



MI Flu Focus

Influenza Surveillance Updates
Bureaus of Epidemiology and Laboratories



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Current Influenza Activity Levels:

- **Michigan:** Local activity
- **National:** During March 25-31, U.S. activity declined nationally and in most regions

Updates of Interest

- **National:** A variant influenza A/H3N2 virus, similar to 12 previous human cases in 2011, has been identified in a Utah child

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****Update: Novel A (H3N2) Guidance****

In December 2011, CDC asked all states to conduct surveillance for suspect human cases of a novel influenza A (H3N2) virus by increasing influenza testing. Subsequently, MDCH issued an interim guidance requesting all healthcare providers to forward all positive influenza specimens to MDCH for further testing. MDCH would like to thank the healthcare providers who contributed to this effort. Since no cases of novel influenza A (H3N2) have been identified in Michigan, MDCH is revising this guidance. For surveillance purposes, healthcare providers may now submit up to 5 representative specimens per week to MDCH Bureau of Laboratories, with priority on pediatric or severe cases. Please call the MDCH Division of Communicable Disease at 517-335-8165 with any questions.

Influenza Surveillance Reports

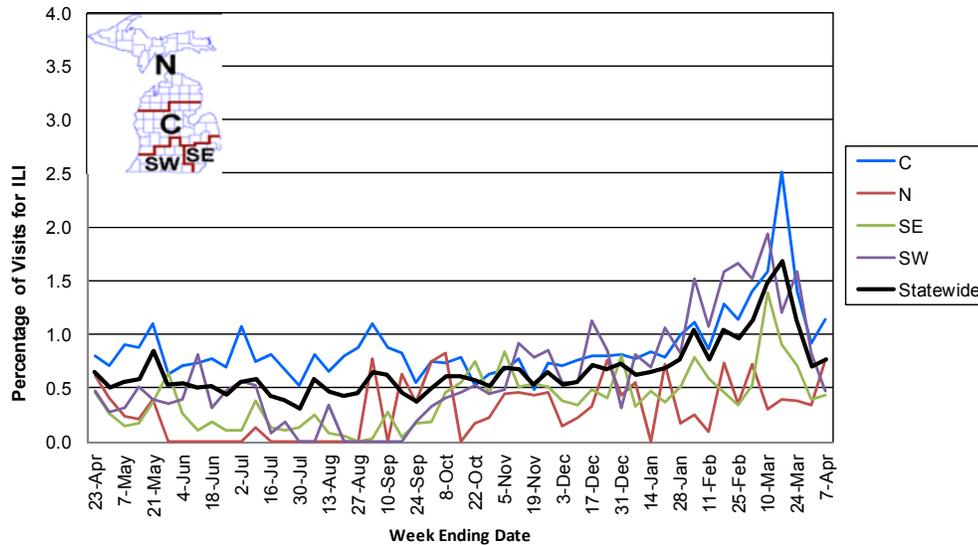
Michigan Disease Surveillance System: MDSS data for the week ending April 7th indicated that both individual and aggregate reports significantly decreased. Recent school breaks may have contributed to the decrease in aggregate reports. Both individual and aggregate reports are similar to levels seen during the same time last year.

Emergency Department Surveillance: Compared to levels from the week prior, emergency department visits from both constitutional and respiratory complaints remained steady. Both constitutional and respiratory complaints are at levels similar to those seen in early February 2012 and are moderately lower than levels reported during the same time period last year. In the past week, there was four constitutional alerts in the SE(1), C(2) and N(1) Influenza Surveillance Regions and seven respiratory alerts in the SE(3), C(3) and N(1) Regions.

