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New fusion ballgame

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A plethora of planets

SMALLPOX

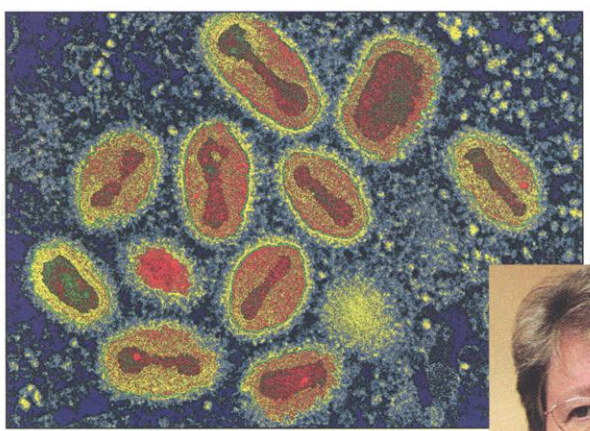
WHO Puts Off Destruction of U.S., Russian Caches

GENEVA—Humankind's worst public health enemy, on death row for more than 2 decades, has won another reprieve. Last week the World Health Organization's (WHO's) governing board agreed to delay destruction of the last known samples of smallpox, now kept on ice at two high-security facilities in Russia and the United States. The decision is a "victory for common sense," says Lev Sandakhchiev, director-general of the State Research Center of Virology and Biotechnology, which houses Russia's smallpox facility.

The decision reflects a new consensus that the stocks may be needed to defend humanity against the possible use of smallpox as a bioweapon, fears heightened in the wake of last fall's World Trade Center attack and anthrax-tainted letter campaign. "We regard the potential release of smallpox as a critical national and international security issue," says Kenneth Bernard, special adviser for national security, intelligence, and defense at the U.S. Department of Health and Human Services.

In staying an execution scheduled for this December, WHO's board has handed a dramatic victory to researchers hoping to develop drugs and a better vaccine. "There's been a sea change in thinking—and that's very good news," says virologist Peter Jahrling of the U.S. Army Medical Research Institute of Infectious Diseases in Fort Detrick, Maryland, whose team is developing a potential monkey model for the disease. The board acted on a recommendation from WHO Director-General Gro Harlem Brundtland, who based her decision on a report last month from a scientific advisory committee.

One sticking point, however, is whether WHO should set a new date to destroy the stocks. The two countries holding all the publicly acknowledged smallpox cards—the United States and Russia—favor an open-ended research program. Setting a deadline "would make it impossible to carry out some research," insists Yuri Fedorov, chief of the Russian health ministry's emerging disease unit. However, China, Cuba, and several other nations are expected to lobby hard for a deadline out of fear that an open-ended program increases the risk that terrorists could steal the virus or that the virus could escape in a lab accident. Observers speculate that the World Health Assembly (WHA) could set a deadline of 2005 or 2006 to destroy the stocks when it meets in May.



Not terminated. WHO's board has approved Gro Harlem Brundtland's recommendation to continue research on the known smallpox stocks.

Smallpox is thought to have claimed hundreds of millions of lives in a reign of terror that began with the first human settlements. But *Variola major*, which kills nearly one in three people it infects, has an Achilles' heel: Humans are its only hosts. That weakness allowed WHO to mount a successful global immunization campaign that led to its eradication in 1980. All nations with declared stocks of live smallpox complied with a WHO request to incinerate these samples, with the Soviet Union and the United States permitted to hold on to live smallpox for research.

These stocks were slated for destruction in 1993, but two developments helped persuade WHA to delay that order. A well-placed defector revealed that the Soviet Union amassed tons of weaponized smallpox virus after the country had lobbied hard for the disease's eradication and had signed a 1972 treaty outlawing bioweapons development. And after the Gulf War, an Iraqi researcher admitted to United Nations inspectors that he had done research on camelpox, a close cousin of smallpox that does not harm humans. Analysts suggested that the work was a surrogate for smallpox research, says Jonathan Tucker of the Monterey Institute of International Studies in Washington, D.C., who described these concerns in *Scourge: The Once and Future Threat of Smallpox* (Atlantic Monthly Press). The allegation heightened concerns about clandestine smallpox stocks in other countries as well.

In 1999, WHO's variola advisory committee proposed a research program to extract as much information from the virus as possible before putting it to death at the end of 2002. Working at the U.S. repository, the Centers for Disease Control and Prevention (CDC) in Atlanta, researchers have sequenced 10 strains. The sequences are highly conserved, particularly in regions coding for proteins essential for replication. Such proteins would be good targets for potential drugs.

One intriguing development is a potential animal model for smallpox, which could be important for testing drugs and vaccines. "The grand old gentlemen of smallpox eradication have been claiming for years that it was impossible to create smallpoxlike disease in primates, and thus there was little reason to keep the virus around," says Jahrling. And indeed, he says, "our initial attempt to infect primates at CDC was a dismal failure." But in a presentation last month to WHO's variola panel, Jahrling described how his team succeeded at infecting cynomolgus macaques after switching to a strain very similar to one that the Soviet Union had weaponized. Nearly all the animals died within a week from a condition that included skin pustules and other hallmarks of smallpox.

The model still has several shortcomings, however. Jahrling's group injected the macaques with large amounts of smallpox, whereas humans would normally contract the disease through the air. The disease was also more deadly than what's observed in humans. Although critics say this suggests that the ani-

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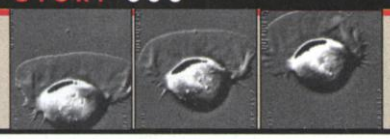
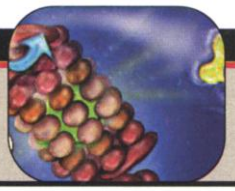




mal model would be a poor surrogate, Jahrling says that he expects to refine the model by testing lower doses and alternate infection routes. The Russian repository has won funding to ramp up its smallpox effort this year, and it too hopes to vet the monkey model.

