A Revisionist Timetable for The Ice Ages
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the breakdown of membranes in dead cells (a process that produces a flood of free radicals, which can kill healthy cells). And for spinal cord injuries, emphasize doctors, saving even a small percentage of the cord's axons can mean the difference between complete paralysis and useful motor function.

Promising as the new treatments are for preventing secondary damage, though, some people are too severely injured to start with to get much benefit from them. And, of course, these drugs can't help people injured long ago. But other drugs under development may be able to restore lost function in neurons that have already been damaged. Take for example a drug called 4-aminopyridine (4-AP), which is now going into the first clinical trials in human patients. As Keith Hayes, a clinical neurophysiologist at the University of Western Ontario in Canada, explains: "Until recently, paralysis and weakness were thought [to be] due only to physical damage to axons. But some of the paralysis may be due to the loss of insulation—the myelin." When the myelin sheet is damaged, adds Hayes, potassium channels on the nerve cells are exposed and ions flow out, creating a "short-circuit" that prevents nerve impulses from being transmitted normally. 4-AP helps restore the conductivity of those naked cells by blocking the channels.

"There has been a revolution.... We have a whole new armament of therapies to consider."

–Ira Black

Transplanting the cure

Other researchers are trying to grow the insulation back by transplanting myelin-producing cells known as Schwann cells into the injured area. The idea, says Richard Bunge, the scientific director of the Miami Project to Cure Paralysis, one of the leading groups exploring that approach, is to obtain Schwann cells from paralyzed patients, grow them in culture, and then transplant them into the original patients' spinal cords. And Schwann cells may do much more than just restore myelin coating. Within the past decade, says Bunge, researchers have discovered that the versatile cells secrete substances, such as NGF, that encourage axons to grow.

Another transplant strategy, the use of fetal nerve tissue, also stirred interest at the APA meeting. Either grafts of solid nerve tissue or an injected slurry of fetal nerve cells restored, on average, 40% of lost motor function to cats paralyzed by contusion-type spinal injuries; some even regained near-normal walking ability, reported Paul Reier of the University of Florida Brain Institute and Douglas Anderson of the Veterans Affairs Medical Center in Cincinnati. Their study expands on earlier fetal tissue work in rats and is considered significant because the animal model used by Reier and Anderson strongly mimics the damage most often seen in human spinal cord injuries.

The fetal tissue grafts apparently don't work the way the researchers expected, however. The original rationale for the experiment, says Anderson, was that the fetal nerve tissue might actually form new functioning nerve cells. But there has been little evidence of that, he says, and he and his colleagues now believe that, like some of the strategies mentioned earlier, the fetal tissue somehow "turns back on" intact fibers that don't conduct or function correctly. Exactly how that happens is still a mystery, admits Anderson.

There's also the possibility that the fetal transplants didn't actually help the animals after all. Researchers like Reier and Anderson have to be careful in interpreting their results, since the evaluation of, say, whether a cat is walking better or not is a subjective test. There are few effective quantitative measures that can test motor function in animal models. Moreover, an intriguing effect called "patterning" keeps experimenters wary about whether their treatments actually work. Research has shown that cats with severed spinal cords can, via a treadmill, be taught to walk, apparently by training local nerves to function without the brain's control. Indeed, though the cats cannot balance themselves, some investigators are trying to see if patterning can help human spinal cord patients. Anderson doesn't think that patterning explains his cats' improvement, however, because he tried to minimize the effect by evaluating the cats only once a week.

But the fetal tissue work may have a more important hitch: While such research can be helpful in elucidating the basic science of spinal cord injury, abortion politics may prevent the technique from progressing past cats. The federal government, for example, refuses to fund any experiments involving transplants of fetal tissue into humans.

Rapid growth in sight

Even though researchers have made dramatic progress within the past decade of spinal cord research, they caution that numerous obstacles must be overcome before a cure for a paralysis rises above the horizon. First off, the majority of spinal cord research is still in test tubes and animal models, not humans. "We have no miracles yet," warns Bunge. "This is a field in its infancy," agrees Black. But like infants at many stages of their development, spinal cord research is showing signs of rapid growth.

–John Travis

PALEOCLIMATOLOGY

A Revisionist Timetable for The Ice Ages

In terms of sheer mass, there's no contest. In one corner, there's a land-based record of ice age climates that takes the form of a single carbonate cylinder about the size of the cardboard tube in a roll of paper towels. In the other corner, there's the marine record, which draws on the tons of deep-sea mud cored around the world during the past 20 years. But a group of researchers argues in this issue of *Science* (pp. 255 and 284) that the lone continental record, drilled from a wall of calcite in Devil's Hole, Nevada, is enough to unseat the conventional wisdom about the causes of the ice ages.