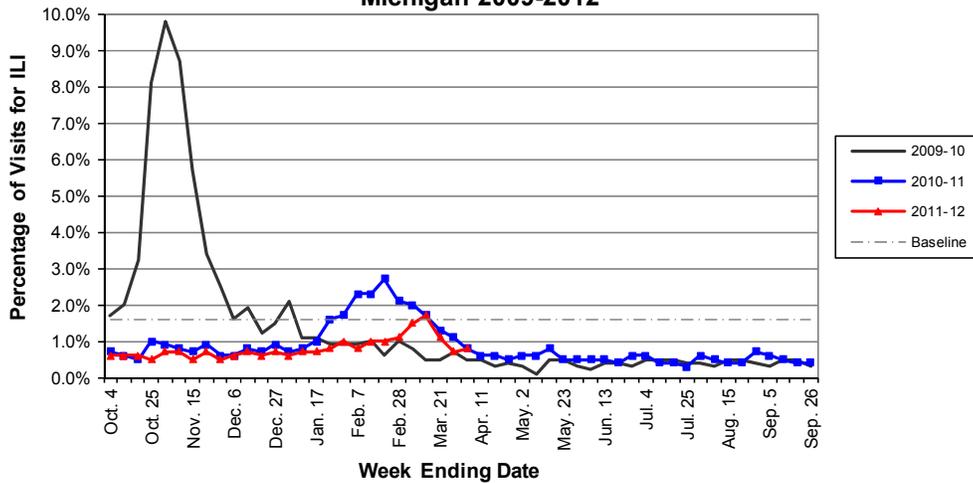
Sentinel Provider Surveillance (as of April 12): During the week ending April 7, 2012, the proportion of visits due to influenza-like illness (ILI) slightly increased to 0.8% overall; this is below the regional baseline of (1.6%). A total of 62 patient visits due to ILI were reported out of 8,023 office visits. Twenty-nine sentinel sites provided data for this report. ILI activity increased in two surveillance regions: Central (1.1%) and North (0.8%); activity remained the same in one surveillance region Southeast (0.4%); and activity decreased in the remaining surveillance region: Southwest (0.5%). Please note these rates may change as additional reports are received.

As part of pandemic influenza surveillance, CDC and MDCH highly encourage year-round participation from all sentinel providers. New practices are encouraged to join the sentinel surveillance program today! Contact Cristi Carlton at 517-335-9104 or CarltonC2@michigan.gov for more information.

**Percentage of Visits for Influenza-like Illness (ILI)
Reported by Sentinel Providers, Statewide and Regions
2010-2011 and 2011-12 Flu Seasons**



**Percentage of Visits for Influenza-like Illness (ILI) Reported by the
US Outpatient Influenza-like Illness Surveillance Network (ILINet):
Michigan 2009-2012**



Hospital Surveillance (as of April 7): The Influenza Hospitalization Surveillance Project provides population-based rates of severe influenza illness in Clinton, Eaton and Ingham counties. 2 lab-confirmed influenza hospitalizations were reported during the week ending April 7, 2012. For the 2011-12 season, 24 influenza hospitalizations (9 adult, 15 pediatric) have been reported in the catchment area.

The MDCH Influenza Sentinel Hospital Network monitors influenza hospitalizations reported voluntarily by hospitals statewide. 7 hospitals (SE, SW, C, N) reported for the week ending April 7, 2012. Results are listed in the table below. Total hospitalizations were adjusted to reflect amended reports from past weeks.

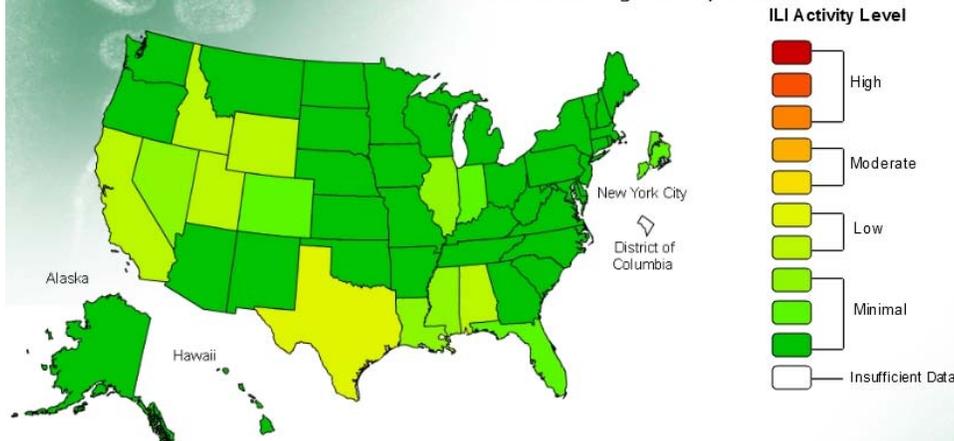
Age Group	Hospitalizations Reported During Current Week	Total Hospitalizations 2011-12 Season
0-4 years	0	18
5-17 years	0	14
18-49 years	1	25
50-64 years	2	21
≥65 years	3	28
Total	6	106

