Thursday, 08/21/1997
Section: FOREIGN NEWS Letter: A Page: 12 Words: 467

CDC to probe deadly flu strain
Virus common to birds kills boy in China

By M.A.J. McKenna/STAFF WRITER

A 3-year-old child in Hong Kong has died after being infected with an influenza virus that never had been seen in humans. Mindful of flu's potential for evolving into world-wide epidemics, the Atlanta-based Centers for Disease Control and Prevention has sent a team to investigate.

Chinese health authorities announced Wednesday morning that the boy contracted a strain of flu, H5N1, that usually infects birds and has recently killed 4,500 chickens on a Hong Kong farm. The child died in May in a Hong Kong hospital, but the virus was only identified last week by CDC and European laboratories.

"The important task for us in the next four to eight weeks is to trace the source of the disease," said Dr. Margaret Chan, Hong Kong's director of health. "If the virus has gone through major change ... it may increase the potential for a big epidemic."

CDC's investigators left for Hong Kong Tuesday. Nancy Arden, an epidemiologist with the agency's National Center for Infectious Diseases, said little is known so far about the new virus. For instance, she said, it isn't clear whether the flu strain itself, or other medical complications, caused the child's death; knowing that will help determine how dangerous the virus is.

"The main objective is to try to determine if there is any evidence that this strain is being transmitted among the population," Arden said. No other cases of flu from this virus have been identified, she said, adding that a Hong Kong lab affiliated with the World Health Organization has analyzed more than 4,000 samples of local flu cases without finding a match for the virus found in the child.

"That is a pretty good indication that it either hasn't spread at all, or that if it has spread, the impact has been minor," she said.

The Hong Kong case is of particular concern because avian flus so seldom cross directly into humans. The more common path is from birds to pigs, which, because they can contract both bird and human viruses, act as a sort of genetic mixer for new viruses.

"It is just not a common occurrence for a human to be infected with avian virus," Arden said. "Theoretically, it could be the start of a new strain in humans."

That is worrisome because flu, considered an underappreciated disease by virologists, has the potential to be lethal on a global scale.

There have been three flu pandemics this century, in 1968, 1957 and 1918. The 1968 epidemic also began in Hong Kong; the 1918 or "Spanish" flu, which began in the U.S., killed more than 20 million people worldwide.

“This may be just a blip, but it is the kind of thing that has to be watched for,” said Dr. Robert Webster, a prominent flu virologist in Memphis who this week published a scientific paper examining the likelihood of another
flu pandemic.

Friday, 08/22/1997
Section: NATIONAL NEWS Letter: A Page: 20 Words: 669

CDC says no new bird-to-human flu cases uncovered

By M.A.J. McKenna/STAFF WRITER

Health authorities so far have found no evidence that the potentially fatal new strain of influenza found in Hong Kong is spreading in humans, a finding they called encouraging but not definitive.

“If it were easily transmissible, we would expect to have seen at least some other people infected,” Nancy Arden,
an epidemiologist in the flu branch of the Centers for Disease Control and Prevention, said Thursday. “But the population of Hong Kong is enormous,” so cases may not yet have been detected.

CDC said Wednesday that analysis of a virus isolated from a 3-year-old child who died in a Hong Kong hospital in May revealed a type of flu that has never infected humans before. The flu strain, known as H5N1, is a form that
infects several bird species. It is highly unusual for avian flu to jump directly to humans, CDC said.

CDC dispatched a four-person team Tuesday to join Chinese and Japanese experts already studying the virus. They expect to spend about four weeks studying human and animal samples in Hong Kong and elsewhere in southern China, Arden said. “We really felt it was important to find out more about the child’s death ---what kind of
contact the child might have had with birds, for instance, whether other family members have been ill, whether the
disease can be transmitted asymptomatically in the way that swine flu can,” she said.

Among the things to be discovered: Whether the new virus was the cause of death. In its first official statement on
the investigation, released late Thursday, CDC said: “It is possible that this single case represents an unusual sporadic infection with an avian influenza strain, followed by a rare but well-recognized complication of influenza
and other viral infections in children.”

Experts are concerned about influenza’s potential to develop without warning into worldwide epidemics, which has happened three times this century.