Some countries are troubled by an open-ended research effort. "A final date for destruction should be determined, and no excuses should be given for further delay," says Sha Zukang, China's Permanent Representative to the United Nations in Geneva. But China, which is not on the governing board, is unlikely to find many allies to press that point. An Indian representative, for example, sat quietly throughout the discussion at the WHO board meeting, although his country had until recently advocated swift destruction of the stocks.

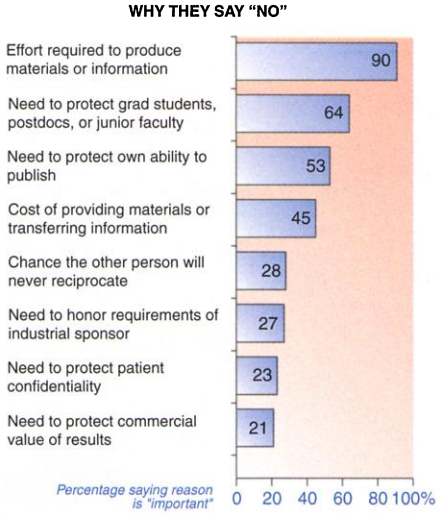
The heightened concern about bioterrorism has led some health experts to question the central tenet that stocks of any microbial killer should be destroyed once it is eradicated in the wild. But proponents of eradication say that steps are also being taken to address a bioterror threat. With respect to polio, "efforts have been under way for some time to inventory laboratory stocks and to develop a framework for specimen storage and future research," says James Hughes, director of the CDC's National Center for Infectious Diseases. The fact that the debate is taking place at all, however, represents another example of the expanding legacy of last fall's tragic events. **–RICHARD STONE**

PROFESSIONAL ETHICS

Data Hoarding Blocks Progress in Genetics

More than a quarter of U.S. geneticists say they can't replicate published findings because other investigators won't give them relevant data or materials. And the rejections are more than a breach of professional etiquette; they say that data hoarding actually retards progress in the field.

The results of a new survey, led by researchers at Massachusetts General Hospital in Boston, tarnishes what has traditionally been a badge of honor among scientists: the sharing of information that allows others to replicate or disprove the original finding. "That's a pretty big deal," says Robert Cook-Deegan, a science policy analyst at the Kennedy Institute of Ethics at Georgetown University in Washington, D.C. "And it's getting in the way of reliable science."



Too much trouble. The amount of effort required tops the list of reasons that geneticists don't share data.

The survey team, led by David Blumenthal and Eric Campbell of the hospital's Institute for Health Policy, compared the responses of 1240 geneticists with 600 other life scientists from the 100 universities that receive the most funding from the National Institutes of Health (NIH). The results appear in the 23/30 January issue of the *Journal of the American Medical Association*.

The survey explores a bread-and-butter issue: 84% of the geneticists report that they have asked another researcher to provide information, data, or materials related to published research. But almost half (47%) said that at least one request had been denied in the previous 3 years. The rejections had a significant impact on their work: 28% say that they had been forced to end a collaboration, and 21% had abandoned a promising line of research. The most likely requests to be thwarted were for biomaterials such as mice or viruses (35% had been denied such a plea), followed by sequence data (28%), findings (25%), phenotypes (22%), and lab techniques (16%).

Despite the widespread rejections, the survey found that naysayers were a distinct minority. Only 12% of geneticists reported that they had denied a request. This number may be an underestimate, Campbell explains, because researchers don't like to admit they resisted sharing their data. The most common reason cited for denying a request was the amount of effort required to produce the data (see table). Indeed, the more requests received, the more likely the scientist was to say no. Those engaged in commercial activities were also more likely to deny requests.

Geneticists say this proprietary behavior is having a negative impact on their field. Some 73% felt that withholding of data slowed progress in genetic research in general, and 58% said it had limited their own work. About the same fraction reported that it hindered the training of students and postdocs. More than twice as many scientists (35% to 14%) thought that withholding had risen rather than fallen over the last decade, although a bare majority (51%) said they hadn't noticed any change.

Campbell and his colleagues suggest that researchers might be more forthcoming if funding agencies provided money to defray the costs of meeting requests. Another step, they say, would be to make material transfer agreements more user friendly. "It's a legitimate cost of doing research," agrees Wendy Baldwin, NIH's deputy director for extramural research, adding that researchers could either list the cost in their grant application or apply for a supplemental award.

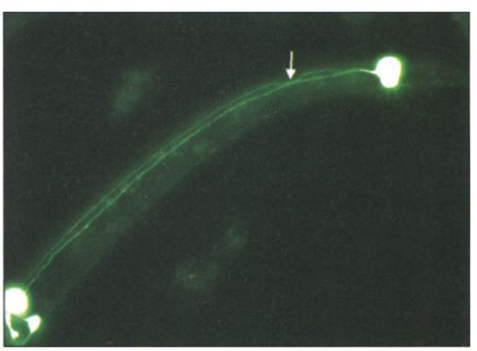
NIH could also put more pressure on researchers to behave civilly, says Cook-Deegan, including a better system to track who's being uncooperative. "There's no shaming strategy available here," he says.

–ERIK STOKSTAD

NEUROSCIENCE

Genes Keep Neurons' House in Order

As any homeowner knows, timely maintenance is vital for keeping a building functioning properly long after construction is finished. The same is evidently true for the complex architecture of the nervous system



Out of line. Axons in *Caenorhabditis elegans* stray from their proper places (arrow) when ZIG proteins are missing.

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