Laboratory Surveillance (as of April 7): During April 1-7, 45 influenza A/H3 (31SE, 10SW, 3C, 1N), 2 influenza A/H1N1pdm09 (1SE, 1SW) and 4 influenza B (2SE, 1SW, 1C) results were reported by MDCH BOL. For the 2011-12 season (starting October 2, 2011), MDCH has identified 1002 influenza results:

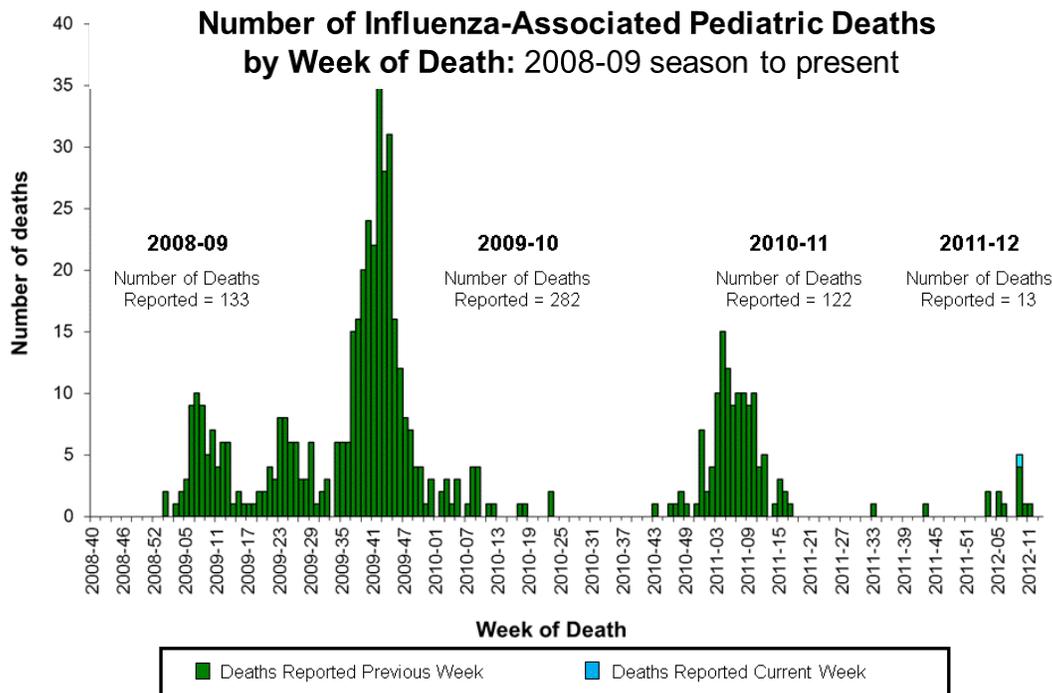
FLUVIEW

A Weekly Influenza Surveillance Report Prepared by the Influenza Division
Influenza-Like Illness (ILI) Activity Level Indicator Determined by Data Reported to ILINet

2011-12 Influenza Season Week 13 ending Mar 31, 2012



This map uses the proportion of outpatient visits to healthcare providers for influenza-like illness to measure the ILI activity level within a state. Therefore, outbreaks occurring in a single city could cause the state to display high activity levels. Data collected in ILINet may disproportionately represent certain populations within a state, and therefore, may not accurately depict the full picture of influenza activity for the whole state. Data displayed on this map are based on data collected in ILINet, whereas the State and Territorial flu activity map are based on reports from state and territorial epidemiologists.



