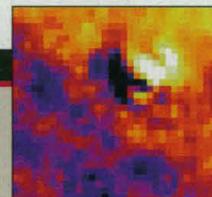


The heart of the proton



How snakes lost their legs



Feeding a black hole

Hassner Sharav steered patient-critics to NBAC in September 1997, where they presented claims that clinical researchers were needlessly distressing patients in challenge trials. Later she asked NBAC to look into the use of ketamine, an anesthetic that has been given in small doses to hundreds of mental patients to provoke psychotic symptoms. Ketamine has short-lived effects like the hallucinogen PCP, causing weird auditory and visual disturbances. Based on its own review, NBAC recommended new protections for mental patients (*Science*, 27 November 1998, p. 1617).

Clinicians say the heaviest blow, however, came in late November, when the *Boston Globe* ran a devastating four-part series full of research horror stories. It concluded with an editorial asking the Justice Department to conduct a criminal investigation into challenge and drug-withdrawal studies. Research leaders were shaken. Within weeks, Hyman spoke publicly about the need for a new scientific panel to approve risky research.

Researchers doing the kind of work that has been criticized tend to see Hyman's move as a surrender to critics, and they don't like it. "I think it would be foolhardy," says William Carpenter, director of the Maryland Psychiatric Research Center at the University of Maryland, Baltimore. Carpenter's colleagues were among those criticized for conducting ketamine studies. Singling out clinical psychiatry for an extra review would be wrong, Carpenter says, because it stigmatizes that area of biomedicine. "It will discourage the best young investigators," he thinks, for "why would you go into a field that has a politicized review process, when others don't?" Like his peers, he insists that other medical researchers use probes that are at least as risky as those used in psychiatry.

Carpenter worries that once created, the new safety panel will slip out of NIMH's control. Critics "will see an innate conflict of interest" in allowing NIMH to watch over its own studies, he warns, and will take it over and "politicize" it. As a warning, he points to the attack on ketamine studies, which he defends as an important way of learning about the efficacy of schizophrenia drugs. He claims that through ketamine trials, people are finding that widely used antipsychotic drugs don't block the underlying pathological brain activity. As for side effects, "ketamine doesn't seem to cause much anxiety or distress," he says. At a 1 December meeting at NIMH, Carpenter reported that data from about 60 patients in ketamine trials at NIMH,

Yale, and Maryland reveal few signs of distress. The effects in the worst cases lasted no more than 2 days, he said, and most effects were over within 90 to 180 minutes. However, two patients were distressed enough that they dropped out of the research.

Donald Klein, a professor at Columbia University and a psychiatrist at the New York State Psychiatric Institute, also feels that a national safety review panel for psychiatry could stifle research. His own work for the past 2 decades has involved inducing panic in people with panic disorder by injecting them with sodium lactate. It has led him to a theory that many cases of panic disorder arise from an innate derangement of the suffocation alarm, a hypersensitivity to carbon dioxide. This research could never have been done, Klein says, without challenge studies, and he wonders whether it would have been permitted by a national safety panel.

Although a few senior clinicians like these are hostile to Hyman's proposal, others are keeping their powder dry. The president of the American College of Neuropsychopharmacology, David Kupfer, chief of psychiatry at the University of Pittsburgh, says he's pleased that NIMH is trying to be "proactive," but doubts that a national safety panel can do better than existing, local ones.

Hyman is aware of resistance within his community. But he believes NIMH must move ahead with the reforms. Given the attention being focused on the ethics of mental health research, he said at a meeting last December, the community needs "to get our house in order."

—ELIOT MARSHALL

BIOMEDICAL RESEARCH

Ruling May Free NIH to Fund Stem Cell Studies

Scientists eager to begin studies on two new types of human stem cells got some good news this week: The National Institutes of Health (NIH) announced that, contrary to what many had feared, U.S. law does not bar federal support for this burgeoning field. Grant money could be approved as early as this fall, according to NIH staffers. Researchers hope to use the cells for studies ranging from basic research on early human development to the development of new technologies for tissue transplantation.

NIH director Harold Varmus announced on 19 January that, in the Administration's reading, "current law permits federal funds

to be used for research using human pluripotent stem cells"—cells that have the potential to develop into a wide variety of human tissues. During a talk at a meeting of the National Bioethics Advisory Commission (NBAC) in Washington, D.C., Varmus released a memo on stem cell research by Harriet Rabb, general counsel of the Department of Health and Human Services. Rabb makes it clear that there is no legal reason why funding of stem cell research cannot begin now.

Rabb's ruling sets aside some of the concerns that arose in November, when researchers first announced that they had derived stem cell lines from human embryo and fetal tissue (*Science*, 6 November 1998, p. 1014). NIH officials were concerned that congressionally imposed rules on some types of embryo and fetal tissue research might restrict the use of the new stem cells to private labs. For example, a clause added to the 1999 NIH appropriations bill makes it unlawful to spend federal funds on the creation of embryos "for research purposes," and it blocks support of research in which embryos are "destroyed, discarded or knowingly subjected to risk of injury or death. ..." An earlier statute also restricts interstate transfer and the therapeutic use of fetal tissue.

In her memo, Rabb makes a distinction between federal support for the development and the use of stem cell lines. The congressional language would prohibit the development of cell lines from embryos but not necessarily from fetal tissue, she wrote. (Both stem cell lines announced in November were developed with private funds.) But the law doesn't apply to the use of stem cells from either source, she said. The law focuses on making a human "embryo" or "organism" for research, she notes, but stem cells are not organisms—or even precursor organisms, in her view—for they cannot develop into an embryo even if implanted in a woman's uterus.

Varmus discussed these detailed legal issues at the first of six meetings NBAC is planning for an ethics review of stem cell research. NBAC hopes to have a draft report by



No legal barrier. Varmus hopes to move ahead later this year.

