxin, has discovered ways to disarm it.

The toxin has three components, Collier explains. One of them, called edema factor (EF), prevents cells called macrophages from gobbling up bacteria. Another, called lethal factor (LF), kills the macrophages and eventually the host, too. The third component, protective antigen or PA (so called because it can be used as a vaccine), helps shuttle the other two into macrophages. The latter process could also be the bug's Achilles' heel, says Collier. Seven PA molecules must bind to receptors on the sur-

PROFESSIONAL TRAVEL

NIH Chafes at Limits On Attending Meetings

Some 200 scientists at the National Institutes of Health (NIH) may be no-shows next month at the year's biggest neuroscience meeting, thanks to a management directive by the Bush Administration to limit government travel. NIH officials hope that a personal appeal by several institute directors will persuade their bosses at the Department of Health and Human Services (HHS) that the policy could hinder progress in biomedical research.

"There's a lot of unhappiness," says a source, who requested anonymity. "We're all trying to figure out ways of explaining to the Administration how pernicious this is to the process of science."

Until recently, NIH scientists who wished to attend a scientific meeting needed clearance only from their institutes. But early this year HHS Secretary Tommy Thompson decreed that those wanting to attend meetings in foreign countries would have to get permission from his office. A few months later, the rule was extended to domestic travel. At NIH, the policy applies to groups of five or larger.

Several NIH officials none of whom was willing to have his or her name used-told Science that the rationale doesn't appear to be financial. Instead, says one source, people in Thompson's office seem to "have the impression that traveling to meetings is a junket" rather than an essential part of the job. An HHS official says the policy is "just part of being a good steward of the taxpayer's dollar."

The policy first showed its bite in June, when HHS lopped the list of NIH participants in the annual meeting of the Research Society on

California dreaming? The Bush Administration wants to cut the number of NIH scientists attending these two fall meetings in San Diego.

NEWS OF THE WEEK

Alcoholism in Montreal, Canada, from 70 to 39. The annual meeting of the American Society of Human Genetics, which ended this week in San Diego, went on without onethird of the 170 NIH people who had asked to attend. Dean Hamer of the National Cancer Institute says that one of his graduate students was permitted to go to a "premeeting" on gene linkage but was not allowed to stay on for the main affair. "It makes no sense whatsoever," Hamer says.

Scientists are now trying feverishly to overturn an HHS ruling that would allow only 550 of 761 researchers who requested permission to attend the Society for Neuroscience's annual meeting next month in San Diego. "Word keeps coming back to me that we are facing a stone wall," says one source. The wall appears to be the person of Ed Sontag, recently installed as assistant secretary for administration and management. Sontag, who has a Ph.D. in education and advised Thompson on educational matters when he was governor of Wisconsin, could not be reached for comment.

NIH officials thought they were making headway this summer after Thompson visited the Bethesda, Maryland, campus and heard from postdoctoral fellows upset at the prospect of being cut out of scientific meetings. "Thompson said, 'We need to fix this,'" reports an observer.

But nothing happened. In August, Michael Gottesman, NIH deputy director for intramural research, wrote to Thompson about the value of scientific meetings not just as a source of knowledge but also as a way to monitor grantees, recruit new talent, and nurture the careers of postdoctoral fellows. A visit by a contingent of institute directors headed by Francis Collins, director of the National Human Genome Research Institute, is also in the works. Their message will be simple, says one source: Meetings are the lifeblood of science.

-CONSTANCE HOLDEN

BIOMEDICAL PHILANTHROPY

Klausner Makes Case For New Foundation

Richard Klausner this month traded # his biomedical research battleship for a speedboat, and he's looking forward to feeling the spray on his face. His transition from the \$3.7 billion National Cancer Institute (NCI)—the flagship of the National Institutes of Health—to the Case Institute of Health, Science and Technology, a small outfit in Washington, D.C., has E left colleagues curious. Last week, in an interview with Science, the 49-year-old

biologist for the first time laid out his

plans and how they will be funded.

Although the details are still being finalized, Klausner says the institute hopes to inject about \$100 million over the next few years in two areas. One is a life sciences informatics initiative, aimed at developing better computerized systems for organizing and analyzing data; this will be largely in-house research. The other is a "molecular monitors" program that will disburse grants to develop technologies for identifying and monitoring specific chemicals linked to particular diseases and biological processes. The two thrusts, he says, are the "logical next steps to the things I loved to do at the cancer institute: large projects oriented toward the linkage of science and technology" that connect researchers in many fields.

With the explosion of knowledge in the life sciences, Klausner isn't worried about stepping on other funders' toes. The institute's areas of interest fall within "crowded fields," he admits, but they offer "some

The new institute is funded by America Online founder Steve Case and his wife, Jean Case (Science, 14 September, p. 1967). Rather than drawing on the interest from an endowment, the institute is likely to operate on a pay-as-you-go basis, with the Cases providing fresh funds each year. The budget "would be driven by the science," Klausner says. "I like that [approach], rather than having to worry about investing the endowment.'

The institute will soon occupy five buildings in Washington's central Dupont Circle neighborhood, with room for administrators, visiting scientists, and a significant in-house informatics program. Klausner's first top hire is MaryAnn Guerra, his former deputy director for management at NCI, who was tapped this week to be a vice president.

As for the rea-

son he left NCI.

Klausner said he

relished the op-

portunity to lead

a new organiza-

tion that could

change direction

quickly. He also

noted that instead

of having scores

of political boss-

es, he now an-

swers to "a board

of two people"-

the Cases. The

couple, he says,

have been "very

supportive" of



Catching the wave. Richard Klausner says the Case institute will be agile.

letting him chart the institute's course. -DAVID MALAKOFF

ScienceSc⊕pe

Sanger Secure The future of the Wellcome Trust Sanger Centre, which sequenced one-third of the human genome, is looking pretty secure. On 12 October, the trust—Britain's mammoth biomedical charity—announced that the Hinxton, U.K., institute

will get \$435 million over the next 5 yearsenough money to take it soaring into the postgenomic era.

The new funds will be divvied up among a number of priorities, including \$123 million for sequencing new genomes such as those of the mouse and the zebrafish, and \$30 million



for recruiting new scientists. Another big winner is the Sanger's 2-year-old Cancer Genome Project, which has already identified more than 80 genetic abnormalities implicated in human cancer. Wellcome originally awarded the project \$14.5 million for its first 5 years; that figure will now more than triple to \$52 million. The extra funds, says project codirector Richard Wooster, "will take us into full production scale."

Pediatric Research OK in Maryland The Maryland Court of Appeals last week reassured worried researchers that a controversial recent decision was not intended to bar most studies in that state involving children.

Universities and biomedical groups feared that language in the 16 August decision—involving a home lead paint cleanup study by the Kennedy Krieger Institute (KKI) associated with Johns Hopkins University—would outlaw studies involving "any risk" to children (Science, 28 September 2001, p. 2367). KKI filed a motion asking the court to reconsider. On 11 October the court denied the motion but stated that "by 'any risk' we meant any articulable risk beyond the minimal kind of risk that is inherent in any endeavor." Several groups that filed an amicus brief, including Hopkins and the Association of American Universities, say the clarification puts Maryland law back in accord with federal regulations allowing pediatric studies involving "minimal risk."

The court was not asked to reconsider its overall ruling, which found that the lead study was unethical. The case will now go to a trial court.