That conventional wisdom was established about 10 years ago, when the timing of the deep-sea record seemed to confirm an idea proposed 50 years ago by the Serbian astronomer Milutin Milankovitch: that the great ice sheets waxed and waned in response to the changing distribution of sunlight as Earth's spin axis wiggled and wobbled and its orbit stretched and squeezed over tens of thousands of years. But after analyzing the Devil's Hole timetable of the ice ages, says hydrogeologist Isaac Winograd of the U.S. Geological Survey in Reston, Virginia, "we just found no support" for the influence of orbital variations. Winograd first raised that possibility 4 years ago, but now, drawing on a longer, better dated core and on other climate records, Winograd thinks he's got powerful ammunition against the orbital theory.

Few other climatologists are ready to abandon their interpretation of the marine record and accept Winograd's conclusion that the ice ages, far from being driven by external factors, result solely from an internal oscillation in the climate system. "It's premature," says paleoclimatologist Thomas Crowley of Applied Research Corp. in College Station. Some think the Devil's Hole record itself is suspect, but Crowley and others agree with Lawrence Edwards of the University of Minnesota, who calls the record "an exciting, fantastic data set." Perhaps both records are valid, they say; the records seem to disagree because they tap into different parts of a climate system that is far more complex than had been hoped.

The reason a single stick of carbonate has received all this attention is the unique resource it contains: a precisely dated continental climate record of the past 600,000 years. The record was deposited from ground water, which carried a measure of air temperature in the form of the water's oxygen isotope composition. As the water seeped into Devil's Hole—an open, water-filled fault zone—carbonate crystallized out, locking up some of the water's oxygen and building up a climate record layer by layer. Drilling into the walls of the fault, Winograd and his colleagues retrieved a core spanning layers formed between 60,000 and 560,000 years ago, as measured by high-precision uranium-thorium dating. And accurate dating is where Winograd thinks he has an edge. "Devil's Hole has one thing nothing else does," says Winograd. "It is well dated; there's nothing else in its league. It's an order of magnitude better dated than" the marine record.

Winograd has no quarrel with the way oceanographers trace past ice ages: by monitoring changes in the oxygen isotope composition of microfossils in ocean-floor sediments. Although some of those changes reflect changes in water temperature, others seem to reflect the amount of water that has been taken out of the ocean and locked up in ice sheets. But the dating of those records, which were compiled by the Spectral Mapping (SPECMAP) group under the direction of John Imbrie of Brown University, is another matter. The marine record has only a few points that can be dated by radioactive techniques like uranium-thorium.

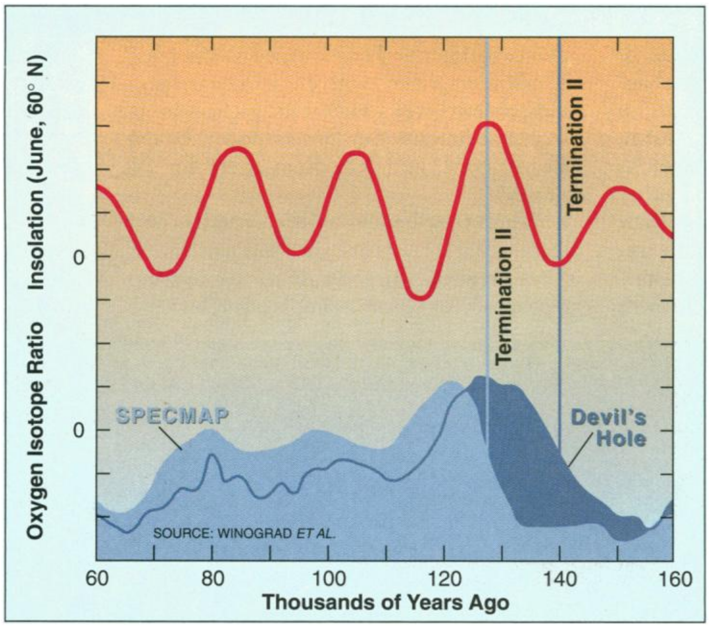
Instead, the record of ice ages was dated by counting—in a sophisticated fashion—the shorter-term isotopic variations that reflect the cyclic wobbling and nodding of Earth's axis with periods of 41,000 and 22,000 years. The resulting record of changing climate over the past 800,000 years seemed to show that the ice ages tended to end when an orbital cycle lasting 100,000 years would have brought stronger summer sunshine to high northern latitudes.

