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

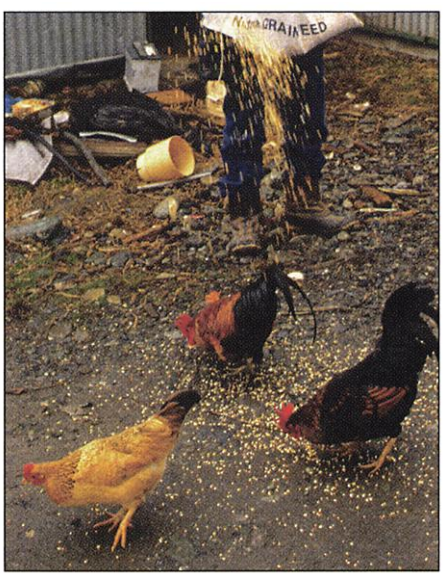
Livestock Feed Ban Preserves Drugs' Power

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.

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]."

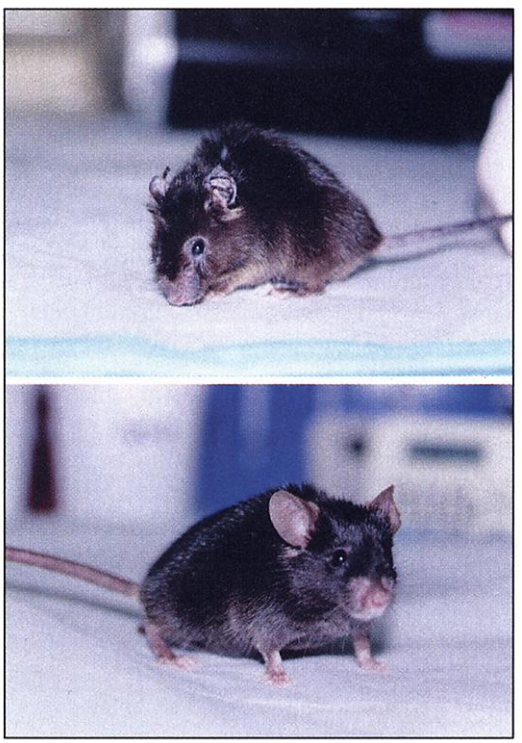
The Belgian results "confirm what people thought might happen in the clinic," says pharmacologist Michael Dudley of Microcide Pharmaceuticals in Mountain View, California. The results mean that antibiotic resistance flows like water from the farm to the clinic, he says, and by stopping the use of avoparcin,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