time the temperature of the surface changed abruptly, creating a region of changing temperature in the compacting snow. The lighter nitrogen isotope would tend to diffuse through the snow's nooks and crannies, up the thermal gradient toward the surface, while the heavier nitrogen would tend to move downward. When the nooks and crannies finally closed off, they would trap nitrogen with a distinctive isotope ratio. And Severinghaus found a sharp peak in the ratio of the two isotopes at the end of the Younger Dryas, 11,600 years ago.

This isotopic spike alone doesn't provide a temperature, but the thickness of ice that separates it from the oxygen isotope shift that also marks the warming does. The oxygen isotope shift was recorded at the surface, in the snow that fell at the time of the warming, but the nitrogen isotope spike formed at the depth where snow was changing to ice. The gap indicates how long the conversion of snow to ice took—826 years, at the end of the Younger Dryas. And that interval depended on the temperature, among other things. After accounting for those factors, Severinghaus found that the air over Greenland was 14° ± 3°C colder than today at the end of the Younger Dryas, twice the 7°C indicated by oxygen isotopes.

Not only did the nitrogen thermometer show that this last cold snap in Greenland was twice as deep as thought, but another gas in the bubbles, methane, suggested that it must have extended far beyond Greenland. Although signs of the Younger Dryas have been turning up around the world (*Science*, 24 December 1993, p. 1972), some researchers have argued that it might have been strong only around Greenland. Methane seemed to offer an answer, because the gas comes from plant decomposition—which is sensitive to temperature and moisture variations—far from glacial ice. Researchers had already shown a sharp rise in trapped methane at about the end of the Younger Dryas, implying a widespread climate shift. Now the nitrogen isotope spike in the bubbles has allowed Severinghaus to show that the methane rise, as measured by Brook and Sowers, began within 20 years of the warming that ended the Younger Dryas in Greenland. So the warming must have affected a broad area of the middle latitudes, says Severinghaus, if not the entire hemisphere.

"Most of the warming in Greenland occurred in about 50 years. The gas rose in a century or so," says White. "That's pretty remarkable; it's a fundamental shift. We've seen nothing like that in the last several thousand years." Now he and other researchers will be applying the new thermometer—and any others they can get their hands on—to work out what threw Earth's climate into crisis.

–Richard A. Kerr

IMMUNOLOGY

Simple Mice Test Antibody Complexity

The world, from an immune system's view, is filled with enemies: a mind-boggling multitude of bacteria, viruses, and parasites just waiting to pounce. And the system has to maintain levels of a staggering range of antibodies tailored to take on these threats. Antibody-producing cells called B lymphocytes somehow mutate their antibodies to produce this diversity, but there are puzzling questions about how this process is controlled. The intricacy of the immune system makes them hard to answer, however. So researchers have been looking to make a simple system suitable for a rigorous test.

Now, on page 1649, Matthias Wabl's group at the University of California, San Francisco (UCSF), reports doing just that. They have "knocked out" various antibody-producing genes from mice and "knocked in" a preformed genetic package so that the animals are born with the ability to make only a few antibody types that recognize just one invader, or antigen. Yet despite this genetic near-uniformity, these so-called "quasi-monoclonal" mice developed, at first look, a near-normal repertoire of antibodies as they grew.

ELEMENTS OF ANTIBODIES

	Normal mouse		Quasi-monoclonal mouse
Heavy chain locus	250 $V_H \times 12\ D \times 4\ J_H$	= 10,000	1
κ locus	200 $V_\kappa \times 5\ J_\kappa$	= 1,000	0
γ locus	$V_\gamma J_\gamma$	= 3	3
Antibody repertoire	Heavy × light chains	= 30,000,000	3

Born to lose. The genetically altered "quasi-monoclonal" mouse has fewer components with which to construct antibody diversity.

Although the mice may be simple, scientists think they have a lot of potential. "This is a poorly understood facet of immunology, and this is a very clear result," says immunologist David Nemazee of the National Jewish Hospital in Denver. Although researchers are still in the dark about the apparatus controlling antibody diversity, the immunologically simple mice should help them shed some light on the matter. These mice, says Nemazee, "provide a potential model for studying what the control mechanisms are."

In previous work on other experimental animals, researchers "knocked out" or "knocked in" antibody-producing genes to restrict the diversity of the animals' immune systems, yet many developed a near-normal repertoire of antibodies. But it was hard to establish valid controls for many of these genome disruptions.

Wabl's group elected to manipulate the genome more precisely, to eliminate as many antibody-producing genes as possible while leaving the ability to produce antibodies to just one antigen. Antibody molecules are made up of elements called light and heavy chains, and the mouse genome normally contains genes for thousands of varieties of each, which combine to form millions of different types of antibodies. The UCSF researchers deleted or inactivated all the genes for the heavy chain and all but three of the light chain genes, and inserted a gene construct for just one heavy chain. The resulting combinations produced antibodies capable of binding only to a chemical called NP.

Yet by the time the mice reached adulthood, about 20% of the B cells were making different antibodies—they no longer bound NP. Overall, the UCSF team found that the amounts of different antibody types in the quasi-monoclonal animals were similar to those of genetically normal litter mates. When the scientists examined the serum for antibodies secreted by B cells, they found few antibodies that were specific for the original NP antigen, suggesting a greater diversity of antibodies had emerged in the circulation. The results implied that the animals were able to switch from just one major antibody type, which occurs early in development, to several types in adulthood—just like normal mice. "These results show that once a B cell expresses an antibody, the specificity is not etched in stone—it still has other options to produce other antibodies, but we don't know how," says immunologist Martin Weigert at Princeton University.

One test that's now possible with this new model is to examine how the interaction between antibodies and other cells in the immune system, such as the T cells that actively direct various aspects of immunological function, might do the job. Wabl hopes to tease these out by boiling the mouse system down still further, perhaps by coming up with an animal with a restricted range of T cells as well. Such simplicity, he hopes, will hold the key to some complex problems.

–Nigel Williams