

## CLINICAL RESEARCH

## Shutdown at Hopkins Sparks a Debate

nents, who have the ears of Senate Majority Leader Tom Daschle (D-SD) and panel member Senator Tim Johnson (D-SD), say that impending plans to flood the former Homestake mine forced them to act quickly.

In contrast, the antarctic astrophysics project, dubbed Ice Cube because of its 1-kilometer-per-side dimensions, has worked its way through NSF's review process. The proposed \$243 million muon and neutrino detector would vastly expand an existing array beneath the South Pole. The expansion was approved last year by the NSB and made it into NSF's draft budget last fall. But it was booted out by the president's diktat.

Project leader Francis Halzen and others at the University of Wisconsin, Madison, which would run the facility, didn't give up, though; they won over Representative David Obey (D-WI), the ranking member of the House Appropriations Committee. At his urging, the committee approved a \$15 million down payment on the project. "There's a long backlog of projects, and I've been told that we were top ranked," says Halzen, explaining his decision to seek help from a powerful friend. "There's also a European project coming along, and we want to push forward and retain our advantage."

This year's final spending bill is also likely to include money for a research plane that was endorsed by the NSB in 1998 but never included in NSF's budget request. The \$80 million project, called High-Performance Instrumented Airborne Platform for Environmental Research (HIAPER), would be operated by the National Center for Atmospheric Research in Boulder, Colorado, which persuaded Congress to put in \$20 million over the last 2 years. In keeping with the panel's philosophy of finishing what it starts, the House this year added the remaining \$35 million needed to start bending metal. Last week, NSF announced that it had begun negotiating with Gulfstream to build the plane.

Left behind in this free-for-all are supporters of EarthScope and the \$100 million National Ecological Observatories Network, a collection of 10 instrumental field stations. These two projects were part of NSF's 2001 budget request, at \$17 million and \$12 million, respectively, that legislators declined to fund. And they were bumped from NSF's draft 2002 budget.

Unlike the teams involved in Ice Cube, HIAPER, and the underground lab, the earth scientists who hope to carry out EarthScope have agreed to bide their time until NSF is able to reinsert them next year into its major research equipment and facilities account, at a proposed \$32 million. However, so far that strategy has netted them nothing but a pat on the back. "They agreed to play by the rules, and so far they have lost out," notes one NSF official.

—JEFFREY MERVIS

The federal government abruptly suspended all U.S.-funded human studies at Johns Hopkins University in Baltimore last week. Then, in a turnabout 3 days later, it allowed about 700 of the more than 2400 that were affected to resume, although with restrictions. The crisis sent a shock through the clinical research world, mainly because Hopkins is regarded as one of the country's most conscientious overseers of research. And it seemed likely to raise questions anew about how best to protect research subjects.

These events grew out of an inquiry into the death on 2 June of a healthy volunteer in a Hopkins asthma study. Hopkins completed its own investigation of the tragedy on 16 July, finding relatively minor flaws in the study (*Science*, 20 July, p. 406). Then on 16 to 18 July, investigators from the U.S. Department of Health and Human Services (HHS), who had been checking other issues at Hopkins since fall, conducted an urgent site visit. One day later, they found Hopkins deficient on 31 points and issued the shutdown order.\* Among the alleged infractions: failure to approve every study in a "convened meeting" of the Institutional Review Board (IRB), lack of proper informed consent, exposure of subjects to a drug not approved for human use, and failure to report an adverse reaction.

Unlike a half-dozen other institutions that have been punished in this way, Hopkins didn't meekly swallow HHS's medicine. Instead, university officials contested some of the allegations and lashed out at the regulators. The same day Hopkins received the notice of deficiency from HHS's Office for Human Research Protections (OHRP), Edward Miller, CEO of Johns Hopkins Medicine, appeared before cameras on Hopkins's front steps to protest what was happening. And in a public statement,<sup>†</sup> the university called the research shutdown "unwarranted, unnecessary, para-

\* [ohrp.osophs.dhhs.gov/detrm\\_lettrs/jul2001.htm](http://ohrp.osophs.dhhs.gov/detrm_lettrs/jul2001.htm)

<sup>†</sup> [www.hopkinsmedicine.org/press/2001/JULY/010719.htm](http://www.hopkinsmedicine.org/press/2001/JULY/010719.htm)

lyzing," "draconian," and "outrageous." University officials also contacted members of Congress. Both of Maryland's senators, Democrats Barbara Mikulski and Paul Sarbanes, responded with faxed protests to HHS Secretary Tommy Thompson.

Over the next few days, Hopkins and HHS reached an understanding. The university submitted a plan to correct the claimed deficiencies by specific deadlines. And HHS agreed that people could continue to be treated in Hopkins clinical studies if the investigators could verify that this would be "in the best interests" of the subjects. Most studies, however, have been placed in limbo and must be reapproved.

This compromise, reached over a weekend of hectic activity at Hopkins and in government offices, seemed to cool the rhetoric. But it was clear early this week that Hopkins

and OHRP still disagree sharply on important points and that a wider debate may be brewing. Observers differ markedly: Some are exasperated with the detailed reporting imposed by the regulators—which they dismiss as mere paperwork that doesn't necessarily improve the protection of research subjects—whereas others think the oversight system needs even more support and authority.