The entire weekly report is available online at <http://www.cdc.gov/flu/weekly/fluactivity.htm>.

International (WHO [edited], March 30): This influenza season started late, but seems to be reaching the peak or is decreasing in most countries of the northern hemisphere temperate regions. Severe acute respiratory infections was mainly observed in the age group above 65 years. The most commonly detected virus type or subtype throughout most of the temperate areas of northern hemisphere temperate zone has been influenza A(H3N2), although the proportion of influenza B detection is increasing. In Mexico influenza A(H1N1)pdm09 is the predominant subtype circulating; China and the surrounding countries which are still reporting a predominance of influenza type B virus. Increasing genetic and antigenic diversity has been noted in H3N2 viruses in the later part of the influenza season. No significant change in antiviral resistance has been reported so far this season.

The entire WHO report is available online at www.who.int/influenza/surveillance_monitoring/updates/latest_update_GIP_surveillance/en/index.html.

MDCH reported **LOCAL ACTIVITY** to the CDC for the week ending April 7, 2012.

For additional flu vaccination and education information, the MDCH *FluBytes* newsletter is available at http://www.michigan.gov/mdch/0,1607,7-132-2940_2955_22779_40563-125027--,00.html.

Novel Influenza Activity and Other News

WHO Pandemic Phase: Post-pandemic – Influenza disease activity has returned to levels normally seen for seasonal influenza. It is expected that the pandemic virus will behave as a seasonal influenza A virus. It is important to maintain surveillance and update pandemic preparedness/response plans accordingly.

National, Human (Weber-Morgan County Health Department press release, April 11): Weber-Morgan Health Department received confirmation from the Centers for Disease Control and the Utah Department of Health that a Weber County resident has tested positive for a novel flu virus that has been identified in several isolated cases in the United States.

The individual was not hospitalized and recovered at home. As a precaution, all known contacts have been advised to watch for fever, cough and other flu-like symptoms and to contact their physician if necessary.

While considered novel, the virus, *A/H3N2v*, is genetically similar to those which circulate in pigs. It is common practice for the CDC to monitor diseases that are capable of transmitting from animals to humans, says Gary House, director of the Weber-Morgan Health Department.

Fortunately, this individual is getting better, House says. We know there have been 12 other cases with in the past year in the United States that have also fully recovered. We are working with the CDC, the Utah Department of Health and Utah Department of Agriculture and Food to determine how the individual was exposed to this particular flu virus.

As with all other flu viruses, House reminds the community to take preventive measures such as covering coughs and sneezes, staying at home while ill and washing hands frequently.

'We learned from the H1N1 experience of 2009 that the public's willingness to follow these simple precautions is the best line of defense.' House says.

The press release is online at http://www.webermorganhealth.org/view_press.php?press_id=23&id=1.

National, Research (CIDRAP, April 6): US researchers say they found no evidence of increased virulence in a novel reassortant H3N2 influenza virus (H3N2v) from one of the 12 human cases identified in the United States last year or in several related H3N2 viruses from pigs. The 12 H3N2v infections detected last summer and fall involved swine-origin H3N2 strains that included the M (matrix) gene from the pandemic 2009 H1N1 (pH1N1) virus. The report in the *Journal of Virology* says that swine H3N2 viruses with triple-reassortant internal genes (H3N2-TRIG) have been widespread in the United States since 1998. Transmission of the pH1N1 virus from humans to pigs resulted in reassortant H3N2 viruses that included genetic elements from pH1N1, which the authors call rH3N2p. They say their genome analysis of H3N2 viruses collected from swine from 2009 to 2011 revealed six different rH3N2p genotypes in the US swine population, all of which include the M gene from pH1N1. The team compared the pathogenic, transmission, genetic, and antigenic properties of a human H3N2v isolate and two swine H3N2 isolates—an H3N2-TRIG and an rH3N2p. They found that in pigs, the H3N2v and rH3N2p viruses were no more virulent than the background H3N2-TRIG strain, with most infected pigs showing mild illness. The authors also found that some recent rH3N2p isolates seem to be forming a separate genetic cluster with the human H3N2v strain. The findings, they say, add to the evidence that influenza A viruses readily pass between humans and animals and that pigs play a role in generating reassortant viruses. "Continued monitoring of these H3N2 viruses is necessary to evaluate evolution and potential loss of population immunity in swine and humans," the report concludes.

