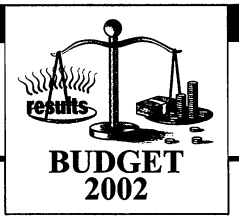


PAGE 2229
Hopeful signs on US budget

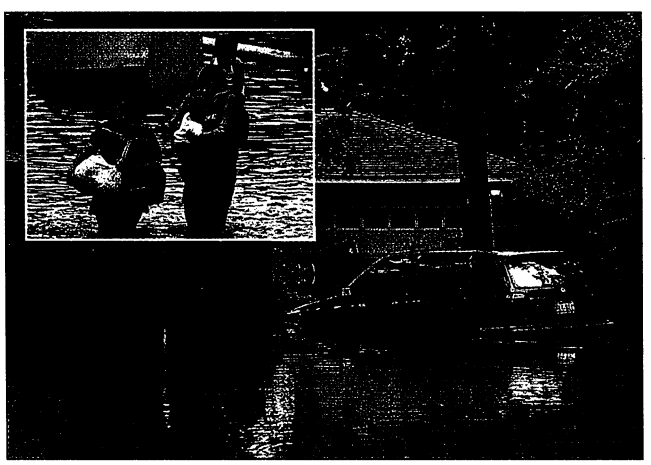
2231
How cancer cells evade a wonder drug

NATURAL DISASTERS

Texas Medical Center Staggered By Deadly Tropical Storm

HOUSTON—Building on a Houston floodplain is a dicey proposition, and last week the dice came up snake eyes for the Texas Medical Center (TMC). Years of scientific work were destroyed, millions of dollars' worth of equipment crippled, and thousands of lab animals drowned when the region was hit with a second burst from Tropical Storm Allison. All research at TMC was shut down as scientists set to the grisly task of clearing out carcasses before they rotted in the sweltering Houston heat.

The TMC is the largest collection of medical research facilities in the world, including the University of Texas M. D. Anderson Cancer Center (MDACC), the University of Texas Medical School at Houston (UTMSH), and Baylor College of Medicine. It also sits at the bottom of an 8-kilometer-square bowl-like depression in the Houston landscape bordered to the south by the Braes Bayou.



Under water. Massive flooding like this wreaked havoc on biomedical facilities in Houston's bayou region.

Rains from Allison's first assault on 7 June had already filled the bayou to the brim. So when Allison unexpectedly returned from the Gulf of Mexico on 9 to 10 June to drop another 36 centimeters over the research complex—an event that occurs on average less than once per century—the water had nowhere to go but into the TMC buildings. "There is no way any [flood prevention] system could survive that amount of rain," says Rice University flood expert Philip Bedient.

A full accounting of the disaster, which claimed up to 24 lives and cost the region billions of dollars, may take months, but the flood's toll on TMC research is already staggering. "We had 2500 animals, from mice to large animals, and we believe we have lost all of them," says UTMSH dean Maximilian Buja, adding that the floods and resulting power outages probably also destroyed the school's new experimental nuclear magnetic resonance facility, ruined a cyclotron used for positron emission tomography scans, and shut down freezers that preserve valuable tissue samples and antibodies.

Flooding at Baylor damaged at least three multimillion-dollar electron microscopes, possibly irrevocably, and killed animals in the older of their two vivariums. "We got everything from the cows down to the rabbits out in time," says Claire Bassett, vice president for public affairs at Baylor. But 30,000 mice and rats may have drowned, she says. The MDACC miraculously escaped serious damage, however, and its researchers worked through the weekend to help others save perishable materials, says MDACC Chief Academic Officer Margaret Kripke.

Insurance and federal aid money should replace most of the lost material, but researchers can never get back the time they have invested. For example, some of the drowned transgenic mouse colonies at UTMSH took a decade to build, and only a minority can be regenerated from breeding pairs sent to other universities. "This is a devastating loss," says George Stancel, dean of the graduate school of Biomedical Science at UTMSH.