“The variations in the flu virus from year to year are usually minor ---enough to avoid the immune system’s safeguards against it, but not enough to make most people really sick,” said Dr. Jeffrey Steinberg, an associate professor in the infectious disease division of Emory University School of Medicine. “But every 20 years or so, there is a major change to a strain that our immune systems just haven’t seen before, and that’s when horrible flus
emerge.”

There have been three flu pandemics so far this century. In 1968, 34,000 people in the United States died; in 1957,

the U.S. toll was 70,000. In 1918 and 1919, 500,000 died in the United States alone, and an estimated 20 million around the world.

According to a scientific paper published this week, it is absolutely certain that another pandemic will occur, and highly likely that it will emerge in Asia, the historic home of the flu virus. The only question is how soon, and the
only potential remedy is increased surveillance of both humans and animals so new viruses can be identified as quickly as possible.

“We must devote as much effort and as many resources as necessary to draw up a defensive strategy and a battle plan for dealing with what could be a potential catastrophe,” Dr. Robert G. Webster, chief of virology and molecular
biology at St. Jude Children’s Research Hospital in Memphis, said in the Journal of Infectious Diseases.

The relatively quick identification of the Hong Kong case indicates that early-warning surveillance set up by the World Health Organization is working, he added in an interview.

Because it is completely new to humans, there is a chance that the new flu found in Hong Kong could pose a serious risk. On the other hand, according to CDC, it may be so foreign that it lacks the ability to infect humans efficiently. The case in the child could be a random event.

“We know it’s very unusual,” Arden said. “We just don’t have an explanation of why it happened. If, when we look even harder, we don’t find evidence of spread within the population, it would be very reassuring.”

The Atlanta Journal - Constitution
Tuesday, 12/16/1997
Section: FOREIGN NEWS Letter: A Page: 1 Words: 437

CDC studies Hong Kong strain of flu seen in humans for 1st time

By M.A.J. McKenna/STAFF WRITER

Seven Hong Kong residents have been infected with a new influenza strain never before seen in humans, putting public health officials on high alert and sparking fears the outbreak may be the start of a global epidemic.

Five epidemiologists from the Atlanta-based Centers for Disease Control and Prevention arrived to begin investigations early last week, and a sixth member leaves today. The team will conduct a news conference in Hong
Kong today.

The flu strain, which has killed two of the seven people infected, appears to have passed directly from birds to humans, an unusual route that can lead to more deadly strains of the virus.

“CDC in general is extremely concerned about the situation and is doing everything it can to assist the Hong Kong
department of health in investigating the outbreak,” Dr. Brian Mahy, director of the agency’s division of viral and
rickettsial diseases, said Monday.

CDC staff members have been examining the new flu since last summer, when the death of a 3-year-old boy was reported. Now, in a second bloom of cases, all within Hong Kong, a 54-year-old man has died; two other people, a
teenager and a woman in her 20s, are in intensive care; and three others are less seriously ill or have recovered. There may be others who have contracted the flu, Mahy said: “We have a number of suspect cases in various

stages
of confirmation."

The outbreak is generating concern because the virus is behaving unusually. Flu viruses originate in waterfowl and commonly move through several species, chiefly pigs, before infecting humans. This one, of a type called H5N1, jumped from birds directly to humans, meaning that it could be so different from previous flu viruses that humans might be fatally vulnerable to it.

Its appearance in southern China increases the concern: The area was the source of the last two worldwide flu epidemics, in 1968 and 1957. Some authorities fear another pandemic ---which in the past has killed millions ---already may have begun.

"The scientific community throughout the world is gearing up as though this is the real event," Dr. Robert Webster, a Memphis virologist who has been investigating the outbreak, said in a phone interview from London. "The pandemic plan is being rolled out."

Hong Kong authorities have instituted some public-health measures, and no one outside southern China is believed to be at immediate risk. But scientists are concerned that the infection could mutate and infect people more
rapidly. A new vaccine would be needed to protect against this flu strain, and flu vaccine production takes four to six months.

Tuesday, 12/16/1997
Section: FOREIGN NEWS Letter: A Page: 24 Words: 564

Public health officials keep close watch on new flu

By M.A.J. McKenna/STAFF WRITER

The world's public-health authorities are watching tensely as the Centers for Disease Control and Prevention investigates the ongoing outbreak of influenza in Hong Kong.