The journal abstract is online at <http://jvi.asm.org/content/early/2012/03/29/JVI.00197-12.short?rss=1>.

National, Research (MMWR abstract, April 13): Since August 2011, a total of 12 human infections with influenza A (H3N2) variant viruses with genes from avian, swine, and human viruses (i.e., A [H3N2]v) that had acquired the M gene from influenza A (H1N1)pdm09 virus have been reported to CDC. Eleven of the cases occurred in children aged <10 years. In six cases, no history of recent exposure to swine was noted, suggesting that human-to-human transmission had occurred. This new gene constellation for A (H3N2)v viruses and its temporal association with an increase in human cases of A (H3N2)v highlight the need to better understand the risk for human infection with these viruses and the extent to which current seasonal vaccines might elicit cross-reactive antibodies to them. CDC conducted a preliminary analysis to evaluate the age-specific presence of serum cross-reactive antibody in U.S. populations vaccinated or not vaccinated with the 2010–11 seasonal trivalent influenza vaccine (TIV). The results indicated that 1) little or no cross-reactive antibody to A (H3N2)v exists among children aged <10 years, 2) immunization with the 2010–11 TIV had no impact on cross-reactive antibody levels in those aged <3 years, 3) cross-reactive antibody was detected in 20%–30% of those aged ≥10 years, and 4) among adults, vaccination with TIV provided a modest boost to the level of cross-reactive A (H3N2)v antibodies. Receipt of seasonal influenza vaccine continues to be recommended to protect against circulating human influenza viruses for all age groups and might provide limited protection against A (H3N2)v infection in the adult population. A vaccine virus specific for A (H3N2)v has been developed and could be used to produce an H3N2v vaccine, if needed.

The article is at http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6114a1.htm?s_cid=mm6114a1_e.

National, Antivirals (CIDRAP, April 6): The intravenous antiviral peramivir was used in close to 1,300 severely ill patients under an emergency authorization during the 2009 flu pandemic, but its impact and safety profile remain unclear, in part because of patchy data collection, according to reports and commentary published in *Clinical Infectious Diseases* (CID) this week.

The Centers for Disease Control and Prevention (CDC) estimated that 1,274 patients received the IV drug under an Emergency Use Authorization (EUA). Food and Drug Administration (FDA) officials estimated that about 16% of the patients died, which is in the range of fatality rates reported for hospitalized H1N1 patients generally, according to the reports.

Also, many adverse events were reported in the treated patients, but those were generally attributed to their already-severe illness at the time of treatment and other factors. Rashes were the only adverse reactions that seemed clearly related to the drug, but data gaps left the overall safety picture incomplete.

"Despite extensive and thoughtful efforts, the post hoc data collection described in this issue provided a limited and incomplete view of the experience," wrote Andrew T. Pavia, MD, a pediatric infectious disease expert at the University of Utah, in a commentary. "The EUA mechanism as described in the Project BioShield Act of 2004 was not designed for prospective data gathering."

Peramivir is a neuraminidase inhibitor, like oseltamivir (Tamiflu, given orally) and zanamivir (Relenza, given by inhalation), but is not yet licensed by the FDA. The FDA issued an EUA for peramivir on Oct 23, 2009, for the sake of seriously ill patients who needed an IV antiviral. The EUA remained in force until June 2010. The CDC managed distribution of the drug to clinicians who requested it.

In one of the CID reports, CDC officials write that they received 1,371 clinician requests for peramivir and delivered 2,129 5-day adult-treatment course equivalents to 563 hospitals.

