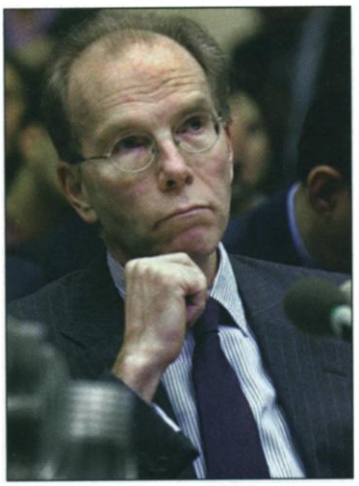
PUBLIC HEALTH

CDC Head's Resignation Expands Leadership Void

Jeffrey Koplan, who guided the Centers for Disease Control and Prevention (CDC) in Atlanta through the country's first fatal bioterrorism attacks last fall, is stepping down on 31 March. Koplan unexpectedly announced his resignation last week, exacerbating the leadership vacuum at U.S. public health agencies. Three other top jobs are currently vacant, even as the nation struggles to face the continuing threat of bioterrorism.



Help wanted. Koplan's departure leaves another top health job vacant.

Koplan, who declined an interview request, did not give a reason for quitting, and in newspaper reports he denied that he was pressured to leave. Health and Human Services (HHS) Secretary Tommy Thompson called Koplan's departure a "loss," adding that "I am going to miss [Koplan's] counsel, leadership, and dedication to public service." But public health experts say there had been friction between Koplan and top HHS officials, including Thompson, in part over CDC's handling of the anthrax crisis.

Some members of Congress and media outlets criticized Koplan last year for an apparent lack of control during the bioterrorism episode and for failing to communicate effectively with local public health experts and the public. "Koplan is a very knowledgeable and credible doc," says Tara O'Toole, who heads the Center for Civilian Biodefense Strategies at Johns Hopkins University in Baltimore, Maryland; "the country would have been better off if it had seen more of him." But O'Toole adds that it's unclear whether Koplan ducked the limelight on his own initiative or at the request of others in the Bush Administration. Eventually, National Institute of Allergy and Infectious Diseases (NIAID) director Anthony Fauci became the government's prime anthrax spokesperson.

Koplan served CDC from 1972 to 1994 and took the centers' top job in October 1998 after a 4-year stint in the private sector. As a member of the agency's Epidemic Intelligence Service in the 1970s, he helped eradicate smallpox in Bangladesh, one of the scourge's last hideouts. In the early 1980s, he chaired the Public Health Service Executive Committee on AIDS. O'Toole and others credit Koplan for his steadfast push to improve public health infrastructure nationwide and his efforts to replace the agency's dilapidated facilities. "CDC has crummy old labs, and he did a superb job of getting a new building plan under way," says C. J. Peters, a former head of CDC's special pathogens branch, who is now at the University of Texas Medical Branch in Galveston.

Koplan's departure comes at a time when the Bush Administration is proposing to spend $5.9 billion next year to prepare for bioterrorism, some $1.6 billion of which would go to CDC. The National Institutes of Health, slated to receive $1.5 billion in bioterrorism funds, has lacked a director for 2 years. Fauci was long rumored to be the front-runner but is now out, according to media reports. Why the deal crumbled is unclear: Some attribute it to Fauci's wish to stay involved in NIAID; others say his candidacy was unpalatable to conservatives, who prefer an outspoken opponent of abortion and embryonic stem cell research.

The Administration is also trying to fill the top slot at the Food and Drug Administration, as well as find a successor for Surgeon General David Satcher, whose term expired this month. Now that Koplan is leaving too, says O'Toole, "Tommy Thompson is truly home alone." –MARTIN ENSERINK

EPIDEMIOLOGY

Battle Heats Up Over Mammography Benefits

The top U.S. health official last week fired the most dramatic salvo to date in a long, drawn-out war over the benefits of mammography. But it is unlikely to be the last shot on the subject.

