animal feed to keep infections from spreading through a flock or herd. The antibiotics also help fatten animals on less feed, although researchers aren't sure why. But antibiotics almost inevitably spur some bacteria to develop resistance to the drugs, and researchers have long warned that the bugs, or the resistance genes they harbor, can make their way through the food chain to the human gut. That, in turn, could make it harder to treat dangerous infections with antibiotics akin to the drugs used on the farm (*Science*, 5 May 2000, p. 792).

This concern prompted the European Union to ban avoparcin from livestock feed in 1997 after more than 2 decades of use. Avoparcin and a human antibiotic called vancomycin kill bacteria by preventing them from building cell walls. Earlier studies showed that avoparcin-resistant gut microbes in chickens and hogs also resist vancomycin. That could be bad news for hospital patients, who receive vancomycin to fight enterococci that cause life-threatening infections when they escape from the gut during surgery. Researchers suspected that the avoparcin ban would help prevent the spread of vancomycin-resistant enterococci (VRE) in humans.

In monitoring the ban's effects, researchers have found a dramatic drop in VRE among pigs, chickens, and supermarket chicken meat. Fewer VRE were also found in the human population. But it wasn't clear whether this trend extended to patients in hospitals, where most opportunistic enterococci infections occur.

To find out, microbiologist Greet Ieven of the University of Antwerp and her colleagues cultured enterococci from stool samples of 353 patients in May and June 2001 and tested how many microbes survived high levels of vancomycin. Just three of the enterococci cultures, or 0.6%, stood up to vancomycin—a big drop from the 5.7% resistance rate in 1996, when avoparcin was still widely fed to livestock. Molecular genetic analysis confirmed that the prevalence of a key vancomycin resistance gene plummeted from 5.7% to 0.8%. Because the use of vancomycin in Belgian hospitals hasn't changed in recent years, Ieven says, the results "confirm the hypothesis that VRE in Europe originates [on farms]."

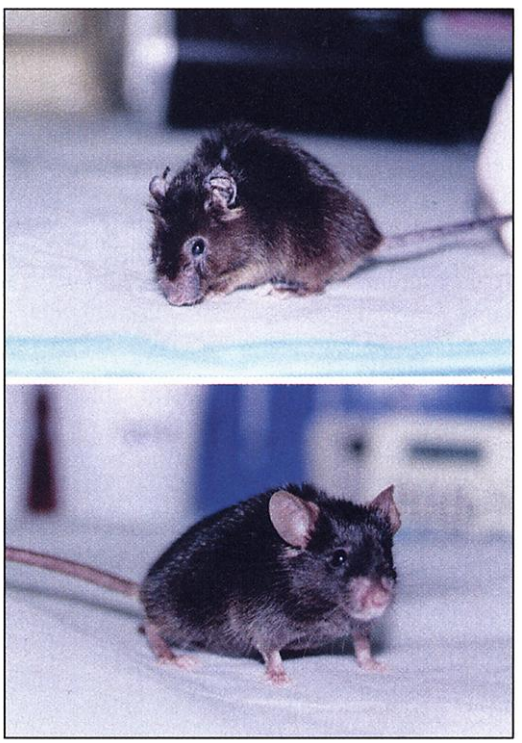
The Belgian results "confirm what people thought might happen in the clinic," says pharmacologist Michael Dudley of Microcide Pharmaceuticals in Mountain View, California. The results mean that antibiotic resistance flows like water from the farm to the clinic, he says, and by stopping the use of avoparcin, "you stop the tap."

Two other classes of farm antibiotics have come under scrutiny lately because they resemble human drugs, and the U.S. Food and Drug Administration has proposed banning them from livestock feed. They include virginiamycin, which breeds enterococci that resist a recently developed drug called Synercid that kills tough enterococci infections; and enrofloxacin, a member of the widely used class of human antibiotics called fluoroquinolones that includes ciprofloxacin (Cipro). Abbott Laboratories, the maker of enrofloxacin, is fighting the ban. A final FDA decision is not expected for at least another year. **–DAN FERBER**

AGING RESEARCH

Cancer-Stalling System Accelerates Aging

Fending off cancer: a good idea? Maybe not. A mechanism that thwarts deadly tumors might come with a major drawback. Overactive p53—a protein that foils potentially cancerous cells—causes symptoms of old age and hastens death in mice, report Lawrence Donehower, a molecular biologist at Baylor College of Medicine in Houston, and colleagues in the 3 January issue of *Nature*.



