MI FluFocus

Influenza Surveillance and Avian Influenza Update

Bureau of Epidemiology
Bureau of Laboratories

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New updates in this issue:

- **Avian Influenza:** New H5N1 avian influenza outbreaks in poultry reported in Vietnam.

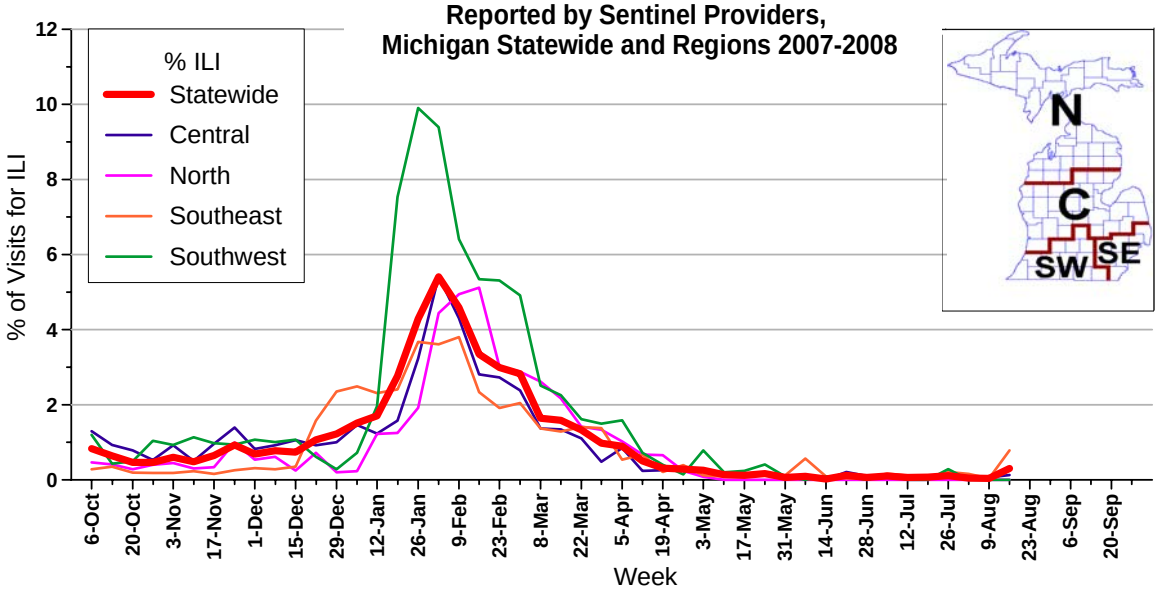
Michigan Disease Surveillance System: The week ending August 16 saw both aggregate flu-like disease and individual influenza reports remain steady near last week's levels. Both aggregate flu-like illness and individual influenza reports are expected to fluctuate near baseline levels until the fall.

Emergency Department Surveillance: Emergency department visits from both constitutional complaints remained steady near last week's levels, while respiratory complaints increased slightly. Both constitutional and respiratory complaints are consistent with numbers seen this time last year. Eight constitutional alerts in the C(6) and SW(2) Influenza Surveillance Regions and four respiratory alerts in the C(1), N(1) and SE(1) Influenza Surveillance Regions, including one statewide alert, were generated last week.

Over-the-Counter Product Surveillance: Overall, OTC product sales were mixed last week. Children's electrolytes showed a slight drop in sales, cough and cold medication held near last week's levels, and the remainder saw a slight increase. Indicator levels are comparable to those seen at this time last year.

Sentinel Surveillance (as of August 21): During the week ending August 16, 2008, 0.3% of all office visits reported by Michigan influenza sentinel sites were due to influenza-like illness (ILI). This represents 10 cases out of 3252 total patients seen. These cases were reported in the Central and Southeast surveillance regions. Fifteen practices provided data for this report. Note that these rates may change as additional reports are received.

Percentage of Visits for Influenza-like Illness (ILI) Reported by Sentinel Providers, Michigan Statewide and Regions 2007-2008



As part of pandemic influenza preparedness, CDC and MDCH highly encourage year-round participation from all sentinel providers. New practices are encouraged to join the sentinel surveillance program today! Contact Rachel Potter at 517-335-9710 or potterr1@michigan.gov for more information.

