Antibiotics in the Barnyard

The FDA wants to curtail the use of drugs in feeds, but the National Academy of Sciences finds the FDA's case unproven

Rare indeed is the health commissioner who says that further study of a controversial issue is *not* what the public demands. Yet that is what one hears from Lester Crawford, director of the Bureau of Veterinary Medicine at the Food and Drug Administration (FDA). It is time for the government to limit the use of antibiotics in animal feeds, as the FDA proposed to do 2 years ago, Crawford thinks, even though he has no irrefutable evidence that doing so will improve the public's health. In theory, the FDA's proposal will make for a healthier environment, and that, he says, is justification enough.

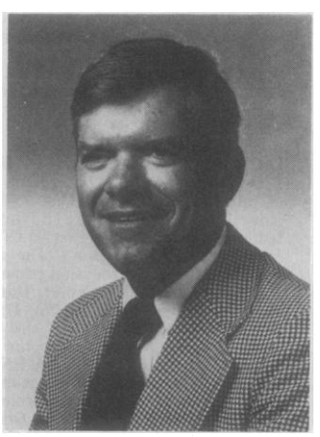
Crawford finds moral support for his outlook in a study completed in March by a committee of experts at the National Academy of Sciences (NAS).* Their outlook, too, was unusual. For how often does a panel of academics turn away a study proposal? Yet that was the choice of the NAS committee. Congress had asked the NAS to recommend a course of study that would answer, once and for all, the question of whether or not it is safe to add antibiotics to feeds. The committee effectively said that could not be done.

Congress made the request precisely because members representing the farm states did not like the sound of FDA's ban on antibiotics. In 1978 Congress instructed the FDA not to act until the NAS had conducted an objective review, and it set aside $1.5 million for the project.

The NAS committee, chaired by Reuel Stallones, dean of the School of Public Health at the University of Texas in Houston, considered the possibilities for study for 7 months and concluded that it would be technically impossible to come up with the definitive answers sought by Congress.

In the words of the committee, the review of the literature found (i) that the case against the use of antibiotics in feeds had been "neither proven nor disproven," (ii) that although there may be a real danger here, "the research necessary to establish and measure a definite risk has not been conducted," and (iii) that it is "not possible to conduct a feasible, comprehensive epidemiological study of the effects on human health . . . partly because it is impossible to determine the antibiotic history of the animal from which a particular piece of meat came."

Since the threat to human health is potentially serious, the committee did suggest that more work be done to find alternatives to the use of antibiotics in feeds. And it proposed four narrowly focused studies designed to give some quantitative data on a problem which until now has been described largely in theoretical terms.



Lester Crawford

Reuel Stallones

Crawford of the FDA took this conclusion to be an "essential affirmation" of the FDA's policy. He thinks it would be a waste of public funds to launch a major new study. Virgil Hays, professor of animal science at the University of Kentucky at Lexington and chairman of another study group at the Council for Agricultural Science and Technology, read the NAS report differently. (Microbiologists on the CAST committee quit last year, charging that Hays exercised a prodrug bias in editing their work.) To Hays, the new report is a repudiation of the FDA's proposal. What it means, he said, is that "We just do not have the information that would justify the decision the FDA has proposed." Like much of the farm industry, he favors delay and further study. He thinks a modest 7-year project would be a good starter. Stallones, the chief author of the report, said he thought that the FDA had been neither supported nor repudiated. He felt a bit like an arbiter in a theological debate, ". . . and as you know, there can be no compromise in a holy war." His committee's point was simply that science cannot provide a definitive critique of the FDA's proposal, for it is impossible to determine whether it would or would not make the environment safer.

As the debate rages among the partisans, the public remains in the dark as to what is being proposed or opposed in its behalf. Congress is not much better informed. The scientists' data are scant. Expert opinion is divided. Yet if the FDA is correct, the government may be acting irresponsibly if it allows the problem to fester.

The concern is that modern animal husbandry, in addition to being an efficient breeder of pigs, chickens, and cattle, may also be an efficient breeder of new forms of disease. As meat production became more systematized in the last 30 years, farmers and lot operators found it economically advantageous to

*Members of the Committee to Study the Human Health Effects of Subtherapeutic Antibiotic Use in Animal Feeds included Reuel Stallones of the University of Texas (chairman), E. Russell Alexander of the University of Arizona, Charles E. Antle of Pennsylvania State University, Pierce Gardner of the Pritzker School of Medicine, Edward H. Kass of the Harvard Medical School, Carl Keller of the National Institute for Child Health and Human Development, J. Michael Lane of the Center for Disease Control, Frank J. Massey, Jr. of the University of California at Los Angeles, Robert H. Rownd of the University of Wisconsin, Paul R. Sheehe of the State University of New York in Syracuse, and Vernon L. Tharp of Ohio State University.

