and Gahring monitored the girl's anti-GluR3 antibodies and found that they dropped as her condition improved. But, as often occurs with plasma exchange, the treatment lost effectiveness over several months, and the girl relapsed. The team reported the results in last July's *Science* paper.

Meanwhile, Rogers and Gahring had moved to the University of Utah in 1993. There they teamed up with neurologist Roy Twyman, who applied the antibodies to cultured neurons and found that the antibodies activate glutamate receptors. This was the first case of autoantibodies activating a receptor for a neurotransmitter.

That finding, reported in the *Neuron* paper, suggests a model for how Rasmussen's might develop. Normally, the blood-brain barrier, which surrounds blood vessels in the brain, prevents antibodies from reaching brain tissue. But Rasmussen's often begins with a mishap such as a bump on the head or a fever, which can cause a leak in the barrier. That wouldn't be a problem ordinarily, but if a child had autoantibodies to the glutamate receptor, the antibodies could enter the brain and activate the receptors, exciting neurons and causing a seizure. A vicious cycle could then develop, because seizures themselves cause rifts in the blood-brain barrier, allowing more antibodies and inflammatory immune cells into the brain and intensifying the immune attack.

Given that Rasmussen's starts locally and "eats its way out, like Pac-Man," says pediatric neurologist John Freeman of Johns Hopkins University, the idea that the disease starts from a small breach of the blood-brain barrier seems "very logical." It is less clear, says Freeman, whether GluR3 antibodies start the process, or "whether there is something else which causes focal autoimmune disease, and as you damage neurons, you have GluR3 released, and you form antibodies to it." But Lindstrom, now at the University of Pennsylvania, points out that "you can model the disease by immunizing an animal [with GluR3]. That is very good evidence," he says, that the GluR3 antibodies are causal.

Rasmussen's is a very rare disease, affecting only a handful of children each year. But McNamara speculates that "a small subset" of cases of more common forms of epilepsy may be autoimmune as well. University of Pennsylvania neurologist Marc Dichter agrees. The Utah and Duke teams are both working to develop a simple test for glutamate receptor antibodies that would allow wide screening of patients. "Once the antibody test becomes more available, I would guess we would see more patients with uncontrolled focal epilepsy who will fit into this category," Dichter says.

Glutamate receptor antibodies have also been found in another group of neurological patients, those with PNS, a very rare condition in which a tumor—often of the lung, ovary, or breast—causes the body to make autoantibodies to various parts of the brain. The Utah group teamed up with University of Utah neurologist John Greenlee, who studies the condition, and examined the serum of PNS patients. They reported in last month's issue of *Molecular Medicine* that six of seven patients had antibodies, not to GluR3, but to several other glutamate receptor subunits.

Moreover, Twyman found that, while the antibodies alone don't activate the glutamate receptors as GluR3 antibodies do, they make the receptors hypersensitive to glutamate. Because overactive glutamate receptors can kill neurons, the antibodies could contribute to the progression of PNS, says Greenlee. But he cautions that "we haven't proven that's what happens." If such a mechanism were proven, however, it might provide an important key to intervention.

Intervention based on the current findings seems to be closer at hand for Rasmussen's patients than for those with PNS. Indeed, since last July's *Science* paper, a handful of neurologists, including Dichter and McNamara, have had some success using plasma exchange and other treatments for autoimmune disease on Rasmussen's patients. They have just submitted their results for publication.

But complicating the clinical decision-making is the fact that there are no foolproof therapies for autoimmune diseases at present, and if a patient may need a hemispherectomy eventually, it is better done soon, because a younger brain is better at adapting. Removing the left hemisphere of the brain of a child more than 10 years old carries with it a serious risk that language skills will not transfer to the right side of the brain. And removal of either hemisphere becomes riskier the older the child gets.

Because of that risk, Freeman and his colleague Eileen Vining have just scheduled two Rasmussen's patients, both nine-year-olds, for hemispherectomy. Nevertheless, Freeman laments, "it does seem incredibly dumb to be taking out half the brain for an autoimmune disease." At least this rare syndrome is now hitched to the bandwagon of autoimmune diseases, where the search for better treatments is intense. And so the days of hemispherectomies may be numbered.