But it could have been even worse. Only four of the nine stacked racks of mouse cages in the Baylor vivarium were underwater, says Baylor molecular biologist Joe Bryan. "We lost critical experiments," says Bryan. "But we still have breeding stock for most of the lines." Bryan estimates that it will take 6 to 8 months to regenerate his mouse herd.

A higher priority is the cleanup. Last week Bryan and other scientists donned hazard suits, rubber boots, and gas masks before descending into the basements to gather dead animals and dump them into biohazard bags destined for the incinerator. Dehydration from the intense Houston summer heat forced most people back to the surface within 45 minutes. And the smell? "I'll leave that to your imagination," says Bryan.

Emergency power and communications systems have now been restored to almost all of the buildings, but the air conditioning was expected to take a few more days. All research remains on hold as faculty members join forces with relief workers to dig out—and dry out—after the disaster.

–MARK SINCELL

Mark Sincell writes from Houston.

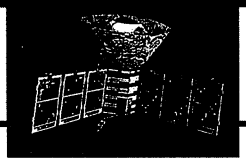
HUMAN SUBJECTS

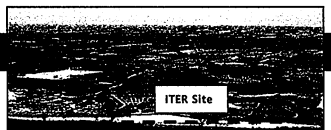
Volunteer's Death Prompts Review

Clinical researchers at the Johns Hopkins University Bayview Medical Center in Baltimore braced for a round of public investigation last week after reporting the death of a volunteer in a study of lung function. The study, funded by the National Institutes of Health (NIH), was directed by Hopkins asthma researcher Alkis Togias, with Solbert Permutt as co-investigator. Healthy volunteers in the experiment inhaled two chemicals that have contrasting effects on the lungs' airways—one constricting and the other relaxing them—yielding data that may shed light on the causes of asthma.

Hopkins made public a short summary of the case on 13 June, saying that an investigation was still under way, but that details would be withheld to protect the volunteer's family. Hopkins later released a copy of the research protocol and consent form. A university official then confirmed press reports that the volunteer, who died on 2 June after several weeks in the hospital, was a 24-year-old Hopkins lab technician named Ellen Roche.

CREDITS: PAT SULLIVAN/AP; (INSET) LM. OTERO/AP





Neither Permutt nor Togias was available to comment. But in a protocol submitted to Hopkins's Institutional Review Board (IRB) last year, Togias explained that the experiment was designed to examine two distinct aspects of normal lung physiology called "bronchoprotection" and "bronchodilation." Togias intended to ask up to 10 healthy subjects to inhale chemicals or saline (as placebo) and breathe into instruments that measure lung capacity. All volunteers were to inhale methacholine, which causes a temporary constriction of the airways, mimicking asthma. And some were to be given hexamethonium, a ganglion-blocking drug that affects the nervous system, lowering blood pressure and relaxing the airways.

"It's proper to characterize this as a mysterious death."

—Joann Rodgers

Hexamethonium formerly was prescribed to lower blood pressure, but that use was withdrawn by the manufacturer. It has not been used in many recent studies, researchers say, although Togias's protocol cites four human studies in the 1980s that used the drug. The protocol suggests that its main risk is that it can induce an excessive drop in blood pressure, and for this reason the protocol calls for a physician to be on hand to oversee its staged administration.

Togias suspended the research in May after Roche became ill. He notified the IRB in a 9 May letter of "a serious adverse event," explaining that a volunteer had reported dry cough, shortness of breath, and flulike symptoms 24 hours after participating in the hexamethonium part of the experiment. The volunteer was hospitalized after an x-ray showed signs of "early pneumonitis." On 17 May, Hopkins vice dean for research Chi Van Dang alerted the U.S. Office for Human Research Protections (OHRP) of the "serious, unexpected" adverse event. Three weeks later, Dang sent notice that the woman had died. He added that the clinicians had performed an autopsy and were investigating many aspects of the study, including the supplier's claim that the hexamethonium was 99.6% pure. OHRP has now begun its own investigation. "It's proper to characterize this as a mysterious death," says university spokesperson Joann Rodgers.