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add small quantities of antibiotic drugs to animal feeds. By a mechanism not thoroughly understood, a steady diet of antibiotics allows animals to gain weight more rapidly. Also, as noted in an appendix of the NAS report of last March, it permits cheaper operating procedures at feedlots and meat packinghouses.

Consider pigs. It is estimated that in 1978 pigs taken to market in the United States consumed about 40 percent (or about 1.4 million kilograms) of the antibiotics used as feed additives. About half the antibiotics produced in the country are now used in feeds. "The swine industry," reports appendix K, written by the Board of Agriculture and Renewable

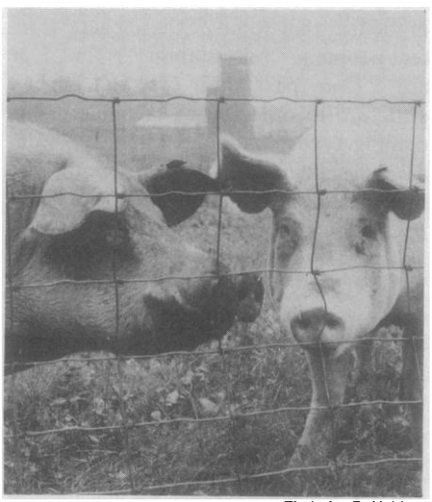

Photo by C. Holden

Drug users.

Resources of the NAS, "has changed from an enterprise that historically employed pasture to one that predominantly employs confinement buildings and concrete lots." (While pig production has increased, the number of pig farms declined from 1.4 million in 1954 to 450,000 in 1974.) The report continues:

> With concentration and confinement production, the enteric diseases and respiratory diseases are the most prevalent problems reported.
>
> As a group, both the large producers and the organized sow-farrowing farms employ an early weaning management system whereby the nursing pigs are weaned at 3 to 4 weeks of age. . . . Because of the high fixed costs, the management places a high priority on total production. With early weaning, the sow can be re-bred within a few days after her pigs are weaned and thereby increase the number of pigs produced per sow per year. . . . In the process of early weaning, natural protection from enteric disease problems in young pigs has been diminished (IgA immune globulins in sow's milk).
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> . . . [T]he introduction and use of feed-additive antibiotics has been concurrent with change in production technology in the swine industry. It is likely that the use of antimicrobial agents has facilitated the development of the concentrated operations.

Discovery by Decree

A mathematics breakthrough is announced but details are not forthcoming

There never was any doubt in mathematicians' minds that Robert L. Griess, Jr., a visiting professor at the Institute for Advanced Study, was a prime contender to discover the "monster group," a postulated mathematical construct whose existence would be of great theoretical importance. Griess is one of several who defined the group and for the past 6 years he has been openly working on a proof that it exists. On 14 January of this year, Griess announced that he had done it. He sent a cryptic mimeographed note to his competitors and other interested parties saying that he had constructed the group and that his construction is "direct, explicit, and carried out entirely by hand. I like it." He concluded by wishing the note's recipients a happy new year.

Griess's announcement sent shock waves through the mathematics community. If true, his discovery would be an important result. The monster group truly is a monster—the number of its elements is about 8×10^{53}. It is thought to be the largest of all so-called finite simple groups. Of particular interest is Griess's claim that he constructed it by hand, since other, smaller such groups were constructed with computers. The monster group also seems to be related, in an as yet obscure way, to certain areas of number theory.

But as the weeks drag on since Griess's announcement, mathematicians are growing increasingly curious about the result. Griess refuses to tell anyone just how he constructed the group or even to commit himself to a date when he will release the details of his discovery. *Science* asked Griess what the details of his proof are, when he will write the proof up, and why he announced the result without being willing to release any details. To all of these questions, Griess replied "no comment."

Still, Griess is getting publicity and credit for his reputed discovery. In February, the National Science Foundation (NSF), which funded his work, issued a press release that said Greiss "succeeded in constructing" the monster. Alvin Thayler of the NSF explains the agency's action by saying, "Griess is a first-class researcher. There is no reason not to believe him. I trust him."

In May, *Scientific American* will publish an announcement of Griess's discovery in its Science and Citizen section. Judith Friedman of *Scientific American* says she decided to go ahead and write the story because it is her feeling that the mathematics community believes Griess. She was able to reach Griess by telephone but got nowhere with her requests for details of his proof. "I really tried to get something out of him and it was impossible. I said, 'give me a hint, anything' and he said 'no,' " she says.

Even those who know Griess well say he refuses to tell them how he did his work. Daniel Gorenstein of Rutgers University in New Brunswick, who is a leading authority on finite simple groups, says, "Sure, I know Griess. He comes to our seminars. I even go out to dinner with him sometimes." But Gorenstein is no more informed than anyone else on the construction of the monster.