The still-unanswered question: whether the seven cases and two deaths seen so far mark the start of a worldwide pandemic that could threaten tens of thousands.

"We have to prepare for it," Dr. Robert Webster, a leading expert on flu in animals, said Monday from London after several weeks in Hong Kong investigating the new flu. "There have been enough cases that we have to prepare
in case something happens."

The seven cases have no known connection to one another. And they have occurred outside Hong Kong's regular flu season, which begins next month. But their most unsettling aspect is the source of their flu: The strain infecting
them is known to be lethal to chickens but never has attacked humans before.

Against that unnerving information, the scientists can lay one hopeful piece of data: There is as yet no evidence that humans are infecting other humans with this strain of flu.

"Every case we have seen so far behaves as though it is an introduction from an outside source," Webster said. "We hope the virus doesn't acquire the high transmissibility that is required for it to really take off in the population.
But at this stage, we have to presume it will acquire it."

CDC staff have been in Hong Kong for a week and are not expected to return until after Christmas. They are conducting surveys and drawing blood samples from health-care workers and family members of the victims. The
samples are being analyzed at CDC and other international flu centers in London, Melbourne and Tokyo; the effort
is being coordinated by the World Health Organization in Geneva.

“This has been a remarkable outbreak because of the unrelatedness of geographical position and ages in the different
cases,” said Dr. Brian Mahy, whose division at the Centers for Disease Control and Prevention includes the influenza
branch. “We have not found a common link that we could point to. If we get more cases over the next few weeks,
this could change.”

Flu is an unpredictable infection. Because it makes many errors when it replicates itself inside cells, it produces minor genetic changes that account for flu’s ability to infect humans year after year. Each virus is just different enough to evade the immune system’s protection.

But every 30 years, the flu makes a major genetic jump. Scientists believe that happens when viruses from birds and viruses from humans mix in the cells of pigs, which are vulnerable to both.

The viruses that emerge are often lethally infectious; they are believed to have caused flu pandemics as serious as
the one in 1918, when up to 40 million died.

The new flu appears to have jumped directly from chickens to humans, sparking fears that the human immune system will have no defense against the virus at all.

Hong Kong authorities have attempted to cope by discouraging contact between children and pets or farm animals, closing a wholesale chicken market, and inspecting birds coming from the southern Chinese mainland.

That may not be enough, Webster said: Because so few of the victims have had contact with chickens, investigators theorize that an additional animal ---possibly a rat or a mouse ---may be carrying the infection as well.

The Atlanta Journal - Constitution
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Section: HEALTH WATCH Letter: B Page: 3 Words: 1139

HEALTH WATCH
Flu strain alarms experts
Rare Hong Kong virus could bring worldwide epidemic, CDC says

By M.A.J. McKenna/STAFF WRITER

The number of cases in the Hong Kong flu outbreak has risen to 10 and includes three people in the same family, sparking fears that the virus may have acquired the dangerous ability to pass from person to person.

Officials at the Centers for Disease Control and Prevention in Atlanta and on site in Hong Kong said Tuesday that
two new cases, a 2-year-old boy and a 3-year-old girl, are cousins of a 5-year-old girl who is already hospitalized.

“This is the first time we have seen any link between cases,” said Dr. Brian Mahy, director of the CDC’s division of viral and rickettsial diseases, who is coordinating the flu effort from the CDC’s Atlanta headquarters.

Scientists around the world have been watching the Hong Kong situation tensely, waiting for evidence that the virus has mutated enough to be communicable between people. That would increase the possibility of the virus’ causing a global epidemic, which could threaten tens of thousands of people.

Though Tuesday’s news was deeply unnerving, Mahy said officials still aren’t convinced that this flu virus can spread from one person to another.

“(The cousins) spent quite a bit of time together in an apartment with their grandmother,” he said. The cause of the
infection “could be common exposure to the same environment. It doesn’t really get us clear evidence of human-to-human transmission.”

The outbreak now includes a potential 10 cases: seven that have been confirmed by genetic analysis at the CDC, including two who have died; one who is strongly suspected of having had the virus, but has recovered; and an additional two cases whose blood samples are awaiting analysis.

