Use of Antibiotics in Animal Feed Challenged

A study linking antibiotics in animal feed to subsequent illness in people has reinforced efforts to promulgate new regulations

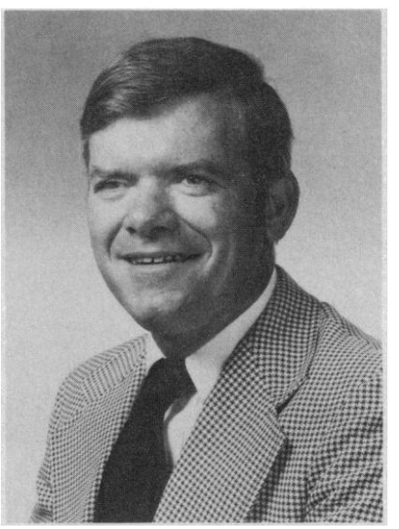
"Like the air we breathe, the water we drink and the food we eat, we find that bacteria are not the exclusive province of any one country, any one part of the body, any one person or even any one species of animal . . . The discovery of the specific mechanisms by which resistance to antibiotics is transferred between living things reminds us that in spite of our biological diversity we are all, in the last analysis, inextricably joined."—ORVILLE SCHELL, author of *Modern Meat: Antibiotics, Hormones, and the Pharmaceutical Farm.**

For 30 years, American farmers have added low levels of antibiotics to animal feed to promote growth in cattle, poultry, and swine, and for the past 20 years, some scientists have been advocating an end to this practice. In the past 2 years, new important scientific evidence has accumulated, substantially bolstering the case for a ban. Most notable is the publication last month of an epidemiological study in the *New England Journal of Medicine*. Researchers conclude in the 6 September issue that there was a direct connection between the use of antibiotic feed additives in beef and the occurrence last year of 18 cases of severe *Salmonella* poisoning in the Midwest (*Science*, 5 October, p. 30).

As a result of this new data, there appears to be a consensus among scientists that the federal government should take steps to limit the use of antibiotics in animal feed. Although it was too late for Congress to address the issue before the current session adjourned, the new studies have set the stage for an enormous battle next year. Restrictions have been proposed before, but lobbies representing the pharmaceutical companies and the farm community have always successfully thwarted these plans. Thus far, the publication of the *Journal* study has elicited an enthusiastic, but cautious, response on Capitol Hill and at the Food and Drug Administration (FDA). In 1977 FDA tried to ban the use of penicillin and tetracycline in animal feed but was promptly blocked by Congress. The proposal has been in regulatory limbo ever since.

The drug companies have a substantial amount at stake. According to the Animal Health Institute, the trade association representing companies that produce animal drugs, sales of antibiotic feed additives last year totaled $270 million. Almost half the antibiotics manufactured domestically are fed to animals, according to a 1979 report by the Office of Technology Assessment (OTA).

How antibiotics promote growth is hotly debated among scientists. But a majority of scientists agree that the use of subtherapeutic doses of antibiotics in animal feed—principally penicillin and tetracycline—has already weakened their value in human disease. Antibiotics in animal feed kill off vulnerable bacteria, leaving the more competitive, and often more virulent, microbes to flourish. When these bacteria are then passed through a contaminated food source, such as meat, eggs, and raw milk, and consumed by people, illness can be prolonged because conventional antibiotic therapy is ineffective against these drug-resistant organisms.



Lester Crawford of FDA

"This study is about as good as we're going to get."

Scientists are also worried about the fact that the genetic material controlling drug resistance can be transferred from bacteria to bacteria. "Every animal or person taking an antibiotic (therapeutically or subtherapeutically) becomes a factory producing resistant strains through selection of existing and newly emerging resistant organisms," said Tufts microbiologist Stuart Levy in an editorial that accompanied the *New England Journal* study last month and stressed the urgent need for a ban. The study was headed by Scott D. Holmberg of the Centers for Disease Control (CDC).

Drug companies and farmers have consistently argued for years that a direct link has not been proved, that the degree of risk is unknown, and that food costs will rise if antibiotic use in feed is prohibited. The biggest manufacturers of antibiotics for animal feed are American Cyanamid and Pfizer Inc., which make tetracycline derivatives. Other companies that manufacture antibiotics for animal feed include Eli Lilly & Co., American Hoechst Corporation, and Upjohn Company. The American Farm Bureau Federation has actively opposed a ban.