As to why Griess is behaving in this eccentric way, mathematicians have two hypotheses. One is that he is trying to milk his method as much as he can before he releases it to his competitors. The other is that Griess is still checking to see whether his proof really works but he decided to announce the result anyway to establish priority.

Whichever hypothesis is correct, Griess did manage to be credited with discovering the monster. There are few other examples in modern science of a claim being established simply on the basis of a note saying essentially, "I did it and I like it." But, as is frequently pointed out by Griess's colleagues, he'll look awfully stupid if he doesn't eventually come up with some details.—GINA BARI KOLATA

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The report also notes that, if antibiotics were removed from feeds, the present structure of the swine industry might break down. Piglets would have to be suckled longer to get the natural bacteria killers in their mothers' milk. Sows would breed less frequently. "More labor and time would be required to thoroughly clean and disinfect between groups of pigs." And because of increased costs, farmers might have to return to "pasture production." The seasonal nature of natural pig life "would mean large month-to-month variability in marketings reminiscent of historical patterns and would be disruptive for today's packing industry." In this way, the pig industry has become dependent on drugged feed.

The drugs that keep the animals healthy have a negative effect, however. When used steadily in small doses—as is the case today—they create an environment with a strong selective bias. Bacteria genetically endowed with the strength to survive in a sea of antibiotics flourish. Those without it die. Thus, modern feedlots are marvelous breeding farms for resistant strains of bacteria. The potential threat to human health lies in the fact that some of these bacteria infect people as well as animals, and some are able to pass their resistant genetic structure to other types of bacteria, including types that infect humans. (*Salmonella* and *Escherichia coli* are the two most frequently mentioned.) As the microbiologists say, these feedlots act as reservoirs for drug-resistant genes.

No research has linked a human epidemic with the perceived threat in using low levels of antibiotics, but the threat itself was enough to persuade Great Britain to ban the use of human-disease antibiotics as a feed additive in 1971. By all reports, however, farmers in Britain have circumvented the government by obtaining the drugs by prescription from veterinarians, and adding it to the feed privately. They could do the same here.

The FDA in 1978 proposed to ban the use of penicillin and tetracycline as feed additives because these two drugs are the most important for human therapy. According to Virgil Hays, the properties that make them valuable for humans also make them valuable in animal feeds: they are "broad spectrum" bacteriocides without peer. Just as the FDA was preparing to go into regulatory hearings, Congress intervened and stopped the process.

Crawford says, "We are ready to go to hearings right now and regulate." But there is a "catch-22." If new evidence relevant to the issue turns up, the FDA must consider it before taking final action. "It would be a little stupid to go to hearings unless we could see what the light at the end of the tunnel is," according to Crawford. The FDA, he thinks, will probably go to Congress and ask what should be done next.

To judge by the comments of the House Agriculture Committee staff, Congress is not recommending any action at the moment. And it is not difficult to understand why. Limiting antibiotics

Rain Forests Vanishing

Barring a change in human nature, virtually all the world's remaining rain forest will have disappeared within the next generation. Although a committee of the National Research Council does not label this a "crisis," it makes it clear in two new reports that nothing less than an emergency effort is called for to mitigate the effects of this loss.

The reports, on "conversion of tropical moist forests" and on research priorities (the latter to be produced at the end of May) relate that the world's tropical forests are being destroyed at an even faster rate than anyone thought, by commercial timber harvesters, forest farmers, cattle raisers, and fuel wood gatherers. An area the size of Massachusetts is being permanently converted every month, and by the end of the century the only

Monteverde Cloud Forest Preserve in Costa Rica.

Photo by G. Powell

sizable areas remaining will be the remote parts of the Amazon and areas of equatorial Africa. But these, too, will probably disappear in 40 or 50 years. Actually, it may happen sooner as 90 percent of world population growth over the next 20 years is expected to occur in tropical countries.

The committee, headed by Peter H. Raven of the Missouri Botanical Garden, says that very little is known about the complex and fragile tropical ecosystems. Of the 4 to 5 million species of plants and animals in the world, 3 million are found in the tropics, and no more than one-sixth of these have been taxonomized. In addition to research on tropical ecosystems, the committee emphasizes the need to accelerate biological inventories, collect specimens, set up gardens, zoos, and seed banks to preserve the fast-diminishing tropical gene pool, and increase by four or five times the number of tropical experts in the world, who now number about 1500.

Norman Myers, a Nairobi-based wildlife expert who collected information for the committee, says the picture is not as bleak as it might be as the government of Brazil, which owns one-third of the world's rain forests, has come to recognize the ecological and economic losses incurred by rapid and heedless exploitation of the Amazon. But this new sensitivity may only delay the inevitable.