According to the SPECMAP marine record, for example, the end of the penultimate ice age more or less coincided with the peak of summer sunshine 128,000 years ago. But Winograd thinks the SPECMAP people may have miscounted their orbital cycles. The Devil's Hole dating suggests that the climate was already warming 140,000 years ago, and the ice was presumably in full retreat. That and several other inconsistencies cast doubt on the orbital theory, say Winograd and his colleagues: How, they ask, can an effect—rapid warming—come so far *before* its cause—a 10,000-year-long peak in insolation?

Many paleoceanographers have responded that it is Winograd, not themselves, who has misinterpreted the data. Paleoceanographer Richard Fairbanks of Columbia University's Lamont-Doherty Geological Observatory, for example, suspects Winograd might be mistaking peaks in glaciation for peaks in temperature. Winograd could have it backward, Fairbanks says, if the isotopic signal of changing ice volume that is found in the ocean was also picked up at Devil's Hole after being transmitted through the atmosphere. In that case, the record at Devil's Hole might actually support the marine record.

But Winograd says his revisionist timetable is getting support from a new quarter. Coral reefs also preserve a chronology of ice ages, in the form of the ages of ancient reefs that formed when sea level was high, that is, when ice volume was low (*Science*, 6 April 1990, p. 31). Getting accurate dates for the ancient reefs has always been a challenge, but Winograd and his colleagues are encouraged by two efforts by Gerald Wasserburg's group at the California Institute of Technology to date reefs that formed during the previous interglacial warming. One, relying on the uranium-thorium technique, dated the coral reefs formed at the high-water mark (lowest ice volume) in New Guinea as being as old as 135,000 years. If so, the ice had melted back to its present volume 7000 years before the sunlight peak. Another uranium-thorium study dated high stands of sea level in the Bahamas to as early as 132,000 years ago.

Some coral researchers, though, aren't so sure that such work supports Winograd. "At face value, the coral and marine records appear to disagree" at some points, concedes Edwards, a former student of Wasserburg's who perfected the application of the uranium-thorium technique to carbonates like coral. "But the coral dating business is still young, and it's getting more complicated. People are getting hints that the dates can be shifted by diagenesis"—physical and chemical alteration during more than 100,000 years of weathering. The few older ages inconsistent with Milankovitch may be the result of diagenesis that escaped detection, says Edwards.



An ice age out of synch? Whether the end of the penultimate ice age (termination II) fell at a sunshine minimum or maximum depends on the record. (The vertical scale shows standard deviation units.)

As a result, many paleoceanographers expect Winograd to lose if the coral dating ever yields a decisive verdict on sea-level changes. But that wouldn't mean that the Devil's Hole record itself is wrong. Paleoceanographers on the whole feel comfortable with the possibility that a regional climate signal like a warming in Nevada could appear well before the large-scale melting of the ice sheets reflected in the ice volume signal. They've long known, for example, that the surface ocean in the Southern Hemisphere warms several thousand years before ice sheets begin shrinking. Says Crowley, "There can be significant leads and lags that we don't understand."

Just how Byzantine the interconnections of the climate system might be is illustrated by a computer climate model constructed by Barry Saltzman of Yale University. It has four main components—ice sheets that grow and shrink, bedrock that is depressed by the weight of the ice, the greenhouse gas carbon dioxide in the atmosphere, and the deep sea with its storehouse of carbon dioxide. Each of these components responds slowly to changes in other components.

Even without orbital variations, Saltzman's model produces ice ages of a sort in the form of irregular oscillations that sweep back and forth through the system. That's just what Winograd suggests happens in the real world. But only when Saltzman includes the insolation effects of Milankovitch cycles does he find that the oscillations of the model resemble the observed climate variations. "Something else in the climate system must be operating besides Milankovitch," he says, "but in our model it does play a role in the timing of the major swings. There probably could be quite a bit of variability; the climate system could fall in and out of phase, but [Milankovitch cycles] give it the temporal pace." So Saltzman, for one, isn't particularly bothered by a sloppy match between orbital cycles and the ends of ice ages. And if he is right, the standoff between the two climate records could end with both records intact—and Milankovitch still standing.

–Richard A. Kerr