Because of these powerful interest groups, federal action to ban antibiotics has never gained much momentum. In 1977, FDA, under commissioner Donald Kennedy, who now is president of Stanford University, proposed to halt the use of penicillin and tetracycline in animal feed. Congress stalled the proposal by requesting that the National Academy of Sciences study the issue before the agency acted further.

In 1980, the Academy committee issued its report. It concluded that while a majority of studies reviewed in a literature search said that restrictions should be imposed, it still could not assess the quantitative risk. "The assertion that subtherapeutic levels of antibiotics in livestock feed are hazardous to human health has been neither proven nor disproven. The research necessary to establish and measure a definite risk has not been conducted and, indeed, may not be possible," the report said.

Opponents of a ban seized upon the report's conclusion, and Congress once again mandated more study. This time federal legislators ordered FDA to study the issue some more. Almost a year ago, 300 scientists signed a letter drafted by the Natural Resources Defense Council urging the Administration to issue a quick ban on penicillin and tetracycline in animal feed. Little happened.

Now, 7 years after FDA first proposed

*Random House, New York, 1984.

a ban, many scientists are hoping that the logjam may be broken. Four studies significantly undercut the arguments that a direct link has not been proved.

- In 1982, a study by Harvard researcher Thomas O'Brien published in the *New England Journal of Medicine* reported a new laboratory technique for demonstrating that animal and human bacteria extensively share genetic material that codes for drug resistance.† This genetic material, known as a plasmid, provides a fingerprint that allows researchers to identify their existence and to trace the origins of the host bacteria.
- In August, a team of researchers led by Holmberg of the CDC reported in *Science* (24 August, p. 833) that a majority of outbreaks of drug-resistant *Salmonella* in the United States during the past decade were traced to animal food sources. The fatality rate as a result of these infections was 21 percent higher than for disease caused by *Salmonella* strains that responded to conventional antibiotics.
- Holmberg was also the principal investigator of the critical study demonstrating that tainted hamburger meat from a South Dakota cattle herd infected with *Salmonella newport* led to human illness in four states. The cattle had been fed low doses of tetracycline for months.
- The findings of the Holmberg report are "consistent" with the preliminary findings of 3-year study conducted at the behest of FDA and recently completed, says Lester Crawford, director of the agency's Center for Veterinary Medicine. In a retrospective study, the public health department of Seattle–King County, Washington, sought to measure the extent of illness in the local population caused by animal products. The final report has been submitted to FDA and will now be peer reviewed.

Raoul Stallones, chairman of the 1980 Academy study and dean of the School of Public Health at the University of Texas, said in an interview that if the studies by Holmberg and O'Brien had been available at the time of the Academy's review, "I might not have been as blasé about antibiotics as I was." He adds, "The conclusions that Holmberg drew [in the *S. newport* study] are most reasonable. I think this is as close as one can get to a direct link."

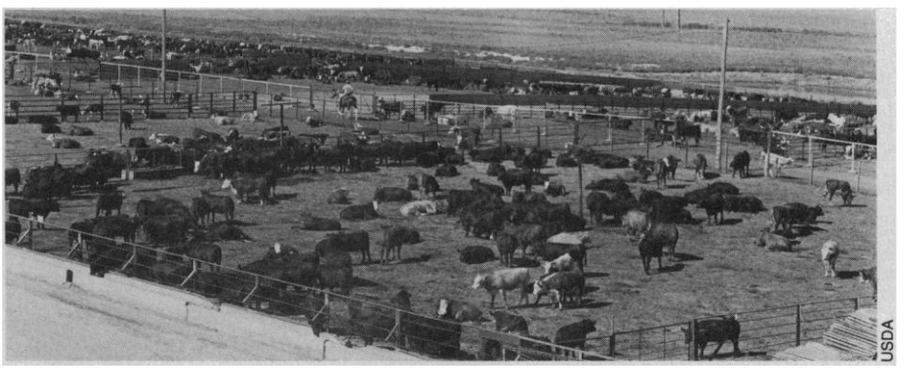
Crawford, who has long advocated a federal ban on antibiotic feed additives, said in an interview that Holmberg's *New England Journal* report "supports our contentions. This study is about as good as we're going to get. I don't see how we can get any better information."