After reading the documents, Norman Fost, a pediatrician and ethicist who chairs

an IRB at the University of Wisconsin, Madison, says he agrees with Hopkins that some government sanctions were "outrageous," probably "unfair," and perhaps even "wrong." For example, OHRP reprimanded Hopkins for ignoring U.S. rules on the use of drugs in basic clinical research, but Fost says the record shows that the government has never clearly articulated them. In contrast, Mary Faith Marshall, a professor of medicine and bioethics at the University of Kansas Medical Center in Kansas City and chair of OHRP's advisory committee, thinks government inspectors were probably justified in taking strong action. "In my experience," she says, "they bend over backward to be fair and do an excellent job." She notes that an HHS inspector general's report in 1998 warned that IRB review panels were overworked and underfunded—putting human subjects at risk.

The university, meanwhile, is trying to



"Outraged." Hopkins Medicine CEO Edward Miller protested a federal shutdown order.

recover from the setback. If OHRP-ordered clinical reviews at other sites are any guide, it will cost Hopkins well over \$1 million and months of labor to get its clinical studies fully on track.

—ELIOT MARSHALL

## HOUSTON FLOOD

### Research Toll Is Heavy In Time and Money

**HOUSTON**—The final group of researchers returned last week to labs at the Texas Medical Center, nearly 6 weeks after Tropical Storm Allison temporarily turned the campus into a lake (*Science*, 22 June, p. 2226). But no one was celebrating. Widespread power outages had destroyed years of work, and the basement laboratories of the University of Texas Health Science Center (UT-HSC) and the Baylor College of Medicine (BCM)—once home to over 35,000 animals that drowned—were declared a total loss.

"This is a real, honest-to-God disaster," says Jim Patrick, BCM's vice president of research. Several large pieces of equipment, including two multimillion-dollar electron microscopes, were completely destroyed by water and floating debris, and Baylor officials are still tallying the damage. The total cost to UT-HSC is expected to be about \$205 million, including a ruined \$50 million cyclotron used for positron emission tomography, says George Stancel, the dean of the graduate school of biomedical science at UT Houston. With insurance expected to pay for only a fraction of the replacement value, both schools are seeking state and federal funds for the restoration work.

Researchers are more concerned about the lost time. Morteza Naghavi saw almost 4 years of work float away when the flood drowned all his research animals. "I lost everything: 800 mice and 35 rabbits," says Naghavi, a cardiology researcher at UT-HSC, about animals bred to be apoE deficient, which predisposes them to heart attacks. It was even worse for Lance Gould, leader of the team that built the ruined cyclotron. "It took 20 years to build that machine," he says.

Allison's destructive clouds have a faint silver lining, however. Gould's team hopes to build a better cyclotron than the one they had, for less money because of improvements in technology, with support from private donors. "The storm was an unmitigated disaster," says Gould. "But we are turning it creatively into an advantage."

The researchers back on the job have shifted to higher terrain, either elsewhere in the hospital or in nearby temporary facilities. And neither institution plans to move them back underground. "That is history," says Patrick. But their upward mobility has creat-



**Damaged goods.** Floodwaters destroyed equipment in the basement of the Texas Medical Center.

ed a space crunch. The two hospitals must each relocate employees in nonessential services, now occupying thousands of square meters, before they can resettle the labs in permanent homes.

—MARK SINCELL

Mark Sincell writes from Houston.

## ANIMAL BEHAVIOR

### New Data Reveal the Sisterhood of Lions

In any pride of lions, a "lion king" typically sires most of the cubs. But whereas male pridemates have a strict pecking order, a new study reveals that there's really no such thing as a "lion queen." On page 690, behavioral ecologist Craig Packer and colleagues Anne Pusey and Lynn Eberly of the University of Minnesota, Twin Cities, report that female lions all bear young with



**Togetherness.** In contrast to males, female lions in a pride have about equal reproductive success and even cooperate in raising their young.

about equal success—an unusual behavior for social mammals.

Packer and his colleagues have been observing lions in Tanzania since the 1960s. A decade ago, their DNA analysis showed a big "reproductive skew" among males, with most of the offspring belonging to one of two dominant males. In this study, they analyzed 36 years' worth of birth records in which they kept track of every cub reaching its first birthday in some 31 prides and identified its mother. "That they looked across a large number of groups over a long time makes this a powerful [study]," notes Jeffrey French, an animal behaviorist at the University of Nebraska, Omaha.

The number of young varied from pride to pride: In some, the females had just one or two cubs a year, whereas in others, they tended to have three or four and occasionally more. But within a pride, Packer says, "there was no hint [that] any females were systematically getting more reproduction than others." Indeed, the more mothers in a pride, the likelier the cubs were to survive.

Such behavior is atypical for social mammals, in which it is common for one female to hold the reproductive reins and actively sabotage the reproductive efforts of others. As a result, subordinate females stop breeding and instead help a more dominant sister or mother with her young. But Packer and his colleagues offer several reasons why this behavior does not occur in lionesses.

For one, the fighting required to set up a pecking order that would prevent low-caste females from breeding would lead, Packer says, to "mutually assured destruction" from the animals' massive claws and teeth. "It's too risky to try to control other females directly," agrees Tim Clutton-Brock, an evolutionary biologist at the University of Cambridge, United Kingdom.

Lionesses also avoid another strategy sometimes employed by alpha females seeking to thwart breeding by potential rivals: killing the rivals' newborn young. This likely stems from breeding in communal locations. But in behavior typical of felines, lionesses go into hiding to give birth and don't rejoin the pride until the cubs are 6 weeks old and much less vulnerable.

Returning mothers then raise the cubs communally and together fend off raids from lions in other prides. "Females benefit from each other's presence," notes Clutton-Brock. In short, Packer adds, "the queen of beasts is a democrat."

—ELIZABETH PENNISI