In a press conference with CDC officials Tuesday, Dr. Margaret Chan, director of health for Hong Kong, said that
65 Hong Kong residents who had contact with the victims have reported flulike symptoms. Lab tests determining whether they were sickened by the so-called H5N1 virus ---named after two proteins, hemagglutinin and neuraminidase, on the virus’s surface ---have not been completed, she said.

Tests conducted so far by the CDC and other international flu labs confirm that the virus originated in birds and remains unique to them and to humans. Influenza typically originates in waterfowl and passes through other animals ---often pigs ---before infecting humans, but genetic analysis shows no evidence that it infected other mammalian species before triggering this outbreak, something that flu experts previously thought impossible.

On Tuesday, the Hong Kong government announced a slate of public health measures, such as increased surveillance of chicken farms and markets to ferret out birds smuggled from southern China. It has begun public service announcements on radio and television and started a 24-hour telephone hotline, which received almost 350
calls in its first 24 hours. There have been reports of residents abandoning pet birds of all species at animal shelters
and jamming emergency departments to ask for flu tests; one hospital has created a 20-bed isolation ward in anticipation of more cases.

There is still some suspicion, Mahy said, that an additional unknown animal vector may be playing a part in this outbreak. “The general argument is that since we are not seeing this flu in poultry handlers, poultry-market workers,
chicken butchers, we perhaps should be looking at some other possible reservoir of infection,” he explained. “The
theory would be that the virus goes from birds into another species ---a rodent, a cat, something of that sort --- and
humans get infected from that source. But we have no evidence of this.”

According to the CDC, the Hong Kong flu outbreak meets two of the three conditions necessary to be called a pandemic: It is a brand-new infectious organism that has been let loose in a susceptible population. Despite Tuesday’s news, it has not yet met the third condition: an outbreak that grows enough to cross national borders or
jump between regions of the world. That condition was added after the 1976 “swine flu” epidemic provoked intense
public concern but then unexpectedly died out.

Nevertheless, public health authorities are implementing a pandemic plan that was accepted internationally after 700,000 people died in the last pandemic in 1968.

The first step of the plan, administered by the CDC and the World Health Organization in Geneva, calls for rapid development of a vaccine against the new strain of flu. The currently available vaccine offers no protection against it,
because it was designed ---as flu vaccines are every year ---to counteract the three flu strains that experts predicted
would be circulating this flu season. The H5N1 outbreak was not predicted.

But the plan has already hit a major bottleneck. The worldwide manufacturing network that produces flu vaccine every year uses fertilized chicken eggs as a growing medium. But the new flu is closely related to a virus that has caused mass chicken deaths in the United States, Mexico and Hong Kong in the past few years. It is "absolutely lethal in chickens," killing them within two days, said Dr. Robert G. Webster, a Memphis-based virologist who has
been investigating the outbreak.

That has left experts scrambling for an alternative. If the Hong Kong outbreak becomes an epidemic, they will have little time to waste, because broad-scale flu vaccine production takes four to six months.

One path, Mahy said, would be to find or develop a genetically similar but nonlethal strain of flu. Another would be to discover a different method of manufacturing large quantities of vaccine quickly. Both have drawbacks.

Because the H5N1 virus has never been seen in humans before, no close match for it exists in the world's flu labs.
The WHO has already uncovered several surrogate viruses, but they must be tested against the Hong Kong strain, a
task that could take several weeks.

If an alternative virus cannot be found, scientists will have to rely on alternative methods of vaccine production. There are several ---growing the virus in cell cultures, using a "cold-adapted" weakened virus that is administered
by nasal spray, and using the purified DNA of the virus by itself. But all three methods are still experimental, Mahy
said; none has been approved by the U.S. Food and Drug Administration, and none is advanced enough to produce
the quantities of vaccine that would be necessary.

One of those methods, a vaccine using purified DNA, is under investigation at the Yerkes Regional Primate Research Center at Emory University. Studies in humans are in very early stages, said the vaccine's creator, Dr. Harriet Robinson. "I can't even comment on a time frame" for availability, she said. "When you have a new approach to vaccination, you have to proceed very cautiously."

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Section: HEALTH WATCH Letter: G Page: 3 Words: 382

HEALTH WATCH
Report on Hong Kong flu may have missed mild cases

By M.A.J. McKenna/STAFF WRITER

In its first official write-up of the Hong Kong flu outbreak, the Centers for Disease Control and Prevention warned
Thursday that the number of cases may have been underestimated.