Even so, Jerry Brunton, a veterinarian and a vice president at the Animal Health Institute, the trade association representing companies that produce animal drugs, says "There's not a shred of evidence to say that the *Salmonella newport* was animal in origin. It took a great leap in logic to come to that conclusion." Brunton argues in particular that other foods may have been the true source of the bacteria. Brunton also contends that the beef could have become contaminated during slaughter or processing. Holmberg disagrees.

Other opponents of a ban, including the American Farm Bureau Federation, concede that the recent studies undercut their arguments that a direct link has not been shown. Instead they are stressing another argument—that a prohibition on antibiotics will cause higher meat prices for consumers because of higher production costs. A study by the U.S. Department of Agriculture came to this conclusion in the 1970's. But Crawford of FDA points out that the department based its conclusion on the assumption that all antibiotics would be banned. FDA in 1977 proposed to ban the two main broad-spectrum antibiotics on the market and left the door open for the use of alternatives.

In 1979, OTA said, "Most of these [animal feed] drugs could be replaced with alternative drugs that are already approved by FDA." The use of such alternatives reduces the chance of transferable drug resistance. Although consumer prices could rise significantly over the short term, the report said, "the long term consequences are less certain, probably resulting in small decreases or no changes in [meat] production and small increases in both consumer prices and overall producer incomes. The trade-off is therefore between immediate economic benefits and future health risks. These decisions involve value judgments that cannot be based simply on monetary considerations."

Farmers in the United States are the only ones in the world to rely so heavily on antibiotics in livestock production. Britain and several other European nations issued a ban on the use of antibiotic feed additives in the 1970s. (Because of a loophole, however, farmers could obtain the antibiotics by prescription from veterinarians. So while use declined, the reduction was not as much as was hoped for. Crawford says that a ban on penicillin and tetracycline here would extend to prescriptions too.)



Beef cattle

Should they be fed antibiotics?

The situation has changed somewhat in the United States. A majority of American poultry farmers once routinely used antibiotics in feed. During the past few years, however, most of them have either switched to antibiotics developed only for animal use or have stopped using them altogether. But FDA officials say that a high proportion of cattlemen and pork producers continue to use antibiotics as a growth promoter. In 1979, OTA had estimated that 70 percent of beef cattle and 90 percent of veal calves and swine in the United States are reared on feed mixed with tetracycline or penicillin.

The agriculture lobby has also argued that they are unfairly being singled out for widespread use of antibiotics. They assert that people indiscriminately use antibiotics as well. Supporters of a ban, such as Mitchell Cohen, chief of the division of enteric diseases at the CDC, and Stuart Levy of Tufts acknowledge that physicians and patients do overuse and misuse antibiotics. Physicians too often prescribe broad-spectrum antibiotics when a more specific antimicrobial could be used as therapy and people too frequently take antibiotics without a doctor's direction. But use of antibiotics in

†*New England Journal of Medicine* **307** (No. 1), 1 (1982).

animals is much more worrisome than in humans because, at any one time, the number of animals feeding on antibiotics vastly exceeds the population of humans being treated, they say. This is compounded by the fact that the length of therapy in humans averages fewer than 10 days, while use of antibiotics fed to animals is "often continuous," according to the OTA report. Levy says, "Depending on the animal's size, its daily fecal excretion can be 5 to 400 times greater than the 100 to 200 grams excreted daily by adult human beings, and dispersal of animal feces is not well controlled." As a result, the disease would be transmitted much more easily to other animals and humans.

Cohen says that the issue in the past may never have found much favor because "people perceive *Salmonella* poisoning as a nuisance illness," which does not create the same concern as a chronic disease such as cancer. "But selective pressure caused by antibiotics chooses more virulent organisms," he says. "Once we have a large number of resistant organisms, it's going to be too late."

