

Vaccinating Birds May Help to Curtail Virus's Spread

As avian influenza continues to ravage Asian poultry, countries are experimenting with a novel control strategy

Fearful that a deadly flu epidemic could be brewing in Asia, some countries are stockpiling drugs, preparing pandemic flu plans, and ratcheting up vaccine production (see p. 394). As these efforts kick into overdrive, animal experts are grappling with the other half of the bird flu equation: the birds. Specifically, they are debating whether a relatively untested strategy of mass vaccination of chickens and other poultry against avian flu will do more harm than good in warding off a human pandemic.

Since its appearance in 1997, global health experts have worried that H5N1 will combine, or reassort, with a human flu virus to produce an easily transmissible strain with H5N1's lethality. To avert such a disaster, last winter and spring seven Asian countries slaughtered more than 100 million birds, decimating the poultry industry. But the virus has resurfaced and appears to be endemic in the region. And the more virus in circulation, the greater the chance of a deadly reassortment.

Animal health officials agree that the best ways to curtail H5N1 are increasing surveillance and improving biosecurity, which includes a host of measures intended to prevent diseases from spreading among flocks and to the public. But now, after years of debate, consensus is building that vaccination of at-risk poultry could also be a critical tool in averting a human pandemic. Indeed, in September, alarmed at the spread of H5N1, the Paris-based World Organization for Animal Health (OIE) and the United Nations Food and Agriculture Organization (FAO) strengthened a previous recommendation encouraging consideration of vaccination in conjunction with other control methods.

But there's a catch, explains Alex Thiermann, a veterinarian at OIE: "If improperly done, vaccination could be dangerous." It could enable the virus to circulate undetected among birds, perhaps spurring its evolution. And no matter how helpful poultry vaccination might be, some countries may decide against it for fear that it would jeopardize

their export market.

So far, Hong Kong requires vaccination of all poultry. Thailand forbids it. China and Indonesia are selectively vaccinating in regions where the virus has appeared.

Risks and benefits

The clear benefit of vaccination is its ability to reduce the amount of wild virus in circu-



Balancing act. Inoculating chickens has its perils but is gaining favor as part of a larger control strategy.

lation. Although vaccination does not always prevent infection—just disease—it takes a much higher dose of virus to cause infection, and vaccinated birds that do become infected shed far less virus than unvaccinated birds. As an added precaution, animal health experts agree that vaccinated birds that become infected should be culled. "By reducing the amount of virus in the environment, you reduce the possibility of the virus spreading to a new flock, and you reduce the risk to humans," says David Suarez of the U.S. Department of Agriculture's (USDA's) Southeast Poultry Research Laboratory in Athens, Georgia.

For a country to undertake vaccination safely, it first must ensure the quality and efficacy of the vaccine. It must be targeted to the virus in circulation, properly inactivated, and tested to determine the adequate dosage.

Then there's the problem of distinguish-

ing vaccinated birds from birds infected by the wild virus. If the vaccine is derived from the circulating virus, both infected and vaccinated birds would appear positive in antibody tests. This problem has limited the use of avian flu vaccines in the past because it prevents epidemiologists from tracking the circulating virus. It could also make it hard to prove that flocks are disease-free so exports can resume once the disease is stamped out. (The use of vaccines to control highly pathogenic avian influenza is so new that there are few precedents to follow in resuming trade once an outbreak is contained.)

Long-term experience with an avian vaccine in Mexico has raised other concerns, as reported by Suarez and colleagues in the *Journal of Virology* in August. Farmers in Mexico have been immunizing chickens against a low-pathogenicity H5N2 virus with the same vaccine for 7 years. Over time, the virus has mutated, in a process called antigenic drift. Although the vaccine still prevents clinical disease, it no longer reduces the amount of virus shed by the chickens. Suarez believes that widespread vaccination probably contributed to the virus becoming endemic not only in Mexico but in neighboring Guatemala and El Salvador as well. To avoid this, the virus must be monitored and the vaccine updated periodically.

A shift in favor

Despite these hurdles, sentiment began to shift in favor of adding vaccination to other avian flu control measures several years ago.

With the increased scale of modern poultry farms, culling in a buffer zone around an infected flock was killing enormous numbers of healthy birds. Some farmers and animal health officials began arguing that vaccination in a buffer zone, instead of slaughter, might be more humane and cost effective.