Surveillance for flu in Hong Kong is conducted primarily through hospitals, the agency said in a special article added to its weekly disease report. But if cases in the community have been missed, it added, they were probably less severe than the ones that have been diagnosed.

“Milder cases may not have been recognized, and the severity of infections identified to date may not be representative of the spectrum of (this) infection in humans,” the agency said.

Health authorities have disclosed a potential 10 cases so far, with eight confirmed by laboratory analysis as of Thursday. Two victims have died, one this month and one in May.

Knowing whether mild cases exist in the community is vital, said Dr. Brian Mahy, director of CDC’s division of viral and rickettsial disease, and not just because it defines the true size of the outbreak.

“The other concern is the possibility of reassortment,” he said. “If this H5N1 virus is replicating in someone who happened to get infected at the same time with a more common human flu virus, H1N1 or H3N2, we could end up
with a much more worrying virus.”

Research into the outbreak is focusing on whether the so-called H5N1 flu virus, which jumped from chickens and
has not been known to cause disease in humans before, has developed the ability to be passed from human to human. That would increase the likelihood of more cases.

With the exception of three toddler-age cousins, most of the cases have been linked to some exposure to chickens.
Over the past week, there have been reports in Hong Kong of large numbers of chickens dying in the wholesale live-bird markets. In the United States, the CDC said, the flu season is proceeding normally. Twenty-seven states including Georgia, and the District of Columbia, have reported some flu cases, overwhelmingly the influenza A virus, type H3N2, that had been predicted for this winter. Though the season does not hit full stride until January, vulnerable people such as the elderly should get flu shots very soon, the agency said; the vaccine takes several weeks to protect recipients fully.

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Focus on HONG KONG FLU
Instead of dipping into eggnog this Christmas, CDC researchers in
Hong Kong and Atlanta are leading an investigation into a deadly new influenza strain spread by chickens and so far suspected in 15 illnesses, including four deaths

By M.A.J. McKenna/STAFF WRITER

In discussions of the Hong Kong influenza outbreak, the word “pandemic” keeps recurring.

To epidemiologists, it has a technical meaning: an epidemic that jumps national borders and spreads to different regions of the globe. To those with long memories, it has emotional resonance, recalling the deaths of hundreds of
thousands, even millions, from the last major worldwide flu epidemics in 1968, 1957 and 1918.

To a small group of scientists, it has the force of an alarm bell ---one that has them moving quickly to create a global network to combat and control the Hong Kong flu, if it continues to spread.

“Within a short period of time, we went from one case to four, and it was chilling,” said Dr. Dominick Iacuzio, influenza program officer at the National Institute of Allergy and Infectious Diseases. “Suddenly we were facing reports that we might be facing a new pandemic strain. It made me take a deep breath.” Iacuzio represents the National Institutes of Health on a federal interagency council on influenza pandemic preparedness, a group that views influenza not as a two-week winter nuisance but as a re-emerging disease that could potentially take thousands of lives.

“We haven’t seen a true pandemic in 30 years, and we have, I guess, been lulled into some complacency,” he said.
“The general public doesn’t fully understand the danger of influenza.”

The group has been working on strategies for countering a major epidemic of flu, from launching new vaccine research to increasing the surveillance that picks up cases of the disease. Greatly increased surveillance in southern
China, the starting point for the last two pandemics, led to early discovery of the new strain ---and may, Iacuzio said, inadvertently have increased alarm over the 15 confirmed and suspected cases so far.

“Our surveillance ---done by the Centers for Disease Control and Prevention and the World Health Organization ---is so much more sophisticated than it was 20, 30 years ago,” he said. “This might have happened in the past, and
we didn’t know about it.”

Most of the cases of the so-called H5N1 influenza strain, a bird virus that has never affected humans before, have
been linked to exposure to chickens. The great question for scientists has been whether the virus will acquire the property of being passed from person to person, an event that could signal an explosion of flu cases to come.

Infectious-disease specialists around the globe are waiting for the next news from the outbreak, which could take one of several forms. If the new strain discovered in Hong Kong remains chiefly a bird virus, the infection could percolate in the area for a while but produce only low levels of disease. It could even die out, if authorities are successful in keeping infected chickens away from Hong Kong residents.