On 21 February Tommy Thompson, secretary of the Department of Health and Human Services (HHS), released a report from an outside group saying that all women over 40 should get breast x-rays at least once every 2 years. This conclusion, published on the HHS Web site last week,* is at odds with some other biostatistical studies that have found little support for screening women in their 40s. Thompson buttressed the report with a personal view: Mammography saved his wife from cancer, he said, adding that "all of you in this audience [should] take these recommendations to heart."

The recommendation that mammography should begin at age 40 comes from the U.S. Preventive Services Task Force, an independent panel of health care experts that advises HHS. After examining published reports over a 2-year period, the task force concluded in January that there is "fair" evidence that mammography for women in their 40s "significantly reduces mortality from breast cancer." Janet Allan, dean of the school of nursing at the University of Texas Health Science Center in San Antonio and a co-chair of the panel, appeared at the HHS press conference with Thompson to defend this finding. The risks and benefits of mammography have become clearer since the panel examined this issue in 1996, she said. Back then, the task force had found "insufficient evidence" to support routine mammography under age 50.

Peter Greenwald, a National Cancer Institute official in charge of cancer prevention, used the press conference to criticize a widely cited analysis questioning the value of mammography. The paper, which appeared last October in *The Lancet*, rejected the methodology in five of seven large studies that have been cited as proving the value of mammography. The authors, Peter Gøtzsche and Ole Olsen of the Nordic Cochrane Center in Copenhagen, Denmark, a biostatistics group, said even the two studies that are reliable fail to show that the benefits outweigh the risks. The false positives that turn up in x-ray testing lead to anxiety and unnecessary surgery, according to the *Lancet* paper, which argued against the routine use of mammography in cancer screening.

The skeptics got another boost in January, according to biostatistician Donald Berry of Houston's M. D. Anderson Cancer Center, when another advisory group began taking a serious look at the Gøtzsche-Olsen analysis. The panel, which reviews medical literature for NCI's online information service known as the Physician Data Query, noted that the benefits claimed for routine screening with breast x-rays are small in public health terms,

Screening supporters. HHS Secretary Tommy Thompson and advisory panel co-chair Janet Allen.

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* www.ahrq.gov/clinic/3rduspstf/breastcancer

about 4 days of added survival per woman, says Berry, a longtime skeptic. "We found a lack of credibility" in many of the studies that claimed to find such benefits for women under age 50, Berry added.

The panel's concerns were written up in *The New York Times*, raising the volume on a debate that has raged for at least 5 years, ever since a "consensus conference" in 1997 sponsored by the National Institutes of Health ruled that the evidence did not support routine mammography for younger women. That ruling brought down the wrath of the U.S. Senate, which issued a resolution favoring mammography by a vote of 98 to 0. Observers say that Thompson's very public endorsement of mammography, including the release of the task force's report on an accelerated scale, was intended to blunt this latest attack.

Larry Norton, current president of the American Society of Clinical Oncology and a researcher at Memorial Sloan-Kettering Cancer Center in New York City, rejects the Gøtzsche-Olsen analysis, dismissing it as a scholarly debate about "30-year-old studies and 30-year-old therapies." But he agrees that the controversy is far from over. Norton says that patients are getting far better diagnosis and treatment now and that mammography can produce a 25% to 30% reduction in mortality. The whole topic, he says, deserves yet another, more impartial, review.

–ELIOT MARSHALL

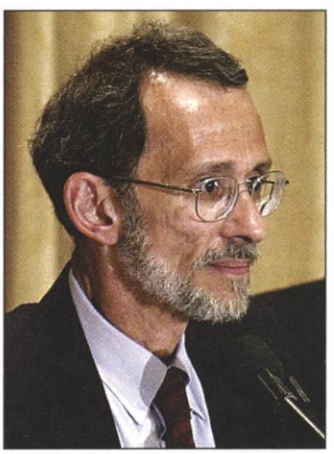
DATA SHARING

Clear-Cut Publication Rules Prove Elusive

A select group of scientists and journal editors met last week at the National Academy of Sciences in Washington, D.C., to chisel out some commandments for their peers on the ethics of publishing. Organizers hoped that the 25 February session would produce clear and simple rules compelling scientists to share data. But the participants clashed on what it means to insist that an author make "freely available" the data backing a published claim—reviving an argument that wracked the human genome community a year ago. After drafting a few broad "thou shalt" phrases, participants failed to agree on how these rules should be enforced. The leader of the session—Thomas Cech, president of the Howard Hughes Medical Institute in Chevy Chase, Maryland—promised that an academy panel will fill in the details later.