–Marcia Barinaga

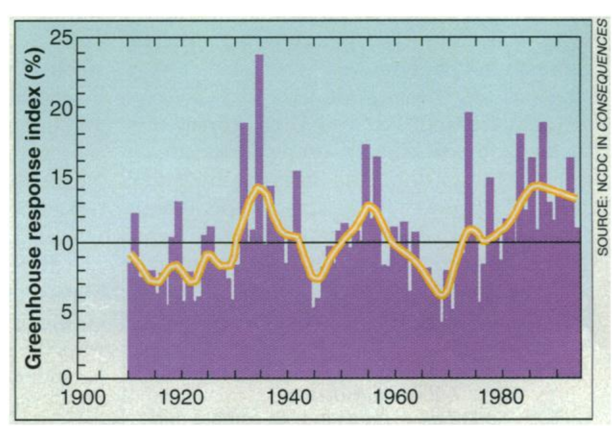
CLIMATE

U.S. Climate Tilts Toward the Greenhouse

Yellowstone was ablaze during the torrid, parched summer of 1988. The Midwest was awash in the great floods of '93. Minneapolis was shivering with a wind chill of –32°C this April. Is this wild and woolly weather a sign that a strengthening greenhouse effect is changing global climate? That possibility is on everyone's lips during a scorching summer or a season of floods, but no single weather event can be conclusive. Only when unsettled weather becomes a persistent trend can it say anything about global change. Now Thomas Karl, senior scientist at the National Climatic Data Center in Asheville, North Carolina, and his NCDC colleagues have found such a pattern—a sign, they say, that the U.S. climate has turned toward a greenhouse regime in the past 15 years.

By combining data on summer droughts, wet winters, drenching rainstorms, and other weather extremes expected to grow more common in a warmer climate, Karl and his colleagues have come up with the Greenhouse Climate Response Index, a handy one-number guide to the state of the U.S. climate. As they report in the premiere issue of *Consequences*, a journal of global change, the index has been stuck at a high level ever since the late 1970s, suggesting that chance variation may not be enough to explain the unusual weather of recent years.

"The trend directions we see in the U.S. are indeed what's projected" for an intensified greenhouse, says Karl. "You shouldn't judge the whole world from the U.S. standpoint, and even in the United States it's not so overwhelming that you'd say the evidence is unequivocal." Still, by showing that recent weather trends are just what you would expect from a greenhouse warming, the index should help give the public and policy-makers a better feel for what global climate



On the wild side. A U.S. climate index based in part on weather extremes has jumped toward values expected in a greenhouse warming. The expected value is 10%.

change could bring in the future, says Karl.

The index gives the most weight to much-above-normal temperature—measured as daily minimums, because that's where climate models predict greenhouse influences will be strongest. But Karl and his colleagues also included yardsticks derived from the generally accepted assumption that a greenhouse climate will be more summery than the norm—not just warmer, but more prone to heavy rainstorms and droughts. The index's four other measures are much-above-normal precipitation in the cool months, extreme or severe drought in the warm months, a much greater than normal proportion of annual precipitation falling on days having more than 50.8 millimeters of precipitation, and reduced day-to-day temperature swings.

For each year since 1910, Karl and his colleagues determined the percentage of land area in the lower 48 states that experienced extremely abnormal climate of each of the five types. Taken together in the greenhouse index, these indicators reveal three episodes of greenhouselike climate: the Dust Bowl years of the 1930s, the drought years of the 1950s, and the 1980s and early '90s. The index values in the current episode are no higher than those of earlier episodes, but they have remained high for longer—since the late 1970s, the same time the tropical Pacific took a turn toward the warm side and global temperatures shot up (*Science*, 28 October 1994, p. 544). What's more, all five index components have contributed to the rise. As a result, Karl and his colleagues estimate a probability of only about 5% that the index's latest surge toward the greenhouse side is just another fluctuation of an otherwise stable climate.

Like Karl, climatologist David Robinson of Rutgers University says that number shouldn't be seen as proof of a greenhouse warming. The components in the greenhouse index "are the key players in recognizing global change," he says, "but they're not the be-all and end-all for identifying global change." But Robinson agrees that the high index is a sign of "some interesting things going on in U.S. climate."