In addition, studies done at the USDA lab in Georgia and reported in *Avian Pathology* in 1999 and in *Vaccine* in 2000 showed that a vaccine based on one H5 virus subtype might provide cross-protection against several others. If so, vaccinating with a strain that differs from the circulating strain could solve the problem of differentiating vaccinated-but-uninfected birds from infected birds. More recently, researchers at the Tai Lung Veterinary Laboratory of Hong Kong's Agriculture, Fisheries, and Conservation Department tested a vaccine based on an H5N2 strain against the H5N1 strains

Asia Struggles to Keep Humans and Chickens Apart

SONG PHINONG, SUPHANBURI PROVINCE, THAILAND—After having 30,000 chickens culled when H5N1 turned up on a farm 2 kilometers away, Boonchu Taeng-orn got serious about biosecurity. When permitted to restock his farm here in the central lowlands 2 hours north of Bangkok, he followed recommendations of Thailand's Department of Livestock Development to the letter. He strung netting from the shed roofs to the tilapia ponds beneath to keep wild birds out. (Biosecurity experts discourage locating chicken coops near open water, but raising tilapia on bird droppings is key to the economics of chicken farming here.) As few workers as necessary go into the sheds, changing first into work clothes kept at the site, walking through a disinfecting mist, and stepping in pails of disinfectant on the way in. The egg crates are disinfected before use, as are vehicles at the gates to each compound. And Taeng-orn follows the all-in, all-out practice: When he fills a shed with new chicks, he keeps them until egg production drops and then sells the entire batch. Sheds and cages are washed and repaired before the next batch arrives. "The emphasis on cleanliness is definitely good. It is more humane for the animals and safer for the workers," Taeng-orn says.

It is also safer for the world. Infectious disease experts agree that keeping zoonotic diseases like H5N1 and severe acute respiratory syndrome from crossing the species barrier into humans will partly depend on the efforts of millions of farmers like Taeng-orn. A greater



Risk on wheels. Current methods of transporting live animals facilitate the spread of avian diseases.

closing its live animal markets. Currently, buyers pick a live chicken at one of more than 800 live animal shops and have it slaughtered on the spot. K. Y. Yuen, a microbiologist at the University of Hong Kong, favors a central slaughtering facility, both to reduce the chances of exposing the general public to avian influenza and to cut the incidence of other infections. "Other advanced countries adopted central slaughter long ago," he says. The government asked for public comment this summer and is now deciding how to proceed.

—D.N.

that caused outbreaks in Hong Kong in 1997 and 2002. Trevor Ellis, senior veterinary officer at the Tai Lung lab, says the vaccine "protected against clinical disease and produced greater than 1000-fold reduction in virus excretion in birds given heavy virus challenge doses."

More convincing than the lab studies was Hong Kong's experience. Since H5N1 first surfaced there in 1997, the territory has progressively strengthened H5N1 biosecurity measures. Despite these efforts, Hong Kong has repeatedly been hit by H5N1 outbreaks. During an outbreak in December 2002 and January 2003, a number of farms were infected. On three of these farms, chickens in infected sheds were culled, but chickens in other sheds were inoculated with a vaccine based on the H5N2 strain. The virus spread to additional sheds on two of these farms, killing some of the recently vaccinated chickens. But as Ellis and his colleagues reported in the August issue of *Avian Pathology*, 18 days after vaccination, when immunity had developed, there were no new cases of disease among the vaccinated birds; intensive monitoring found no evidence of asymptomatic shedding.

In early 2003, Hong Kong added universal vaccination to its control measures. Unvaccinated "sentinel" chickens are placed within each flock, and there is regular serologic and virologic testing. When H5N1

swept through neighboring China early this year, Hong Kong remained virus-free.

Last winter, both South Korea and Japan identified H5N1 outbreaks quickly enough to contain them with limited culling, still the preferred approach. But where stamping out is impractical or uneconomical, vaccination should be considered, says Joseph Domenech, chief of animal health services for FAO.

Hong Kong's experience is not easily translated to other countries, however. Hong Kong's poultry industry is limited to just 150 farms and a handful of families raising backyard chickens. The territory is small and has an infrastructure capable of fully monitoring the use of vaccines. Hans Wagner, FAO's regional director, says, "It's a substantial challenge to extend these measures to an entire country"—and expensive. The vaccine alone costs about 7 cents per bird, not counting the labor of injecting or the monitoring that should accompany it. By contrast, FAO consultants and others who have visited China and Indonesia—which are both vaccinating in areas where H5N1 has been reported—noted several shortcomings. Several of the vaccines in use in both countries are based on the H5N1 strain itself, making it difficult to track the disease. And the use of unvaccinated sentinels and the serological and virological monitoring is spotty at best.

In Thailand, which has reported more than 250 outbreaks in 45 of the country's 76 provinces in the last 3 months, authorities have rejected vaccination, at least for the moment. Yukol Limlamthong, director-general of Thailand's Department of Livestock Development, says they are worried that vaccination might enable the virus to circulate silently among vaccinated birds, exposing farm hands and families to infection. "We don't want to put them at risk," he says. But flu experts elsewhere suspect that commercial concerns factored heavily in the decision.

The OIE Terrestrial Animal Health Code, which governs international trade in animals and animal products, says a country can be considered free of avian influenza if specified levels of surveillance do not turn up the virus—regardless of whether it is vaccinating. But the code is vague and places the burden of proof on the exporting country. Johan Reyniers, a press spokesperson for the European Commission in Brussels, says, "It would ultimately be up to Thai authorities to demonstrate that vaccination is properly implemented."

For now, Thai officials believe it will be easier to convince trading partners that its poultry products are safe if the country can control the disease without vaccination. But whether it can remains to be seen.

—DENNIS NORMILE

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