Laboratory Surveillance (as of August 21): For the 2007-2008 influenza season, the MDCH Bureau of Laboratories has identified 249 influenza isolates:

- 190 A/H3N2: Central (58); Southwest (51); Southeast (49); North (32)
- 4 A/H1N1: Southeast (2); North (2)
- 2 A subtyping unable to be performed: Southeast (2)
- 53 B: Southeast (30); North (10); Southwest (6); Central (6); Indiana (1). 51 have been typed as B/Shanghai/361/2002-like and 2 were B/Malaysia/2506/2004-like (SE).

***As a reminder, the positive predictive value of influenza rapid tests decreases during times of low influenza prevalence. MDCH suggests that during periods of low influenza activity in your community, all positive rapid tests results be confirmed by sending in a specimen for viral culture; this can be arranged through your local health department.

Influenza-Associated Pediatric Mortality (as of August 21): For the 2007-2008 season, MDCH has confirmed one influenza-related pediatric mortality in Michigan. The case was a 13 year-old from the Central region with an influenza A/H3N2 and MRSA co-infection; disease onset was in late February.

***The CDC has asked all states to collect information on any pediatric death associated with influenza infection. This includes not only any death in a child (<18 years) resulting from a compatible illness confirmed to be influenza by an appropriate diagnostic test, but also any unexplained death with evidence of an infectious process in a child. See www.michigan.gov/documents/fluletter_107562_7.pdf for the complete protocol. Please immediately call MDCH to ensure that proper clinical specimens are obtained.

Congregate Settings Outbreaks (as of August 21): Congregate setting outbreaks have been reported in all regions of the state, peaking in the first two weeks of February. Seven outbreaks have been culture-confirmed at MDCH; six as influenza A/H3N2 and one as influenza B for the 2007-2008 season.

Michigan Influenza Season Summary: The 2007-2008 Michigan Influenza Season Summary is now available online at www.michigan.gov/influenza. Overall, this influenza season was moderate in activity with peak activity occurring in early February and was dominated by influenza A/H3N2.

National (CDC): To access the entire CDC weekly surveillance report throughout the influenza season, visit http://www.cdc.gov/flu/weekly/fluactivity.htm. The 2007-2008 national influenza season summary is available at http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5725a5.htm?s_cid=mm5725a5_e.

International (WHO, August 14): During weeks 30–32, the level of overall influenza activity in the world increased. In the southern hemisphere, increase in both influenza activity and detection of influenza viruses was observed. Influenza A (H1), A(H3) and Influenza B circulated. Widespread outbreaks were reported in New Zealand. Countries in the northern hemisphere reported sporadic or no activity.

China, Hong Kong Special Administrative Region. Increase in influenza activity continued, with circulation of both A (H3) and A (H1) viruses. Regarding influenza B viruses detected, B/Yamagata lineage predominated over B/Victoria lineage.

New Zealand. Widespread influenza activity was reported, with influenza A (H3) and influenza B viruses circulating.

Between weeks 30 to 32, sporadic influenza activity was detected in Argentina A (H1), Brazil (A,B), Canada, Chile (A, B), the Islamic Republic of Iran A (H3), Poland (A) Uruguay (A ,B)

Madagascar reported sporadic influenza activity, but no influenza cases were laboratory confirmed

Belgium, Cameroon, Germany, Norway, Portugal, and Slovenia reported no influenza activity.

Seasonal influenza reporting to the CDC has ended for the 2007-2008 influenza season.

For stakeholders interested in additional information regarding influenza vaccination and education, the MDCH publication *Michigan FluBytes* is available online at http://www.michigan.gov/mdch/0,1607,7-132-2940_2955_22779_40563-125027--,00.html. *FluBytes* is published biweekly during the summer months.

End of Seasonal Report

Avian Influenza Activity

WHO Pandemic Phase: Phase 3 - Human infection(s) with a new subtype, but no human-to-human spread or rare instances of spread to a close contact.

International, Poultry (Nhan Dan newspaper, August 16): Bird flu disease has reoccurred in the southern province of Ben Tre [Vietnam], according to the Veterinary Department.

The samples of the infected ducks of two households in An Loi hamlet, An Binh Tay commune and the died ducks in Cau Vi hamlet, My Chanh commune under Ba Tri district were tested positive to the virus H5N1.

By August 14, the bird flu epidemic had occurred in the six poultry raising households in three communes of An Binh Tay and My Chanh and An Hiep, with 1,960 infected ducks including 905 deaths. So far, 2,865 ducks have been culled.

At present, four provinces of Dong Thap, Quang Ngai, Kien Giang and Ben Tre are yet to be free from the disease for 21 days nationwide.

National, Research (Associated Press, August 17): Nearly a century after history's most lethal flu faded away, survivors' bloodstreams still carry super-potent protection against the 1918 virus, demonstrating the remarkable durability of the human immune system.

