Poultry, politics, and antibiotic resistance

A growing body of data suggests that the clinical use of cephalosporins in human beings is under threat because of their widespread use in the poultry industry. Paul Webster reports.

The 18 000 chickens wedged together at John Neil's feet form a vast carpet of feathers, beaks, and tiny red-ringed eyes across the dimly-lit barn where the birds are being raised. Several lines of troughs, delivering food and water, snake through the mass of chickens and every so often pellets of food are released to them. "The food and water most likely contain drugs", says Neil, who audits the disclosure of drug use on 1100 chicken farms for the Chicken Farmers of Ontario, a Canadian industry lobby group. "The chickens are raised in their own excrement", Neil admits, "because that saves farmers the cost of having to change their litter during the 40 days they spend here before slaughter". In this environment, which teams with parasites and bacteria, Neil acknowledges the chickens are likely getting vaccines, anticoccidials, and what he vaguely refers to as "curatives". But on the question of whether the birds are getting antibiotics, Neil demurs, "I'm not seeing a whole lot of antibiotics".

The amount of antibiotics that chickens are receiving in North America is a closely guarded secret. In Canada, although a federal food inspection agency gathers drug-use data from poultry farmers, it refuses to release that data publicly. Even federal researchers tracking antibiotic use on farms are blocked from access to these data, confirms Rebecca Irwin, a Public Health Agency of Canada veterinary epidemiologist who runs the Canadian Integrated Program for Antimicrobial Resistance Surveillance. "Trying to get data on usage is tough", she complains. "Very tough."

The US picture is the same, confirms Tony Poole, a specialist on the use of antibiotics on factory farms with the US Department of Agriculture. "The producers are reluctant to let you in", she explains about her efforts to unearth drug-use data on factory farms. "Those are secrets."

Secretive as the poultry industry may be, in recent years US and Canadian researchers have made substantial headway in probing the usage of one highly controversial category of antibiotics on factory farms. In Canada, both the Food and Drug Administration (FDA) and the Public Health Agency are concerned about the use of cephalosporin antibiotics, which are both popular on farms and categorised as top priority drugs in human medicine. Concern among public health officials has grown in recent years. In 2004, researchers in Spain and Canada confirmed that cephalosporin-resistant bacteria have jumped from being a problem contained to hospitals to being a community-wide problem that is rapidly knocking out the use of one of the last remaining categories of antibiotics available to treat urinary tract infections, pneumonia, and gonorrhoea.

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"There's been a dramatic rise in cephalosporin resistance since 2000", says David Livermore, director of the Antibiotic Resistance Monitoring and Reference Library at the UK Health Protection Authority in London. Pointing to the global dissemination of a category of bacterial plasmids that are impervious to cephalosporins along with several other antibiotics, Livermore warns "this has been picked up in Europe, the Middle East, India, Japan, Korea, and Canada. These are supremely efficient plasmids."

With alarm growing about the increasingly rapid spread of cephalosporin resistance both in hospitals and urban communities, the Public Health Agency of Canada has invested substantially in tracking cephalosporin resistance in bacteria isolated from animals raised for slaughter, in retail meat and poultry products, and in human beings since 2002. "This surveillance has yielded a load of data that has become", as surveillance director Rebecca Irwin recently told a gathering of veterinary scientists, "more famous than probably the poultry industry wants to show".

Irwin's data shows a startling correlation between the use of cephalosporin antibiotics in chicken hatcheries in Quebec and a consequent spike in cephalosporin resistance in bacteria taken both from retail chicken products and human beings—a revelation that made the finding of heightened resistance to cephalosporins in chicken products in grocery stores and in human beings seem like a highly-suspicious coincidence. "We are seeing an animal connection that we never saw before", says Irwin about Canadian patterns of cephalosporin resistance in animals, retail chicken, and human beings.

Those suspicions only deepened after Quebec farmers were persuaded

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by public health officials to voluntarily cease using cephalosporins, with human resistance then quickly subsiding. According to the latest Canadian data released in March, cephalosporin resistance is growing again in Quebec, where farmers have begun using the drug again in hatcheries.