Prepping the audience, Eric Lander of the Whitehead Genome Center at the Massachusetts Institute of Technology began the day with a talk on historical context. The rules being considered by this meeting, he said, were established by the Royal Society in London in 1665 when it began publishing its scientific proceedings. The society offered a simple bargain, according to Lander: Anyone claiming to be an inventor could get the society's imprimatur—as long as the claimant published a detailed description of the discovery. Before this, scientists had often protected their work through concealment, Lander said; but, thanks to the society's bargain, they could achieve honor through disclosure. Lander proposed an updated set of rules, a "uniform policy on access to data and materials" (UPADAM), which he pronounced "up 'n' at 'em." The basic idea is that if you choose to publish a claim, you must release all the "integral data" supporting it, as determined by editors and peer reviewers.

Lander acknowledged a personal stake in this cause. As the principal author of the draft version of the human genome sequence published in *Nature* last year, he strongly disapproves of the way a commercial group—Celera Genomics Inc. in Rockville, Maryland—was allowed to publish a rival paper at the same time in *Science* (16 February 2001, p. 1304). Unlike Lander's group, Celera did not release supporting data through a government-funded repository, GenBank. Instead, Celera allowed readers to view data at a Web site the company controls. Lander said *Science* made "a mistake" and did "a disservice" in agreeing to this form of data release. He asked the academy group to reject what he called "partial data release." Some academic researchers, including Marc Kirschner, cell biology chair at Harvard Medical School in Boston, endorsed this view.



One code? Lander (*right*) proposed a uniform policy; Patrinos (*above*) argued for flexibility.

But several others disagreed. The most outspoken dissenter was Ari Patrinos, director of biological and environmental research at the Department of Energy. DOE pioneered the Human Genome Project, although the bulk of support has come from the U.S. National Human Genome Research Institute (NHGRI) and the Wellcome Trust, a British charity. Patrinos, describing himself as "normally an optimist," said, "I am extremely pessimistic about the outcome of this discussion." It would be "a mistake," he argued, to adopt a simple rule forcing authors to choose between releasing control of all their data at publication or not publishing. He thinks that enforcing such a rule would silence some would-be authors in the private sector.

Patrinos urged people to "recognize the importance of the emerging biotechnology industry" and avoid adopting a set of "feel-good" data-release policies that suit mainly academics. This could cut the academic world off from some of the most exciting research being done now, he said. Patrinos argued instead for a "trench-by-trench" campaign, accommodating the rules of publishing to the circumstances of the author. Noting that private investment in research is increasing, Patrinos also warned that agencies such as DOE and NHGRI may have less clout than before: "Our hands may be more tied than in the past," making it difficult "to enforce the rules you would like us to enforce."

Francis Collins, director of NHGRI, found these comments "puzzling." He said that recently there has been "a blurring" of the rules on data release. "It is hard for me to see how we can step away from" an effort to "nail down" the basic principles and decide how they should be enforced, Collins said. And he argued that Patrinos's trench-by-trench approach would lead to a series of exceptions.

Although the working session did not reach a consensus on who should be the primary enforcer of standards, Cech summed up a few principles he hoped all could agree on. The draft summary states that authors have a responsibility to "undertake reasonable efforts to make data and materials integral to a publication available in a manner that enables replication and further science." Specifically, if authors claim to have created a large database, "the entire database must be available," and in every case, they must make available "enough [data] to support the paper's conclusion."

Cech said he and his panel aim to wrap up a report on this project within "a few months." Meanwhile, he said, the National Institutes of Health is planning to release its own updated set of data release guidelines—along with new grant support to help defray the cost of sharing materials—possibly as soon as next week.

–ELIOT MARSHALL

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