Scientists tested the blood of 32 people aged 92 to 102 who were exposed to the 1918 pandemic flu and found antibodies that still roam the body looking to strangle the old flu strain. Researchers manipulated those antibodies into a vaccine and found that it kept alive all the mice they had injected with the killer flu, according to a study published online Sunday in the journal Nature.
There's no pressing need for a 1918 flu vaccine because the virus has long since mutated out of its deadly form and is extremely unlikely to be a threat anymore, experts said. What's more important in this research, they said, is that it confirms theories that our immune system has a steel-trap memory.

"It's incredible. The Lord has blessed us with antibodies our whole lifetime," said study co-author Dr. Eric Altschuler at the University of Medicine and Dentistry in New Jersey. "What doesn't kill you, makes you stronger."

This is the longest that specific disease-fighting cells have lasted in people, said study lead author Dr. James Crowe, a professor of microbiology and immunology at Vanderbilt University Medical Center in Nashville, Tenn.

But these antibodies don't just survive; they have mutated tremendously and now bind tighter to disease cells than other antibodies. That makes them more potent, he said.

Crowe said he hopes to use similar techniques to boost the potencies of vaccines that would be more useful now against newer bird flu strains that could become epidemics.

The 1918 flu killed about 50 million people worldwide and nearly everybody else was exposed to the virus, Crowe said. The specific 1918 virus was lost to the world for decades, until it was reconstructed about three years ago using genetic material from victims. When scientists tested the antibodies from survivors on infected mice, they did so in a high level biosecurity lab at the Centers for Disease Control and Prevention in Atlanta.

The idea for the new study came from an old TV show, said Altschuler. In an episode of the since-cancelled TV series "Medical Investigation," a town improbably gets infected with the 1918 flu and the doctors treat everyone with the reluctantly donated blood of an old butler who survived the original pandemic, he said.

That prompted Altschuler, a professor of rehabilitation medicine who doesn't normally study flu, to look into the idea of testing people more than 90 years old for antibodies. The National Institutes of Health, which paid for much of the study, connected Altschuler with experts in the field and he found the elderly antibody donors.

The findings make sense, said Dr. Anthony Fauci, director of the National Institute for Allergies and Infectious Diseases in Bethesda, Md., who wasn't involved with the study. Recent studies have estimated that the human immune system should last many decades, but this gives real proof, he said.
"This is the mother of all immunological memory here," Fauci said.

International, Research (CIDRAP, August 18): Public health officials from Indonesia recently published an analysis of nearly all of the country's H5N1 avian influenza cases, revealing that death was more likely in those who received antiviral treatment late, were not part of a cluster, and lived in an urban area.

The study, published online Aug 15 in *The Lancet*, was authored by officials from Indonesia's Directorate General of Disease Control and Environmental Health, the country's health ministry, as well as authorities from laboratories and health organizations. It includes data from public health investigations and, when available, patients' clinical information.

The evaluation covered all confirmed human cases between Jun 22, 2005, when Indonesia recorded its first H5N1 infection, to Feb 1, 2008. Included were 127 patients, 103 (81%) of whom died.

The case-fatality rate (CFR) rose from 65% in 2005 to 86.8% in 2007. However, Indonesian officials say the rate has declined so far in 2008. According to a report that appeared Aug 15 on the Web site of the health ministry's avian influenza committee, the CFR from January through July was 84.2%, based on the 19 cases and 16 deaths recognized by the nation (as of this writing, the World Health Organization has recognized 18 cases with 15 deaths).

Only 2 of Indonesia's 127 infected patients were not hospitalized. One had a mild infection and received outpatient care, and one refused treatment and died at home.

Emerging patterns
A review of 108 clinical histories showed that symptoms during the first 2 days after onset were nonspecific in most cases. Thirty-two (30%) patients had fever and cough, and nine (8%) had fever and dyspnea.

Of the 125 patients who were hospitalized, 104 were diagnosed with pneumonia immediately or shortly after admission.

Eighty-eight (69%) of the case-patients were treated with oseltamivir, and the median time between symptom onset and treatment was 7 days (range 0 to 21). Patients who received the drug early were more likely to survive; those starting treatment more than 5 days after onset were more likely to die.

The authors report there were 11 case clusters that involved 28 patients. Infected patients who were not part of clusters were more likely to die, but researchers did not find any differences between cluster patients and noncluster patients in terms of when they presented to a healthcare facility, whether they received oseltamivir, or how soon they received the drug.