If it's not one thing, it's another. Cancer-resistant mouse (top) appears to grow old faster than normal mouse (bottom).

CREDIT: L. DONEHOWER/BAYLOR COLLEGE OF MEDICINE

The work suggests a trade-off between cancer prevention and sustained vigor. "A robust surveillance mechanism against cancer is important for getting the animal to reproductive age," says Leonard Guarente, a molecular geneticist at the Massachusetts Institute of Technology in Cambridge. But if the system's gauge is set high enough to protect against cancer, it might thwart normal cells as well. "This might be good early on but bad later in life," says Guarente.

Most research on p53 has focused on how a deficiency of the protein causes cancer. The protein prevents genetically marred cells from reproducing by sending them to their death or by stalling reproduction until the damage is fixed. Without sufficient p53, corrupt cells run amok and some grow into tumors.

While trying to mimic a common human p53 mutation in mice, Donehower's team serendipitously created a different one. The mutation lopped off about half of one copy of the *p53* gene, causing mice that carried it to build some normal and some stunted p53 proteins. Counterintuitively, the mice behaved as if they had acquired extra dollops of the protein. None of the 35 animals that harbored the altered p53 developed life-threatening tumors, although some acquired small tumors that were discovered on autopsy. But in the 56 mice with two intact copies of the gene, 45% developed deadly tumors. A series of tests led the researchers to conclude that they had inadvertently constructed a mutant p53 that grants the normal protein superpowers.

The mice didn't have a chance to fully enjoy their cancer-free lives, however. By 96 weeks of age, half the mutants had died. Half of normal animals, in contrast, lived 118 weeks or longer. And the oldest mutant barely squeaked by the 136-week mark, while its normal counterpart celebrated 164 weeks.

As pups, the mutant mice seem similar to their normal littermates, but "they start to look decrepit and sluggish in middle age," says Donehower. The mice developed many age-related conditions. They shrunk, for example, their skin thinned, and wounds healed slowly. Many of their organs shriveled as well, apparently because the constituent cells withered. The results suggest that p53 repels cancer at a price: The ability to obstruct rampant cell division might also hamper an animal's ability to replenish essential cells. This idea fits with other work that links p53 with aging. For example, a gene known to extend longevity in worms and yeast—*Sir2*—also promotes survival in mammalian cells by turning down p53 activity.

Guarente cautions that the study doesn't prove that the p53 mutants grow old before their time: "Is this premature aging, or is this just a sick mouse?" But he and others are impressed by the large constellation of old-age traits in the mice. To convince people that the

mice exhibit accelerated aging, "you'd have to knock out p53 and get a longer life-span," Guarente says. But "we already know what happens then: You get cancer."

Researchers can't yet circumvent this problem, but Donehower has managed to collect some preliminary data. Mice that carry one normal and one inactive copy of *p53* suffer from a high incidence of cancer. But two of 217 such animals he studied did not happen to get tumors—and they "lived much longer than any of the wild-type mice," says Donehower. "It's only two mice," he cautions, but he would like to follow up this tantalizing observation to see if small amounts of p53 make for a longer life-span, provided the animal remains cancer-free.

Teasing apart p53's age-promoting and cancer-preventing capabilities might eventually lead to therapeutic interventions, suggests Ronald DePinho, a cancer geneticist at the Dana-Farber Cancer Institute in Boston. Perhaps such an approach would "help the organism age gracefully," he says, without compromising its ability to guard against cancer.

–EVELYN STRAUSS

CLIMATE CHANGE

Reducing Uncertainties Of Global Warming

About all that climate researchers can say with any confidence concerning global warming is that the world has warmed during the past century and much of that warming is probably due to humans pouring greenhouse gases into the atmosphere. How bad could things get as the world continues to warm? Scientists' bottom-up approach—trying to understand the role of every part in the dizzyingly complex climate machine—has left that question unanswered. But in this issue of *Science* (p. 113), a group of researchers take a top-down approach: They plugged different combinations of values for fundamental properties of the climate system—such as its sensitivity to the nudge that humans are giving it—into a computer model and looked to see how well the model's output matched long-term observations. The results are mixed.

