lial cells that humans and Old World monkeys do not make. Primates' immune systems recognize this sugar as a foreign antigen and attack the pig cells, leading to "hyperacute rejection" and organ failure.

Researchers have addressed the problem by endowing transgenic pigs with protective proteins to counter the immune response, which has allowed the organs to function in primates for months rather than days. But the only complete solution is thought to be a pig lacking the gene for the enzyme galactosyltransferase that makes the sugar. Cloning technology raises the possibility of disrupting, or knocking out, this gene in cultured cells, then inserting the nucleus of the modified cells into an empty pig egg to create embryos.

The first cloned pigs were created in 2000 (*Science*, 18 August 2000, pp. 1118 and 1188). Now, animal scientist Randall Prather and his team at Missouri, along with collaborators at Immerge BioTherapeutics Inc. in Charlestown, Massachusetts, have knocked out the galtransferase gene in fetal cells used to make cloned piglets.

To disrupt the gene, the researchers used a "gene trap" vector, a piece of DNA containing snippets complementary to the target gene along with sequences for antibiotic resistance. They moved this vector across the cell membrane and into the nucleus by jiggling the cells with electricity. They then treated the cells with antibiotics to kill all but the cells that contained the inserted DNA, then screened for those that had it in the right location. This replaced gene causes the cell to make a truncated version of galtransferase. Because the odds of a successful insert were only 1 in 5 million, the team didn't expect to get any cells with both alleles knocked out.

The researchers then fused these modified fetal cells with oocytes from which the chromosomes had been removed by zapping the cells with electricity, which kick-started the process of cell division. They implanted these embryos into sows that had just come into heat.

Because fetal cells stop dividing after a few weeks in culture, the team had to move quickly. "We did a bunch of things in the lab differently" to speed up the modification and testing steps, Prather says. All the same, the team had to implant more than 3000 embryos in 28 surrogate sows to get seven live piglets born in September and October, a 0.2% success rate. "It's a rather heroic piece of work," says cattle cloning researcher George Seidel of Colorado State University, Fort Collins. And the work isn't over: The four surviving piglets, all females, still make the galactose link with their good copy of galtransferase.

At least two other companies are hot on the Missouri team's heels. Advanced Cell Technology of Worcester, Massachusetts, say they are close to announcing the birth of pigs lacking the galtransferase gene. And David Ayares of Scotland-based PPL Therapeutics's lab in Blacksburg, Virginia, told *Science* at press time that five pigs appearing to have the knockout allele were born on Christmas Day. Prather says the next step, which his group hopes to achieve within 18 months, is to produce double knockout pigs using conventional breeding methods.

–JOCELYN KAISER

ANTIBIOTIC RESISTANCE

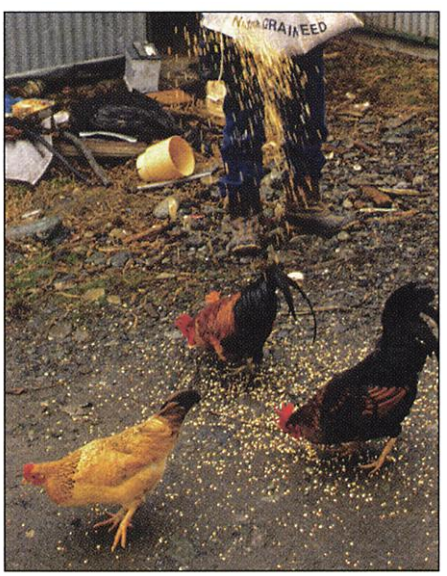
Livestock Feed Ban Preserves Drugs' Power

CHICAGO—It's no secret that livestock fed antibiotics breed drug-resistant bacteria that can cause dangerous infections in people. But a new study suggests that the process is reversible. Banning a drug called avoparcin from animal feed dramatically reduced the chances that potentially dangerous gut microbes in hospital patients would be resistant to an important, related drug, Belgian researchers reported last month at a meeting* sponsored by the American Society for Microbiology.

The results are the first to show that cutting antibiotic use on the farm leads to reduced resistance in hospital patients—those who need antibiotics the most, says microbiologist Stuart Levy of Tufts University School of Medicine in Boston. "This says there's a strong connection between what's done in animals and what you see in people," he says.

Farmers mix low doses of antibiotics into

* The Interscience Conference on Antimicrobial Agents and Chemotherapy, Chicago, 16–19 December 2001.



Just say no. Cutting antibiotics from chicken feed reduces microbes' drug resistance in people.

CREDIT: PHIL SCHERMEISTER/CORBIS

ScienceScope

THE YEAR AHEAD

Weather forecasting models may not be reliable beyond a few days out, but ScienceScope is willing to stick out its neck for an entire year. Here are some likely science-related developments in 2002:

New Faces at NIH A director will finally arrive—and immediately face questions about the best way to adapt to slower budget growth. A report from a congressionally ordered panel due out within a year of the new director's appointment is rumored to be looking at merging several institutes as part of a perennial quest to make the Bethesda biomedical behemoth more efficient.

ITER Inches Ahead Plans for a multibillion-dollar international fusion reactor will continue to crawl forward, with the United States making noises about rejoining the project. The Bush Administration is mulling requests to send observers to planning meetings—although other partners say they don't want the United States present unless it is ready to pony up some cash. In 1998 U.S. officials pulled out of a more costly version of the project.

Kyoto Clash The Bush Administration is still working on an alternative to the Kyoto climate change treaty. In the meantime, dozens of other nations may implement a carbon emissions–trading scheme that would allow some countries to emit more of the gas in exchange for undertaking projects—such as tree planting—to soak up carbon.

To Clone ... Or Not? The U.S. Senate will debate a controversial bill to ban human cloning early in the year, while nations from Germany to China continue to discuss how to regulate their own cloning and stem cell research. Some researchers fear that talent and resources will flow to countries with the most permissive laws.

Deep Dreams Scientists hoping to convert an abandoned gold mine in South Dakota into the world's deepest laboratory will find out whether National Science Foundation (NSF) reviewers think the idea is a good one. Backers haven't waited for NSF's blessing to move ahead with the $300 million project, however. Senate Majority Leader Tom Daschle (D–SD) last month tucked language into a defense spending bill that makes the mine state property, opening the way to future renovations.

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

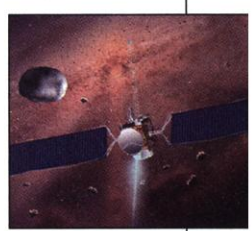
Prospect unclear. Climate uncertainties, such as the effect of this Himalayan pollutant haze, hinder projections of greenhouse warming.

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