Data from three surveys were used to estimate how many patients were treated. The surveys included a reminder survey about reporting adverse events, a hospital pharmacy survey, and a clinician survey seeking patient data. From these, the CDC estimated that at least 1,274 patients, median age 49, received the drug.

The reminder survey results yielded data on 844 patients. Adverse events were reported in 260 (31%) of these, but most of the events could have been due to flu itself or underlying diseases, according to Pavia. Because of the survey design and the lack of a control group, the relationship of the adverse events to peramivir could not be determined, he said.

The clinician survey drew a response rate of only 12%, with data on 127 patients. "The results paint a picture of very ill patients and late treatment," Pavia commented. Ninety-two percent of the patients were on mechanical ventilation when peramivir treatment was started. When treatment ended, 30 (24%) of the

patients had died. The available data did not permit a conclusion on whether the drug influenced outcomes.

The second CID report was written by FDA officials who analyzed reports submitted to the Adverse Events Reporting System (AERS) about peramivir patients. The FDA received 369 reports covering 900 adverse events in 344 patients.

The FDA investigators could not determine if any adverse events other than rash were due to peramivir, as missing data, severe illness, and other factors complicated the review, according to Pavia. The estimated overall mortality among the treated patients, about 16%, "did not differ from overall mortality of 14% to 46% in published series of hospitalized patients with pH1N1 influenza," he wrote.

Despite the limitations, the reports "highlight the first effective use of the EUA to provide a potentially lifesaving medication that was not yet licensed during a large-scale bioemergency," Pavia wrote. "The delivery of drug to more than 1,100 critically ill patients within 24 hours of the request represents an enormous effort and logistical tour de force."

But he adds that the EUA was not initiated until close to the peak of the second wave of the pandemic, "and there may have been missed opportunities to make the drug available earlier."

Pavia suggests that more complete clinical data on patients treated under an EUA could be collected by providing data forms or links to secure Web sites when the drugs are delivered. Clinical research networks established in advance of emergencies would also improve data collection.

The US House-passed version of the reauthorization for the Pandemic and All-Hazards Preparedness Act would expand the FDA's ability to plan in advance for EUAs and to collect data during and after an emergency, but the Senate version does not include those provisions, Pavia said. Passage of the language in the House version is critical, he said.

The article is at <http://www.cidrap.umn.edu/cidrap/content/influenza/swineflu/news/apr0612peramivir.html>.

International, Research (Influenza and Other Respiratory Diseases abstract, April 6): Blyth *et al.* (2012) The impact of bacterial and viral co-infection in severe influenza. *Influenza and Other Respiratory Viruses* DOI: 10.1111/j.1750-2659.2012.00360.x.

Background: Many questions remain concerning the burden, risk factors and impact of bacterial and viral co-infection in patients with pandemic influenza admitted to the intensive care unit (ICU).

Objectives: To examine the burden, risk factors and impact of bacterial and viral co-infection in Australian patients with severe influenza.

Patients/Methods: A cohort study conducted in 14 ICUs was performed. Patients with proven influenza A during the 2009 influenza season were eligible for inclusion. Demographics, risk factors, clinical data, microbiological data, complications and outcomes were collected. Polymerase chain reaction for additional bacterial and viral respiratory pathogens was performed on stored respiratory samples.

Results: Co-infection was identified in 23·3–26·9% of patients with severe influenza A infection: viral co-infection, 3·2–3·4% and bacterial co-infection, 20·5–24·7%. *Staphylococcus aureus* was the most frequent bacterial co-infection followed by *Streptococcus pneumoniae* and *Haemophilus influenzae*. Patients with co-infection were younger [mean difference in age = 8·46 years (95% CI: 0·18–16·74 years)], less likely to have significant co-morbidities (32·0% versus 66·2%, $P = 0·004$) and less frequently obese [mean difference in body mass index = 6·86 (95% CI: 1·77–11·96)] compared to those without co-infection.

Conclusions: Bacterial or viral co-infection complicated one in four patients admitted to ICU with severe influenza A infection. Despite the co-infected patients being younger and with fewer co-morbidities, no significant difference in outcomes was observed. It is likely that co-infection contributed to a need for ICU admission in those without other risk factors for severe influenza disease. Empiric antibiotics with staphylococcal activity should be strongly considered in all patients with severe influenza A infection.