June, according to its chair, Harold Shapiro, the president of Princeton University. But Varmus said he would like to know by March what NBAC thinks of plans to start funding human stem cell research. After hearing from NBAC, researchers, and the public, he hopes to draw up "clear guidelines" describing what can and cannot be done under the law. He plans to distribute the guidelines by midyear, then set up a standing review committee to monitor compliance.

"I am delighted to hear NIH made this decision," said Senator Arlen Specter (R-PA), chair of the subcommittee that approves NIH's appropriation bill, noting that it does not violate the intent of earlier legislation. Specter added that "the last 60 days have seen breakthrough developments on stem cell research," promising "enormous advances" in many areas of disease research.

—ELIOT MARSHALL

PALEOCLIMATE

El Niño Grew Strong As Cultures Were Born

El Niño's comings and goings—and the worldwide effects of this tropical Pacific warming—are by now so familiar that they seem to be a permanent fixture of Earth's climate. But in this issue of *Science* (p. 516), a group of researchers reports that a climate record cored from the bottom of a lake high in the Ecuadorian Andes suggests a much-weakened El Niño between 5000 and 12,000 years ago—or even none at all.

Because older climate records show that in even earlier epochs, El Niño operated much the same as today, the new lake record points to an El Niño that waxes and wanes over the millennia. "It's a really interesting record, an important result if correct," says paleoclimatologist Konrad Hughen of Harvard University. Some researchers argue that the onset of the modern El Niño 5000 years ago may have helped shape the emergence of civilizations around the Pacific, and its vacillations may give clues to our climate future in the greenhouse world. But it will take more records like the one from the Ecuadorian lake to fully persuade the cautious paleoclimate community that El Niño sometimes takes a break.

Paleoclimatologist Donald Rodbell of Union College in Schenectady, New York, and his colleagues were actually searching for evidence about the end of the ice age, not El Niño, when they cored the bottom of Laguna Pallcacocha, a lake 4000 meters up in the Andes of southern Ecuador. Although the ice age record they hoped for didn't show up in the 9.2-meter-long core, hundreds of sedimentary "zebra-stripe" layers did.

After chemical and mineralogical analysis, Rodbell concluded that the alternating

layers of light, organic-poor sediments and dark, organic-rich sediments record the comings and goings of torrential rains spawned by El Niños. In non-El Niño years, moderate rains apparently wash only a little sediment, heavily laden with the dark debris from vegetation, off the steep, bowl-shaped slopes surrounding the lake. In El Niño years, the unusually warm waters just offshore fuel powerful storms that wash large amounts of sediment unsullied by organic matter into the lake, leaving a lighter colored deposit.

A quick look showed a marked shift in the pattern of zebra stripes partway through the record. After Rodbell's team set a time scale for the record with carbon-14 dating and used medical imaging software to count the stripes, they were able to date and quantify the shift. During the past 5000 years or so, the lake recorded extreme rains every 2 to 8 years, following the same rhythm that El Niño has exhibited of late. But before 5000 years ago, that pattern fades away. Extreme rains recurred only at intervals of a couple of decades to 75 years. Only weak El Niños could have persisted in this period, says Rodbell, as they did not spark torrential rains near the lake. But before 12,000 years ago—earlier than could be seen confidently in the lake record—El Niño was going strong, according to new records from western Pacific corals and even Great Lakes sediments.

"It's an interesting story," says Hughen. Still, he says, "this is one record from one lake basin." Although the lake seems to have been a faithful recorder of heavy rains during historical times, changes in the vegetation around the lake, for example, might have obscured the record of earlier strong El Niños. Rodbell and his

El Niño's mark. Frequent storm deposits (light bands) in younger sediments from a lake core (top) suggest that El Niño has strengthened since the time of older sediments (above).



ScienceScope

JAMA Editor Gets the Boot Journal editors are dismayed by last week's sacking of George Lundberg, longtime editor of *The Journal of the American Medical Association* (JAMA). Association brass fired the 17-year veteran for his decision to publish a paper on what college kids think of oral sex—just as President Bill Clinton's impeachment trial moved into its second week.

The paper, which appeared in the 20 January JAMA, was presented by the authors—June Reinisch, former director of the Kinsey Institute for sex research in Bloomington, Indiana, and Kinsey researcher Stephanie Sanders—as a contribution to "the current public debate regarding whether oral sex constitutes having ... sexual relations." It reported that 59% of 599 students surveyed at a large midwestern university in 1991 did not regard oral-genital contact as having "had sex." The authors conclude there is a "lack of consensus" on the topic.

The timing of the paper did not sit well with AMA executive E. Ratcliffe Anderson, who said it had been rushed to publication. In announcing Lundberg's departure, Anderson said that the editor had threatened the journal's "integrity" by "inappropriately and inexcusably interjecting JAMA into a major political debate that has nothing to do with science or medicine." Anderson, who has been at the AMA helm for 7 months, also said other factors had contributed to a loss of "confidence and trust" in Lundberg, but he declined to be specific.

Lundberg's lawyer, William Walsh, branded the firing an "inappropriate intrusion into the historically inviolable ground of editorial independence." And other journal editors were outraged. The board of the Council of Biology Editors said "the firing marked a dark hour for scientific journals worldwide," and that the action "amounts to tacit support for suppression of scientific information that may be politically sensitive." *New England Journal of Medicine* Executive Editor Marcia Angell was surprised by the firing of a "highly successful editor," although she called the Reinisch article "trivial and irrelevant."

Lundberg, 65, has long been at odds with AMA honchos, tackling issues such as the perils of smoking before the association took public stands. Lundberg declined to comment, but according to press accounts Walsh has hinted that litigation might be in the works.

Contributor: Constance Holden