There is some movement on Capitol Hill to address the issue. Representative James H. Weaver (D–Ore.) is currently drawing up a bill that would put into legislation the FDA's proposed ban on the use of tetracycline and penicillin. Weaver planned to introduce the bill before Congress recessed, but it will have to be reintroduced in the next Congress. The bill, according to a staff aide, would probably be reviewed by the House health and environment subcommittee. House legislators introduced a bill in 1980 which embodied the goals of FDA's 1977 proposed ban, but the measure did not get far. The Natural Resources Defense Council is also considering several options to spur FDA action. Karim Ahmed, a senior scientist with the group, says that it may, for example, petition the agency to declare that antibiotics in animal feed pose an "imminent hazard" to human health. If FDA should agree, then an immediate ban would be required.

Renewed efforts at FDA to enact a ban might run aground once again in the Appropriations Committee, which is chaired by Representative Jamie Whitten (D–Miss.). Whitten, the champion of the farm community, oversees the budgets of both FDA and the agriculture department. It was the appropriations committee, under Whitten's chairmanship, which thwarted FDA's proposal and each year since has written into the hearing record that FDA will not proceed with rule-making until the appropriate studies are completed.

The issue appears to be on the front burner again at FDA. The Seattle study represents the final report on Congress' wish list. Crawford is now deciding whether to deliver the report to Congress next spring as scheduled or present the findings now, given the publication of the Holmberg studies. Crawford himself brings an unusual background to his post. He was head of FDA's veterinary branch in 1977, became dean of the University of Georgia's School of Veterinary Medicine, and then returned to the same FDA post in 1982. During his time away from FDA, he chaired a seminar on antibiotic feed additives for the Natural Resources Defense Council, the same group that last year circulated the letter in support of a ban. When he returned to FDA, he was required by law to excuse himself from any discussions for a year. Crawford went beyond this and stayed out of discussions for 2 years "to avoid any appearance of a conflict of interest," he says. Crawford also says he has been a consultant for American Cyanamid. Now new FDA commissioner Frank Young has asked him to take charge of the issue.

Crawford says there might be a better chance to proceed now. Drug resistance fostered by antibiotics is better understood by the general public now, he says. Nevertheless, "we will have to handle this [issue] gingerly. We will have to have the courage of our convictions."

—MARJORIE SUN

Waiting for Sonic Booms

The Air Force and Navy plan to start low-altitude combat training at supersonic speeds over sparsely populated rural areas; local residents are opposed

A year and a half ago, Leland and Gertrude Van Allen drove 50 miles east from their home in Fallon, Nevada, to Dixie Valley, where the Navy had promised to demonstrate what sonic booms sound like. Dixie Valley is in an area of central Nevada which, if the Navy's plans go through, will be subjected to 20 to 100 booms a day from planes flying at low altitudes, often as low as 7000 feet over the residents' heads. The inhabitants of Fallon also expect to hear booms but not so many as their Dixie Valley neighbors.

Before they heard the booms, the Van Allens thought they would not be too bad, that it would be possible to live with them. Afterward they changed their minds.

An F-14 plane made two passes over the area where the Van Allens and other observers stood and they got the full impact of two sonic booms, one of which, a so-called focus boom, put a large crack in the town schoolhouse. Townspeople who were inside their homes saw the walls shake and Edwin Robbins, who lives in Dixie Valley, came home to find that the boom had broken new Sheetrock in his house. A miner said it was "the equivalent of a 50-pound block of gelatin [explosives]."

To the dismay of many citizens in the areas, the Air Force and Navy plan to train fighter pilots by allowing them to engage in low-altitude dogfights at supersonic speeds over sparsely populated sections of New Mexico, Texas, Utah, and Nevada. On 13 September, the Air Force announced that it will fly up to 600 supersonic sorties per month near Holloman Air Force base in New Mexico. The flights will begin in January. As a concession to the opponents, the Air Force has promised to monitor the booms, to restrict the pilots to fly supersonically only in 22 by 28 mile elliptical areas, and to reassess the program after 9 months. The Air Force and Navy plans for Nevada and eastern Utah are not yet finalized.

Defense Department officials contend that pilots need to gain proficiency in flying in combat situations and there simply is not enough airspace available over military ranges. "There are geographical limitations on where we could do these flights," says Gary Vest, deputy for environment and safety to the deputy assistant secretary of the Air Force. It is too expensive to send the