Patients with secondary cases were more likely to survive than primary case-patients, and they received antiviral treatment about 3 days earlier than primary case-patients. The investigators acknowledge that secondary cases may have involved other early interventions as well. They also report that patients who had indirect exposure to the virus were more likely to die.

Death and survival patterns among patients in clusters deserve further study, the authors state. Though close-knit families may be exposed to a common viral source, the role of genetic susceptibility and H5N1 virulence may also play important roles, they note. "Further studies should therefore be done on clusters to elucidate the definitive causes of reduced case fatality."

A need for new strategies
Most patients were hospitalized too late and received oseltamivir too late, the group says. "Training and equipping of all H5N1 referral hospitals across Indonesia, together with increasing the number of referral hospitals, is in progress to address this issue."

The authors emphasize that early identification is often difficult, but more information from agricultural officials about local poultry outbreaks could help healthcare workers increase their index of suspicion for H5N1 infections.

Other measures that could help reduce the country's CFR from H5N1 infections include rapid diagnostic tests for field use and better case-management training for healthcare workers, they write.

Experts call for more rigorous data
In a commentary accompanying the *Lancet* report, two British researchers say more uniform and complete data are needed to shed more clarity on trends emerging from Indonesia's cases—which account for a third of cases worldwide. The researchers are Sheila Bird, a biostatistician at Medical Research Council's biostatistics unit in Cambridge, and Jeremy Farrar, who directs the Oxford University clinical research unit at the Hospital for Tropical Diseases in Ho Chi Minh City, Vietnam.

"Basic clinico-epidemiological data are an essential adjunct to virological surveillance," they write. For example, exposures to the H5N1 should be clearly specified, including dates, they say, adding that lack of full data raises questions about such issues as whether the time frame between H5N1 disease onset and hospital admission has decreased over time.

"Indonesia, with the most extensive experience of human H5N1 patients, has a crucial clinical, epidemiological, and scientific role to play in the world's response to this potentially devastating infection," write Bird and Farrar.

The time to bolster national surveillance for human H5N1 cases is now, and disagreement over virus sample sharing should not hamper the flow of epidemiologic data, they add. "The world also needs to find a more equitable way to ensure that all share in the benefits of such important research. Indonesia could give the lead here."

Michigan Wild Bird Surveillance (USDA, as of August 21): For the 2008 testing season, 616 Michigan samples have been taken so far, comprised of 238 live birds, 339 hunter-killed birds, 14 morbidity/mortality samples and 25 environmental samples.

HPAI subtype H5N1 has not been recovered from any Michigan samples tested to date, or from the 16,080 birds or environmental samples tested nationwide for the 2008 testing season, which will run from April 1, 2008 - March 31, 2009. For more information, visit the National HPAI Early Detection Data System website at http://wildlifedisease.nbii.gov/ai/.

To learn about avian influenza surveillance in Michigan wild birds or to report dead waterfowl, go to Michigan's Emerging Disease website at http://www.michigan.gov/emergingdiseases.

Please contact Susan Vagasky at VagaskyS@Michigan.gov with any questions regarding this newsletter or to be added to the weekly electronic mailing list.

Contributors

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Table 1. H5N1 Influenza in Poultry (Outbreaks up to July 25, 2008)

(Source: http://www.oie.int/downld/AVIAN%20INFLUENZA/A_AI-Asia.htm Downloaded 7/29/08)