"A major reason such data is so interesting", says Irwin, "is that in a rare inside glimpse into chicken farms Quebec chicken farmers have disclosed to veterinary researchers from the University of Montreal that they rely heavily on the practice of injecting cephalosporin into eggs just before they hatch". This practice—which is an unapproved "extra-label" use of the drug—is done to prevent the spread of disease among birds raised in their own excrement. In the USA, according to a summary of a 2001 FDA investigation of 27 chicken and turkey hatcheries obtained by a Chicago-based group, the Food Animals Trust, four hatcheries reported injecting eggs, while four others reported injecting already-hatched birds. The real extent of ceftiofur usage may have been greater; more than a third of the hatcheries "kept poor or no treatment records", the FDA reported.

Frank Aarestrup, a specialist in antibiotic resistance with the Danish Technical University in Copenhagen, who helped to introduce a system of comprehensive surveillance of all veterinary drug use in Denmark since 2000, describes the Canadian surveillance data that matches hatchery usage and human resistance as among the most powerful he has ever seen. "Taken in context with all the other knowledge we have, anyone still opposing a link between antibiotic use in food and animal production and its direct impact on human health does so for other reasons besides science", Aarestrup said after reading the latest Canadian data.

In 2006, just after the first batch of Canadian surveillance data was released, a group of the most senior antibiotic-resistance experts from the US FDA, the Public Health Agency of Canada, France's National Microbiology Laboratory, and Belgium's Veterinary and Agricultural Research Centre warned in a comprehensive review of published data that cephalosporin-resistant bacteria are "frequently recovered from animals and food, with poultry as a primary food source, suggesting that human beings are often infected by these routes".

The Canadian surveillance data cannot conclusively link drug use in poultry with human resistance, says James Johnson, an infectious disease specialist with the Veterans Administration Medical Center in Minneapolis. But like Aarestrup, Johnson thinks the data "is as good as it gets" in terms of signals about the dangers of cephalosporin usage in hatcheries. Canadian veterinarians agree: last year the Canadian Veterinary Medical Association instructed its members not to use cephalosporin for extra-label purposes such as hatchery injections.

In July, 2008, the FDA attempted to do far more. In a "Final Rule" published in the US Federal Register, the FDA boldly proposed to ban the veterinary usage of cephalosporins in unapproved methods including injection into eggs. Unrestricted cephalosporin use "is likely to lead to the emergence of cephalosporin-resistant strains of foodborne bacterial pathogens", the FDA explained. "If these drug-resistant bacterial strains infect human beings, it is likely that cephalosporins will no longer be effective for treating disease in those people."

When it came to mounting a response to the FDA's prohibition of extra-label use of cephalosporins on farms, the industry turned to the American Veterinary Medical Association (AVMA), explains Steve Pretanick, director of Science and Technology for the National Chicken Council—a US lobby group. The AVMA represents 78 000 veterinarians working in the public and private sector.

In their response, the AVMA argued that the FDA's rule against extra-label cephalosporin use was completely unjustified. The Canadian, American, and European studies cited by the FDA fail to directly show that veterinary use of cephalosporin impairs human medicine, the AVMA insists, and the FDA prohibition would put animals at risk. "Extra-label cephalosporin use is medically necessary to relieve animal pain and suffering and allows veterinarians discretion to use drugs judiciously", the AVMA charges.

In late November, 2008, just weeks after the group filed its protest, the FDA reversed course. William Flynn, acting director of the FDA's Centre for Veterinary Medicine, announced the restrictions on cephalosporin use were being withdrawn to allow the agency to "fully consider" comments, including the AVMA's. "We responded through the AVMA", says Steve Pretanick of the National Chicken Council. "They worked up the argument as to why the FDA should not take this action. As a result, the FDA withdrew it. And that's the last I've heard of it."

The FDA now refuses to discuss the matter. But speaking to scientists in Kansas in May, 2009, Flynn suggested the FDA's retreat may not be permanent. That suggestion matches a statement released on July 13 by FDA deputy commissioner Joshua Sharfstein, stating that feeding antibiotics to healthy chickens, pigs, and cattle to encourage rapid growth should stop. Sharfstein's statement was released during Congressional hearings on the Preservation of Antibiotics for Medical Treatment Act, a proposed law that would restrict veterinary use of antibiotics that are important to human health, including cephalosporins.

Supporters of the proposed legislation include the American Medical Association, the American Public Health Association, and the Infectious Diseases Society of America. The AVMA does not support the legislation.

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