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The Skeptic

On the Front: A Pandemic Is Worrisome but 'Unlikely'

By ELISABETH ROSENTHAL

OXFORD, England — The Hospital for Tropical Diseases in Ho Chi Minh City, where Dr. Jeremy Farrar works, has treated about two dozen people with avian influenza in the last three years.

With that tiny number, Dr. Farrar and his Vietnamese colleagues probably have more clinical experience than any other doctors with the A(H5N1) virus — the dreaded germ that international health officials fear may ignite the next flu pandemic.

Yet, Dr. Farrar notes, this trickle of humans infected with bird flu — 186 in all since 2003 — has provoked a flood of scientific meetings on pandemics, accelerating in recent months.

"The ratio of meetings to patients is probably 10 to 1: Hawaii tomorrow. Geneva and Singapore next week," said Dr. Farrar, in jeans and carrying a red backpack, on a break from a conference where he was — naturally — speaking on the topic.

"The interest is phenomenal," he said, clicking at his popular PowerPoint presentation.

Still, Dr. Farrar is not sure that this intensity is entirely rational:

Having observed A(H5N1) for many years in Asia, he thinks it is unlikely that the virus is poised to jump species, becoming readily transmissible to humans or among them. Nor does he believe the mantra that a horrific influenza pandemic is inevitable or long overdue. He points out that the only prior pandemic with a devastating death toll was in 1918, and he says that may have been "a unique biological event."

"For years, they have been telling us it's going to happen — and it hasn't," said Dr. Farrar, director of the Oxford University Clinical Research Unit at the hospital in Vietnam. "Billions of chickens in Asia have been infected and millions of people lived with them — we in Asia are intimate with our poultry — and less than 200 people have gotten infected.

"That tells you that the constraints on the virus are considerable," he continued. "It must be hard for this virus to jump."

Still, a part of Dr. Farrar is terrified of A(H5N1) — "a very nasty virus," he calls it — which he has watched kill healthy young people, devouring their lungs.

In the last year, the virus has extended its range in birds from Eastern China to Western Africa. Over time, it has expanded the variety of species it can infect, including ferrets and cats.

"That is alarming," he acknowledges in the understated British way.

Like all responsible scientists, Dr. Farrar believes the world should prepare. But schooled in places where people die of real and present diseases like malaria and tuberculosis, he finds the "doomsday" predictions sketched out by some international officials unhelpful, more fantasy than fact.

And even if these officials' dire forecasts were to come true, he says, many of their elaborate pandemic preparedness plans are unworkable in developing countries, which do not have the resources or medical facilities to comply.

"I think you have to say we really don't know the odds of pandemic, and people are not comfortable with that," Dr. Farrar said. "It could fizzle out and kill 98 people — one more than the number dead today. Or it could be something like 200 million," closer to an estimate once made by Dr. David Nabarro, chief avian flu coordinator for the United Nations.

"It's terrifying if it happens, but it is very, very unlikely, I think — and it is difficult to balance those facts."

At the Tropical Disease Hospital in Vietnam, doctors have been doing just that, bracing for a pandemic that may never come, since long before it became fashionable in the West.

Before Vietnam began vaccinating poultry in mid-2005, the disease was rampant among birds there. Of the world's 186 confirmed human cases, 93 are from Vietnam. There have been no new cases this year.

But in the Tropical Diseases Hospital, doctors and nurses still don full bio-protective gear when they evaluate suspected cases, because "you don't know if the next one will mark the start of human to human transmission," Dr. Farrar said.

With each new patient, they assiduously try to follow international scientific recommendations. But their on-the-ground experience reveals

holes in the neat strategies coming from United Nations experts in Geneva and Rome.

The World Health Organization suggests that it might be possible to contain a pandemic by quickly diagnosing index cases, identifying contacts, prescribing all antiviral drugs, and quarantining, for example.

In response, Dr. Farrar shows a picture of the home of a patient: a hut on stilts by the Mekong River. When that patient fell ill, he took a boat to the local health station, and was transferred to the district hospital, Dr. Farrar says. Later, an ambulance took him to Ho Chi Minh City, where genetic analysis showed that he had avian influenza, instead of typical pneumonia. If bird flu ever gained the ability to spread easily among humans, that patient would have infected thousands before diagnosis.

"You've got to act quickly, but the process now takes many days," Dr. Farrar said, suggesting that more money for clinics, labs and experts should be flowing to developing nations.

"Then you're supposed to go back to the village and saturate it with oseltamivir?" he asks, using the generic name for the antiviral drug Tamiflu. "What do the villagers do when they hear the man has bird flu? They don't sit still; they get on buses and flee and stay with relatives in other villages," potentially spreading it there.

For doctors in Vietnam, human cases of avian influenza have been a frightening reality for more than three years, and Dr. Farrar vividly remembers the initial terror of the devoted hospital staff, unsure if they could catch bird flu from patients.

"Look at this lung — there's nothing there," he said pulling up the X-ray of a patient who is back at the university, but whose left chest shows a vast empty cavern. Studies from the hospital have taught the world much about A(H5N1): humans took longer to clear this virus than normal influenza, for example, and Tamiflu can quickly breed resistant strains.

But, to Dr. Farrar's chagrin, the treatment options have not really improved.

Flu vaccines are still manufactured by an "ancient strategy" that involves injecting eggs with virus, he complained, even as other vaccines rely on more sophisticated methods. As a result, flu vaccines — including experimental versions aimed at A(H5N1) — are cumbersome to produce, and target just one strain.

"What we need is a vaccine that is effective across strains because the virus can be different each year," he said. "My mom in the U.K. can get a shot every year, but that is not realistic in rural Asia."

More remarkable still, he said, Tamiflu is still the only drug useful against avian influenza, "and we all know that one drug is not adequate to treat any viral disease," he said, noting that multiple drugs are used in [AIDS](#).

Patients at Dr. Farrar's Hospital are given Tamiflu, and it appears to help some. "It's all that we have," he said. "So if I was sick, I'd certainly want to get it."

But, he rues the lack of international research and coordination to tackle a disease that has been in Asia for nearly 10 years. For example, he said, although Vietnam has greatly reduced the number of bird flu outbreaks by vaccinating poultry, no one knows if the vaccine puts pressure on A(H5N1) to mutate to develop resistance to the shot, which could cause a rebound of disease in the coming years.

Personally, Dr. Farrar remains optimistic, believing a pandemic will not come. If A(H5N1) changed so that it readily infected people, it would probably become less deadly, he said.

But if disaster happens, he says: "People will look back and say: 'This was a nasty virus that you knew could sometimes infect other species. Why didn't you do something? All you had was a single effective drug and no vaccine?'"

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This is in response to your request for information on Tamiflu purchases for the Military Services. A contract for Tamiflu was awarded to Roche for 2.4 million bottles (capsules) at a cost of \$68M. The Tamiflu was purchased for use in the event of a flu pandemic and will be issued to the Military Services as needed. There are no forecasted requirements by Service.

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(From Vickie.Otoole@dia.mil 4/26/06 in response to query from office of Rep. Cynthia McKinney)