Says the committee: ". . . the destruction of these vast ecosystems without the development of ways for replacing them with others equally productive foredooms a large portion of the human race to misery and portends instability for the entire globe by the year 2000."—CONSTANCE HOLDEN

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in feeds, as the FDA proposes, would bring an improvement in the environment which is not measurable at a cost which is both measurable and highly specific. Hays estimates that the FDA's regulations could add an expense of about $2 billion a year to the "national food budget"—an ill-defined concept that includes costs borne by farmers and consumers. The figure is disputed, but there is no question but that the policy would give the meat industry and the drug producers some major logistical problems, if nothing else. They are lobbying to prevent action.

Then, too, enthusiasm for taking action is dampened by the fact that feeds and feedlots are such a small part of the problem. At least half the antibiotics used in the country are given directly to humans. It is known that when people regularly consume these drugs, as they do in hospitals, a direct threat to public health is created. The resistant strains of bacteria bred in hospitals are known to prey on humans. But there is no simple way to attack this more serious aspect of the problem.

Thus inertia prevails even in the face of a potentially great threat. And it may be a very long time before we know whether the FDA's estimate of the potential is correct.—ELIOT MARSHALL

NMC Thrives Selling Dialysis

Controversial company may become the AT & T of proprietary medicine

Constantine Hampers, chairman of the board of National Medical Care (NMC), says he never intended to go into proprietary medicine. "It just happened," he recalls. But now he is in it with a vengeance as founder and head of a company that is beginning to invoke the same sort of mixture of fear and respect in the medical community as AT & T does in the telecommunications industry.

NMC is a company rich enough to hire John Sears, Ronald Reagan's former campaign manager, as its lobbyist and to retain the best legal help available. When the company went public in 1971, its sales were $9 million and its profits zero. Its net income and revenues have since grown exponentially. Its profits in 1979 were $19 million and its revenues were $190 million. The company and stock analysts foresee continued growth that should be unaffected by any downturns in the economy.

This is the first of two articles on the politics, economics, and sociology of dialysis.

The story of NMC begins in the 1960's, when Hampers and Edward Hager, now chairman of the company's executive committee, were in charge of artificial kidney machine treatments at Peter Bent Brigham Hospital in Boston. These machines could keep patients with kidney failure alive by cleansing their blood of the toxins ordinarily removed by the kidneys. But the costs were prohibitive—close to $40,000 a year for each patient—and there were few machines available. Hampers and Hager found themselves in the uncomfortable position of deciding with their staff which patients should be given the treatments and which allowed to die.

It was apparent to Hampers and Hager that more dialysis facilities were needed. They asked the Brigham to expand its facilities but were refused. They then asked the state to support expanded facilities but were refused again. "Ted and I were discouraged, we had almost given up," Hampers relates.

Then, in 1966, a patient whom they had treated for years (although not for kidney failure) asked Hampers and Hager to be medical directors of a for-profit extended care facility that he was establishing. The two doctors requested and were granted permission to include artificial kidney machines in the facility. "It worked beautifully," Hampers says, and from that beginning grew NMC, a company that now owns 120 proprietary dialysis centers treating 17 percent of the nation's 48,000 dialysis patients. It also owns a subsidiary, Erika, that makes dialysis supplies and equipment, and a clinical laboratory, Lifechem, that does all the laboratory tests for NMC patients. The company is branching out into obesity control centers, psychiatric care centers, and respiratory therapy, and it continues to explore the possibility of opening dialysis centers overseas. But NMC has become as controversial as it is successful.

The phenomenal growth of NMC is due to the largess of the federal government, which in 1972 decided to pick up the costs of medical care for patients with kidney failure. This is done as part of Medicare under the End Stage Renal Disease (ESRD) program, and it has created a vastly expanded market for dialysis by guaranteeing payments for treatments. The program itself now costs $1 billion a year, and although the ESRD patients are only 0.2 percent of the total Medicare population, they account for 5 percent of Medicare funds.

In the past 8 years, the number of dialysis patients has increased more than eightfold to 48,000, and it is estimated that the dialysis population will plateau at about 90,000 patients. The government set a fee that averages out to about $28,000 a year for each patient treated in an outpatient center. Medicare pays 80 percent of that fee; the rest is paid by the states or private insurance carriers or is absorbed by the centers. The proprietary centers owned by NMC have flourished under this reimbursement scheme because the company is vertically integrated and makes a fetish of being efficient.

The Health Care Financing Administration, suspecting that it may be overpaying for dialysis, is now preparing a new reimbursement scheme that is expected to result in decreased payments to dialysis providers. But no one expects NMC to be put out of business. Instead, say both NMC and its critics, the squeeze will be put on dialysis centers that are barely making it under the current reimbursement scheme, thereby allowing NMC to purchase these centers. "I tell our stockholders that as long as the government rewards efficiency to bear with us for we are efficient," says Hampers.

The company, as well as other dialysis providers, also is in the enviable position of being protected from economic down-

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