That is the best-case scenario. The worst-case version predicts viral cross-breeding between the new strain and a known strain of flu that produces mild illness but is highly infectious ---something that could happen when Hong Kong’s regular flu season begins in February.

No one can say which is more likely. Flu scientists are preparing as though the worst will happen, while hoping for the best.

“We are writing a new chapter here on influenza,” Iacuzio said.

Thursday, 12/25/1997
Section: NATIONAL NEWS Letter: A Page: 20 Words: 535

Focus on HONG KONG FLU
Researchers struggle to replicate virus for vaccine

By M.A.J. McKenna/STAFF WRITER

When news of the first case in the Hong Kong flu outbreak surfaced in August, public health officials thought immediately about the vaccine problem. This strain of influenza, known to scientists as H5, had never been seen in
humans before; current vaccines offered no protection.

Researchers have been struggling ever since to come up with an alternative shot that will work against the Hong Kong strain, in the event the few cases reported so far become a full-fledged epidemic. Typically, flu vaccine production takes four to six months. In addition, the Hong Kong flu strain poses a unique challenge: Standard production for influenza vaccine, conducted every year by pharmaceutical manufacturers in the six months before
the flu season, uses fertilized chicken eggs. But the Hong Kong virus, so lethal to birds that it was dubbed "chicken
Ebola" by influenza expert Dr. Robert Webster, doesn't replicate well in chicken eggs.

The National Institutes of Health is supporting research into several different alternative methods.

One, originated by Dr. Harriet Robinson of Emory University's Yerkes Regional Primate Research Center while she was at University of Massachusetts, uses a segment of DNA from the influenza virus that is introduced into bacteria. When the bacteria reproduce, they reproduce the DNA sequence; when the pure DNA is injected, it produces an immune response that protects against influenza infection.

A variation of that approach calls for inserting a protein from the influenza virus into a second virus, which is used to infect an insect cell. As the cells multiply, they reproduce the protein, which is then used as a vaccine.

But neither method has reached commercial status yet.

A third technique, which appears closer to federal approval, uses a nasal spray to deliver a live but weakened form
of the virus that is called "cold-adapted" because it has been altered to grow at a lower temperature. Its developers at
Aviron of California have taken the spray through several levels of clinical trials and hope to present a license application to the Food and Drug Administration next June.

"Our studies show that it works, and it is well-tolerated," said Dr. Leighton Read, an internist who is Aviron's chairman and chief executive officer. "And because it is a spray, it allows people to take advantage of influenza prophylaxis who are afraid of getting a shot or to whom shots are not available. Giving children an alternative to a
shot is a particular advantage."

Dr. W. Paul Glezen of Baylor College of Medicine in Houston believes the Hong Kong flu outbreak may have an upside, if it leads to new ways of developing flu vaccines that don't involve chicken eggs and may have shorter manufacturing timetables.

"At their best, the eggs (used to develop vaccines) don't adapt to emergencies," he said. "They're ordered ahead of
time to be used at a certain time; it would be difficult even to find enough eggs this time of year to produce large amounts of vaccine. Everyone agrees it would be a good idea to have another (production method) to use."

Friday, 01/09/1998
Section: NATIONAL NEWS Letter: A Page: 16 Words: 411

Hong Kong's flu outbreak may be finished
Case studies show that person-to-person transmission of the virus usually

is not successful.

By M.A.J. McKenna/STAFF WRITER

No new flu cases have been recorded in Hong Kong since Dec. 28, and one previously suspected case has been found to involve something other than flu, sparking hopes that the monthlong outbreak may be slowing down. While it's far too soon to pronounce the outbreak over, "it is some time since we have seen a new case, and that is
very good news," said Dr. Brian Mahy, director of the division of viral and rickettsial diseases at the Centers for Disease Control and Prevention.

With the drop in cases, some CDC personnel will begin returning to Atlanta this weekend, Mahy said. But three investigators and a spokesman will remain, to be joined this week by a new data manager and next week by Dr. Nancy Cox, chief of the agency's influenza branch.