The abstract is online at <http://onlinelibrary.wiley.com/doi/10.1111/j.1750-2659.2012.00360.x/abstract>.

International, Human (WHO, April 5): The Ministry of Health (MoH) of the Kingdom of Cambodia has announced a confirmed case of human infection with avian influenza A (H5N1) virus.

The 6 year-old female from Kampong Chhnang Province developed symptoms on 22 March 2012. After initial treatment at the village, she was later admitted to hospital in Phnom Penh on 28 March. She died on 30 March. Infection with avian influenza A (H5N1) virus was confirmed by Institute Pasteur du Cambodge on 30 March.

It was reported that the patient had contact with sick or dead poultry prior to onset of illness. The National and local Rapid Response Teams (RRT) are conducting outbreak investigation and response following the national protocol. In addition, a public health education campaign is being conducted to inform families on how to protect themselves from contracting avian influenza.

To date, of the 20 cases reported in Cambodia since 2005, 18 have been fatal.

International, Poultry (OIE [edited], April 10): Low path avian influenza H5N2; Chinese Taipei Outbreak: Yuan-Shan Township, I-LAN

Date of start of the outbreak: 13/03/2012; Outbreak status: Continuing; Epidemiological unit: Farm
Species: Birds; Susceptible: 1000; Cases: 20; Deaths: 0; Destroyed: 0; Affected population: Duck

Michigan Wild Bird Surveillance (USDA, as of April 12): For the 2011 season (April 1, 2011-March 31, 2012), highly pathogenic avian influenza H5N1 has not been recovered from 7 Michigan samples or 408 samples tested nationwide. For more information, visit <http://www.nwhc.usgs.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>.

International Poultry and Wild Bird Surveillance (OIE): Reports of avian influenza activity, including summary graphs of avian influenza H5N1 outbreaks in poultry, can be found at the following website: http://www.oie.int/download/AVIAN%20INFLUENZA/A_AI-Asia.htm.

For questions or to be added to the distribution list, please contact Susan Peters at peterss1@michigan.gov

Contributors

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Table. H5N1 Influenza in Humans – As of April 5, 2012. http://www.who.int/influenza/human_animal_interface/EN_GIP_20120405CumulativeNumberH5N1cases.pdf. Downloaded 4/6/2012. Cumulative lab-confirmed cases reported to WHO. Total cases includes deaths.

Country	2003-2005		2006		2007		2008		2009		2010		2011		2012		Total	
	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths
Azerbaijan	0	0	8	5	0	0	0	0	0	0	0	0	0	0	0	0	8	5
Bangladesh	0	0	0	0	0	0	1	0	0	0	0	0	2	0	3	0	6	0
Cambodia	4	4	2	2	1	1	1	0	1	0	1	1	8	8	2	2	20	18
China	9	6	13	8	5	3	4	4	7	4	2	1	1	1	1	1	42	28
Djibouti	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
Egypt	0	0	18	10	25	9	8	4	39	4	29	13	39	15	8	4	166	59
Indonesia	20	13	55	45	42	37	24	20	21	19	9	7	12	10	5	5	188	156
Iraq	0	0	3	2	0	0	0	0	0	0	0	0	0	0	0	0	3	2
Lao PDR	0	0	0	0	2	2	0	0	0	0	0	0	0	0	0	0	2	2
Myanmar	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0
Nigeria	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	1	1
Pakistan	0	0	0	0	3	1	0	0	0	0	0	0	0	0	0	0	3	1
Thailand	22	14	3	3	0	0	0	0	0	0	0	0	0	0	0	0	25	17
Turkey	0	0	12	4	0	0	0	0	0	0	0	0	0	0	0	0	12	4
Vietnam	93	42	0	0	8	5	6	5	5	5	7	2	0	0	4	2	123	61
Total	148	79	115	79	88	59	44	33	73	32	48	24	62	34	23	14	601	354