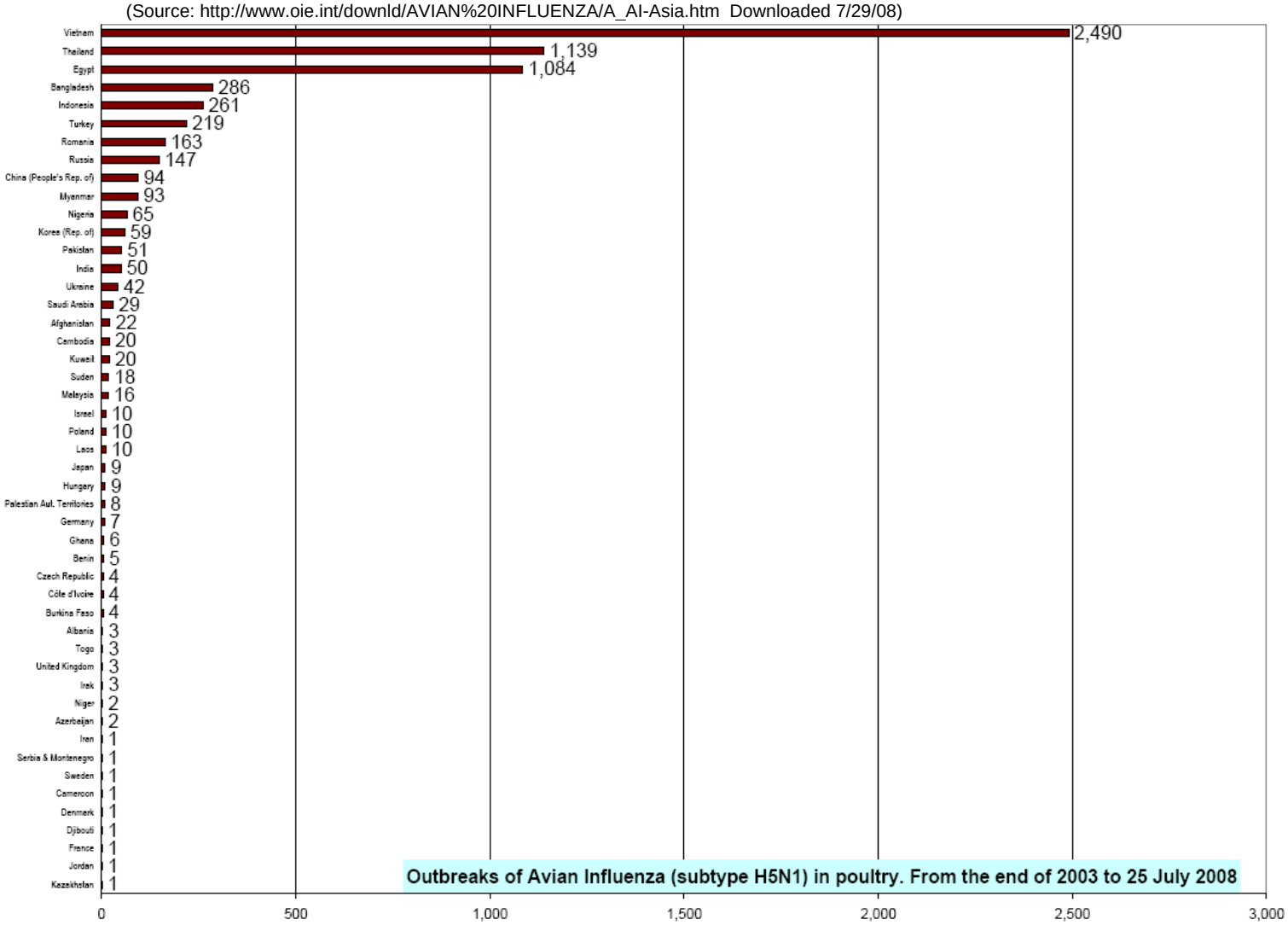

Table 2. H5N1 Influenza in Humans (Cases up to June 19, 2008)

(http://www.who.int/csr/disease/avian_influenza/country/cases_table_2008_06_19/en/index.html Downloaded 6/19/2008)

Cumulative number of lab-confirmed human cases reported to WHO. Total number of cases includes deaths.

Country	2003		2004		2005		2006		2007		2008		Total	
	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths
Azerbaijan	0	0	0	0	0	0	8	5	0	0	0	0	8	5
Bangladesh	0	0	0	0	0	0	0	0	0	0	1	0	1	0
Cambodia	0	0	0	0	4	4	2	2	1	1	0	0	7	7
China	1	1	0	0	8	5	13	8	5	3	3	3	30	20
Djibouti	0	0	0	0	0	0	1	0	0	0	0	0	1	0
Egypt	0	0	0	0	0	0	18	10	25	9	7	3	50	22
Indonesia	0	0	0	0	20	13	55	45	42	37	18	15	135	110
Iraq	0	0	0	0	0	0	3	2	0	0	0	0	3	2
Lao PDR	0	0	0	0	0	0	0	0	2	2	0	0	2	2
Myanmar	0	0	0	0	0	0	0	0	1	0	0	0	1	0
Nigeria	0	0	0	0	0	0	0	0	1	1	0	0	1	1
Pakistan	0	0	0	0	0	0	0	0	3	1	0	0	3	1
Thailand	0	0	17	12	5	2	3	3	0	0	0	0	25	17
Turkey	0	0	0	0	0	0	12	4	0	0	0	0	12	4
Viet Nam	3	3	29	20	61	19	0	0	8	5	5	5	106	52
Total	4	4	46	32	98	43	115	79	88	59	34	26	385	243