Cox will visit the disease-surveillance stations that CDC maintains in China and will meet with health authorities in Beijing in an attempt to answer one of the remaining questions of the outbreak: Whether the unique flu virus, never seen in humans before the initial case last May, has crossed from affluent Hong Kong into the densely populated, underserved Chinese mainland.

In a report published Thursday, CDC set the toll of cases at 16 confirmed and three suspected, with four dead. (One suspected case was disproven by lab work after the publication's Tuesday deadline, Mahy said.)

Analyses appear to confirm that the virus, called H5N1 after certain proteins on its surface, is not passed easily from person to person.

Samples taken from the first seven patients show two slightly different viruses, neither of which contains human influenza genes ---indicating that each person most likely was infected by a bird rather than by another person.

And samples taken from 502 Hong Kong residents who had contact with the first case, or with poultry around the
time that first patient was infected, showed only nine who might have been exposed to the virus, none of whom developed symptoms.

Still, the agency can't yet rule out human-to-human transmission, Mahy said. Four cases, two confirmed and both
of the suspected cases, involve members of the same family. And that first case, involving a 3-year-old child who died in May, may have exposed a day care classmate and a health care worker to the virus. Blood work on both shows that they were exposed to the virus, but neither became sick.

"The message here is that it is not being transmitted efficiently among persons," Mahy said.

Friday, 01/16/1998
Section: FEATURES Letter: F Page: 2 Words: 531

Disease sleuths unraveling Hong Kong virus
Flaw revealed; 2 more die of flu

By M.A.J. McKenna/STAFF WRITER

While the pace of the Hong Kong flu outbreak has slowed, disease detectives are beginning to catch up with the virus that caused it.

On Thursday, Hong Kong health authorities announced that two more victims had died: a 25-year-old woman who was known to be infected with flu, and a 34-year-old woman who had been a suspected case and whose diagnosis was just confirmed by lab work. Their deaths bring the total for the outbreak to six, with 18 cases of flu confirmed and one more suspected.

And today, the journal Science publishes the first genetic analysis of the Hong Kong virus. It reveals a particular genetic flaw that explains this flu strain's behavior and might help scientists develop a vaccine to fight it, if one is needed.

The analysis, made on samples from the first flu case ---a 3-year-old who died in May ---marks an achievement for the research team from the Centers for Disease Control and Prevention in Atlanta, the Agriculture Research Service in Athens and Queen Mary Hospital in Hong Kong. The viral characteristic, a cluster of amino acids at a particular location, was known to exist from chicken samples but had never before been seen in a human.

"It extends our knowledge, because this is the first time it has been isolated from a human in association with disease," said Dr. Kanta Subbarao, chief of the molecular genetics section at the CDC's influenza branch, which is at
the center of global efforts to track, manage and investigate flu outbreaks.

The type of flu virus circulating in Hong Kong, called H5N1 after proteins on its surface, had never been seen in humans before May. But it was well-known for being lethal in chickens; one expert has called it "chicken Ebola."

The genetic sequencing published today explains why, Subbarao said: The extra amino acids allow the virus to infect cells in the brain, heart and blood vessels of birds, as well as the usual sites in the gut and respiratory system.

The analysis doesn't explain whether the H5 virus behaves differently from other flu strains in humans, Subbarao
said. Nor does it clarify whether the Hong Kong strain was spread from person to person or whether each victim was independently infected by exposure to birds.

In Hong Kong, health authorities emphasized that both women who died recently had been sick for weeks. The younger one was hospitalized Dec. 21 and the older Dec. 28, both of them before the massive New Year's chicken
slaughter aimed at eradicating the suspected source of the infection. No new cases have been found in Hong Kong
in almost two weeks, since the 1.4 million chickens were killed to prevent transmission of the "bird flu" to humans.

The outbreak has not spread beyond Hong Kong. In the U.S., which according to the CDC is having a flu season slightly milder than average, a different new strain has emerged: Influenza A/Sydney. But health officials say the Sydney strain is much less serious than the Hong Kong flu and that anyone who receives a flu vaccine should be protected against it.

In Georgia, there have been relatively few flu cases ---14 ---so far this season. None are believed to be related to the Sydney flu.

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DEP: SCIENCE
SEC: B
PG: 05

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.

By M.A.J. McKenna STAFF WRITER

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.”