To see whether the rest of the globe looks just as interesting, Karl would like to broaden the index beyond the 2% of the globe's area covered by the lower 48 states to include places like Russia, China, and Europe. If recent weather there looks as offbeat as it does in the United States, a greenhouse warming could be the only way to make sense of it.

–Richard A. Kerr

Additional Reading

T. R. Karl *et al.*, "Trends in U.S. climate during the twentieth century," *Consequences* **1**, 3 (1995). Published by Saginaw Valley State College, University Center, MI 48710, USA.

MEETING BRIEFS

Anthropologists Overturn Old Ideas About New Developments

Some basic assumptions took tumbles between 28 March and 1 April, when the Paleoanthropology Society and the American Association of Physical Anthropologists (AAPA) held their annual meetings in Oakland, California. Surprises sprang from studies of Neandertal arms, island genetics, and primate birth, among other topics.

Arms and the Man

Fossil skeletons tell prehistorians that humans who looked fully modern first appeared in Europe around 40,000 years ago. But just when these people started *acting* like modern folks—planning their hunting strategies, for example—is another question entirely. "There's been a controversy over the emergence of modern subsistence behavior, like the shift from opportunistic scavenging to planned hunting," says anthropologist Steven Churchill of the University of New Mexico.

One problem is that behavior doesn't fossilize. But bones do, and some types of behavior leave their marks on bone shape and thickness. Based on an analysis of the shape of the upper arm bone, or humerus, in groups of ancient humans, Churchill told colleagues in Oakland that modern behavior seems to have appeared in stages. First, he says, there was a shift in strategy toward more planning, followed thousands of years later by a change in technology, when people developed spears that could be thrown instead of simply thrust. "It's valuable work," says anthropologist Christopher Ruff of Johns Hopkins University. "He's gone in and quantified bone variables related to mechanical loading and thus to behavior."

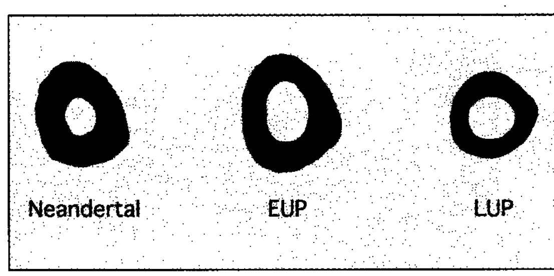
Because outer layers of bone thicken where stresses generated by muscles are the greatest, the amount and distribution of that extra material can reveal overall workloads and particular activity patterns. "It's a fine-grained record of what an individual was doing habitually," Churchill says.

Churchill compared that record in the humeri of three groups of fossil humans, focusing on males because they are almost always the hunters. His sample included seven Neandertals, who lived in Europe until about 35,000 years ago and are not considered anatomically modern; 11 modern-looking humans from the Early Upper Paleolithic (EUP), 35,000 to 20,000 years ago; and 17 humans from the Late Upper Paleolithic (LUP), beginning about 20,000 years ago.

After scaling the bones to account for differences in body size, Churchill found there was a big drop-off in overall humerus thickness from the Neandertals to EUP humans. Apparently, the more recent humans had found ways of easing their workload. "My interpretation is there's been some kind of subsistence shift, a reduction in opportunistic scavenging," he says. "If you are opportunistic, you have to put more effort out than, say, if you are hunting one or two times a week. In the EUP they were doing better—maybe they had better prey intercept strategies. They knew where deer migrated and moved there to catch them."

But the shape of the humerus didn't change until the LUP, around 20,000 years ago. In both Neandertals and EUP human males, its cross section was oval, elongated from back to front. That shape, says Churchill, is a sign that the arm was used heavily for thrusting, an action in which muscles tug on the front and back surfaces of the bone. But in the LUP, the bone's cross section suddenly became rounder. And a round humerus, Churchill argues, is a response to frequent throwing. Throwing an object like a spear generates twisting forces on the upper arm; to cope with these stresses, he says, the body distributes extra layers of bone evenly around the humerus.

That's consistent with archaeological evi-



S. CHURCHILL/UNIV. OF NEW MEXICO

Behavior shift. Upper arm-bone cross sections from Neandertals and Early Upper Paleolithic (EUP) humans are oval, a result of muscles tugging at the front and back. This happens when thrusting a spear. The rounder shape in Late Upper Paleolithic (LUP) humans can be produced by a throwing motion.