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Science Watch

Still battling the 'bird flu'

Alarm over the avian virus that killed six people has eased, but researchers in Atlanta and Athens are still working at a breakneck pace to head off future crises.

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The war against the Hong Kong flu may not be over. But for now, science seems to have fought the virus to a draw.

There have been no new cases of "bird flu" in Hong Kong for 28 days now. The local government has declared the outbreak ended, though scientists disagree; last week, the World Health Organization's leading flu expert said he won't close the book on the novel strain that sickened 18 and killed six until six months have passed.

But the pause is providing flu researchers at the Atlanta-based Centers for Disease Control and Prevention and elsewhere a chance to evaluate the situation. Though work will go on for years, analysis has already provided vital new knowledge about flu viruses. In addition, it has revealed crucial gaps in the global health surveillance system that detects them and the plans being prepared to combat them.

"For those familiar with flu, this outbreak has raised a lot of uncertainty and a heightened awareness of its unpredictability," said Dr. Dominick Iacuzio of the National Institutes of Health. "It is still very early; we're not out of the woods yet."

So much research is under way on the Hong Kong flu --the first in a slate of scientific meetings on flu research opens Thursday in Washington --that little can be said yet with certainty. Some features of the outbreak, such as the discovery that the virus jumped from birds to humans with no discernible genetic change, have sharply challenged conventional knowledge of flu.

"If you had stood up at a scientific meeting before this and declared that a purely avian flu could infect humans, that would have been considered a radical statement," Iacuzio said. "This was an unexpected event, and (suggests) we probably don't know as much as we think."

Conviction has grown in recent years that a worldwide flu epidemic is imminent. Yet U.S. and international plans to respond to a rapidly developing global epidemic have not been made final since they were discussed at a major meeting in 1995.

Among the undecided issues: whether vaccines should be created for each major flu strain known, so that key people --health care workers and law enforcement personnel, for instance -- could be partially protected if a pandemic broke out. "I said this 30 years ago," said Dr. Edwin Kilbourne of New York Medical College, a leading flu scientist. "We should be able to pull a vaccine off the shelf and have it available for people at high risk. But there has been no funding for this kind of research."

Much of the Hong Kong research so far has been conducted in Georgia, at CDC in Atlanta and the U.S. Department of Agriculture's poultry research station in Athens. The pace may have eased in Hong Kong, but the workload has not slackened on Clifton Road.

"We still spend two hours every morning on the phone to Hong Kong, talking to our team out there," said Dr. Brian Mahy, director of the Division of Viral and Rickettsial Diseases, which includes the influenza branch. "And every day at 1 p.m. we have a meeting with other divisions of

CDC who are interested in this problem: the vaccination program, the quarantine program, hospital infections, infectious diseases."

CDC staff have been on high alert for months. Dr. Kanta Subbarao, lead author of the first scientific paper characterizing the virus, said recently that she has had one day off since Thanksgiving. But the agency's efforts are shifting; its remaining staff members return from China in the next few days, and analysis of the reams of data gathered by its epidemiologists in Hong Kong has already begun.

CDC is conducting several sets of studies. One, which is examining blood samples from people who had contact with 10 of the victims, will attempt to determine whether the virus was transmitted from person to person. A second study may identify risk factors that could have increased vulnerability to the virus.

"We have an enormous amount of work to do in the lab," Mahy said. His division faces such a workload that it called two scientists out of retirement and hired two others. It is simultaneously processing thousands of blood samples sent back from Hong Kong, analyzing similar viruses still arriving from labs around the world, and conducting research on improving tests for identifying the virus in Hong Kong.

That last task provided one of the outbreak's unanticipated challenges. The standard test used to identify influenza was not sensitive enough to detect antibodies to avian viruses in blood samples. A research team led by Dr. Jacqueline Katz developed one, and on Jan. 5, she flew to Hong Kong to teach local experts how to run the new test.

"It was tense, and it was very long hours," she said last week in her office at CDC. "We would work all day, I would be in the lab and the epidemiologists would be in an office next door or in the field doing interviews, and then we would do a conference call with Atlanta at 10, 11 at night."

Katz's group has been working under taxing conditions. Because the Hong Kong virus --named H5N1, after two proteins, hemagglutinin and neuraminidase, on its surface --is so extremely lethal to chickens, lab workers must observe many precautions to make sure it doesn't escape: Their work is restricted to a "P3-plus" laboratory, one of the highest levels of biological security, and workers must wear gowns and respirators, and shower and change before leaving the facility. CDC had no such space until it built one several weeks ago by cannibalizing space from other research programs; initially, Katz and colleagues drove to Athens several times a day.

But their work has been eased somewhat by a lucky find. Another H5 virus was sent to CDC by a veterinary laboratory in Weybridge, England, which isolated it from a Malaysian duck held in a quarantine station in Singapore. The virus, dubbed Duck/Singapore/97, is an H5N1 just as the Hong Kong virus is --but it is much less lethal to chickens, so CDC can work with it under regular lab conditions.

Whether the virus will recur and how it will be detected remain urgent questions. Though detection of the initial case in May proved that recently enhanced flu surveillance is working, flu experts are acutely aware of holes in the net of detection.

"There may be other strains, or this strain, elsewhere in the world; in many countries where you could possibly see a new pandemic strain --Vietnam, Burma, Korea --we have almost no surveillance," Mahy said.

In China, CDC supports 12 surveillance laboratories; in the United States, which has about one-fifth of China's population, it has 70. And Chinese hospitals are mostly outside the surveillance network --a gap CDC hopes to bridge, since most of the H5 cases detected in Hong Kong were found in hospitals.

One of the unanswered questions of the Hong Kong outbreak is whether the virus has been vanquished --eliminated over the New Year's holiday with the slaughter of 1.4 million, chickens -- or merely forced underground. The possibility that it may be smoldering at low levels in the local population leaves scientists uneasy; the arrival of Hong Kong's regular flu season next month could encourage the emergence of a virus with the high mortality rate of H5 and the easy transmissibility of a more common flu.

"One of these days, (influenza) is going to hit in a very big way, " Mahy said. "Fortunately, I don't think this particular episode is going to lead to worldwide disease in the next few months.

"But in a year's time, it could be a different story. We just don't know."