Climate dynamicist Chris E. Forest of the Massachusetts Institute of Technology and his colleagues used this new combination of computer simulation and observations to calculate climate properties that had usually been estimated from climate models alone or from polling researchers for their opinions. Using an intermediate-complexity model simple enough to make hundreds of long runs, Forest and his colleagues simulated the climate of 1860 to 1995 under accumulating greenhouse gases. They compared their results to three observational records of temperature that gauge global warming: the changing temperatures of the surface, the upper atmosphere, and the deep ocean.

In the model, they included three adjustable "knobs": the sensitivity of climate to a given amount of added greenhouse gases, the rate at which the ocean can take up heat, and the ability of aerosols—microscopic particles found in pollutant hazes—to change solar heating of the atmosphere. Forest and his colleagues twiddled the knobs over a range of values, ran the model under a large number of setting combinations, and then compared the simulated climate trends with the three observed temperature records. If a three-setting combination produced a reasonable match for all three records, then each of the combination's settings became a possible value of the actual climate property.

By their own concession, Forest and colleagues had varied success pinning down key parameters of the climate system. The rate at which the ocean takes up heat—and counteracts greenhouse warming—couldn't be usefully constrained. "Our result suggests that more research is needed" on ocean heat uptake, they write.

Their lower limit (90% confidence level) on the all-important climate sensitivity—1.4 kelvin for a doubling of atmospheric carbon dioxide—matches the long-cited, subjective 1.5 K lower limit recently repeated by the Intergovernmental Panel on Climate

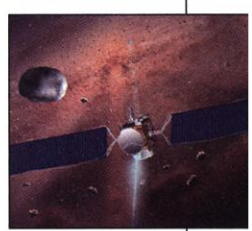
Prospect unclear. Climate uncertainties, such as the effect of this Himalayan pollutant haze, hinder projections of greenhouse warming.

CREDITS: (LEFT TO RIGHT) M. POSFAI *ET AL.*, *JOURNAL OF GEOPHYSICAL RESEARCH* **104**, 21685 (1999); DAWN, WILLIAM K. HARTMANN

ScienceScope

NASA Shakeup Newly confirmed space chief Sean O'Keefe is preparing to name ex-astronaut Charles Bolden, an African American, as his deputy. O'Keefe is filling that job for the first time in a decade as part of his effort to lift the agency from a budgetary morass.

Space scientists are anxious to see how the duo deals with NASA's research program. Earth-based astronomers recently headed off an attempt to chop $550,000 in annual support for the Arecibo radar in Puerto Rico, used to track near-Earth objects. NASA complained that the funding wasn't peer reviewed, but later restored $400,000 for 2002—with no promises for 2003. Planetary scientists, meanwhile, recently won approval for two new missions. Dawn (above) will rendezvous with the largest known asteroids, Vesta and Ceres, while a space telescope called Kepler will search for Earth-sized planets orbiting other stars. Both are slated for a 2006 launch, although budget troubles will delay Kepler for at least a year.



Gene Count Sequencers hope to at least double the number of documented microbial genomes, to more than 50. The number of genes in the human genome, meanwhile, will creep steadily upward from initial estimates of about 35,000. But that total will be dwarfed by the discovery of many more thousands of genes within genes—coding regions for a variety of proteins that begin or end in different places along the sequence of a single gene.

Science & Security Congress will finally pass legislation that increases security at labs working with potential bioweapons, leading some universities to decide that the costs outweigh the benefits of the research. Some scientists, meanwhile, are waiting to see how the Department of Heath and Human Services wields its new authority to classify some information—including lab locations and possibly research findings—as secret.

University researchers will finally get some relief from export regulations that have ensnarled projects—from satellites to supercomputers—involving advanced technology and foreign partners. The State Department is expected to publish new rules that protect academics who allow foreigners access to bona fide research projects.

Contributors: The *Science* News Staff