Claude Lenfant, director of NIH's National Heart, Lung, and Blood Institute, which funded the research, says clinicians seem to have followed the right procedures, and that Hopkins is known to be "ferocious" in getting ethical issues correct. Clinical experiments always contain an element of risk, adds Richard Boucher, an expert on cystic fibrosis at the University of North Carolina, Chapel Hill. He cited the death 5 years ago of a volunteer at the University of Rochester in New York after a reaction to an anesthetic. Since then, he says, "everyone has redoubled their efforts to make this research as safe as possible." **–ELIOT MARSHALL**

NEUTRINO PHYSICS

Polymorphous Particles Solve Solar Mystery

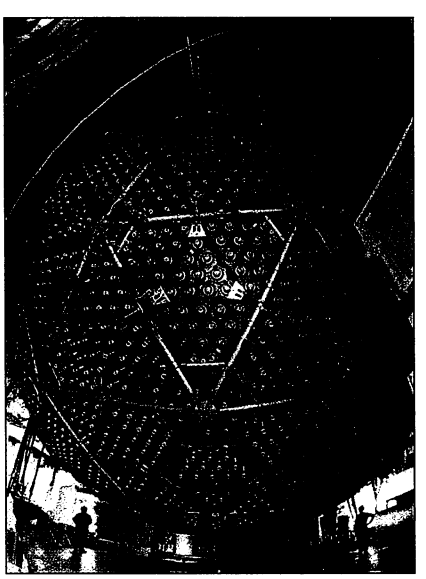
For particles with almost no mass, neutrinos are making quite a splash. On Monday, scientists from three countries announced that they had spotted neutrinos that had been missing for 3 decades.

In the late 1960s, physicists calculated the number of relatively energetic neutrinos that should be streaming from the sun—due to the decay of boron-8 cooked up in the solar furnace—but experiments came up short. There were too few neutrinos. This is the mystery that Canada's Sudbury Neutrino Observatory (SNO) has now cleared up. "I'm thrilled by the precision of the result; I'm thrilled it agrees with the solar model calculations; I'm thrilled we have an answer to the problem," says John Bahcall, a physicist at the Institute for Advanced Study in Princeton, New Jersey.

In fact, SNO has confirmed what several experiments, notably Super-Kamiokande in Japan, had already indicated: The missing neutrinos had simply changed flavor. Neutrinos come in three flavors, named after the particles they are linked with. Electron neutrinos are the type produced by the sun; muon and tau neutrinos, which result from various particle interactions, are harder to detect. In the late 1990s, experiments provided fairly strong evidence that electron neutrinos turn into muon and tau neutrinos as they stream away from the sun—something that can happen only if the particles have mass (*Science*, 4 July 1997, p. 30). The "missing" neutrinos from the sun had merely changed into muon and tau neutrinos and escaped detection.

Buried 2 kilometers underground in a nickel mine in Ontario, SNO has just given a resounding conformation to this picture. The detector measures the neutrinos coming from the sun in two ways. The first method spots the recoil of a neutrino off of an electron. Any of the three flavors of neutrino could potentially cause such a recoil and be detected. The second method detects when an electron neutrino strikes a neutron within a 1000-ton sphere of heavy water. Only an electron neutrino can make the neutron spit out an electron, triggering the detector. The two methods, combined with results from Super-K, reveal just how many neutrinos are coming from the sun and what proportion of them is either muon or tau neutrinos.

"What we find is that there is an appearance of muon and tau neutrinos en route from the sun to the Earth," says SNO project director Art McDonald of Queen's University in Kingston, Ontario. "The electron neutrinos transform into another type." The transformation confirms earlier observations that neutrinos have mass. Better yet, the measurements agree with first-principles calculations of the amount of solar neutrinos created by the sun. "It is in very good agreement," says SNO team member Kevin Lesko, a physicist at Lawrence Berkeley National Laboratory in Califor-



CREDIT: SNO

Neutrino detector. At Sudbury, 10,000 photomultipliers on an 18-meter-wide sphere watch for elusive particles.