



MI FluFocus

Influenza Surveillance and Avian Influenza Update

Bureau of Epidemiology
Bureau of Laboratories



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New updates in this issue:

- **Michigan Surveillance:** Overall influenza activity continues to decrease; statewide activity is “Local”.
- **National Surveillance:** Overall influenza activity decreases slightly but influenza B increases.
- **Avian Influenza:** Egypt reports an additional new case of human H5N1 avian influenza.

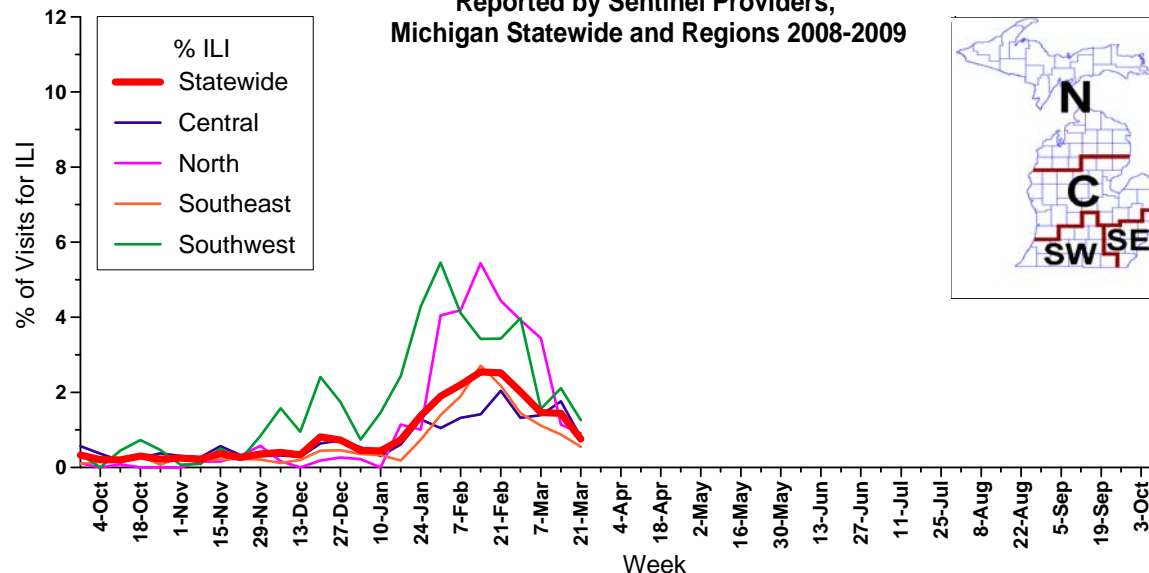
Michigan Disease Surveillance System: The week ending March 21 saw both aggregate flu-like numbers and individual case reports decrease compared to what was seen during the previous week. Individual and aggregate numbers are slightly lower than numbers seen this time last year.

Emergency Department Surveillance: Emergency department visits from constitutional complaints were similar to those during the previous week, while respiratory complaints decreased. Visits due to constitutional complaints are comparable to numbers seen at this time last year, while respiratory complaints are slightly lower. Three constitutional alerts in the C(2), and N(1) Influenza Surveillance Regions and seven respiratory alerts in the SE(1), C(5), and N(1) Influenza Surveillance Regions were generated last week.

Over-the-Counter Product Surveillance: Overall, OTC product sales were mostly steady last week. Unpromoted children’s cough/cold medication sales and thermometer sales increased very slightly in comparison to last week, while remaining indicators saw very little variation. Indicator levels are comparable to those seen at this time last year.

Sentinel Provider Surveillance (as of March 25): During the week ending March 21, 2009, the proportion of visits due to influenza-like illness (ILI) continued to decline and is now below the baseline at 0.8% overall. This represents 68 patient visits due to ILI reported out of 8,977 office visits; 32 sentinel sites provided data for this report. Activity declined in all four surveillance regions: Southeast (0.6%), North (0.9%), Central (0.8%) and Southwest (1.3%). 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 2008-2009



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 Cristi Carlton at 517-335-9104 or CarltonC2@michigan.gov for more information.

Laboratory Surveillance (as of March 25): During the past week, 5 new influenza A isolates and 12 new influenza B isolates were identified at the MDCH Bureau of Laboratories (BOL). For the 2008-2009 influenza season, MDCH BOL has identified 257 influenza isolates (followed by Influenza Surveillance Regions of origin):

- 148 A/H1N1 (54SE, 33SW, 20C, 41N)
- 3 A/H3N2 (1SE, 1C, 1N)
- 9 A subtype pending (1SE, 2C, 6N)
- 97 B (20SE, 31SW, 13C, 33N)
 - 9 B/Florida/4/2006-like (4SE, 1SW, 1C, 3N)
 - 62 B/Malaysia/2506/2004-like (13SE, 19SW, 7C, 23N)
 - 25 are pending characterization (3SE, 10SW, 5C, 7N)
 - 1 untypable (SW)

For the week ending March 21, 10 sentinel labs reported. Influenza A positives are steady to decreasing, with one lab (SE) reporting no influenza A activity. Influenza B reporting is mixed, as 2 labs (N) reported increasing influenza B positives, 1 lab (SW) reported level B activity, and 6 labs reported decreasing B activity (SE, SW, C). RSV activity was level to decreasing at the majority of the labs.

***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.

Michigan Antigenic Characterization (as of March 25): At this time, 24 influenza A/H1N1 isolates have been antigenically characterized by the CDC; results indicate all isolates are A/Brisbane/59/2007-like, which matches the influenza A/H1N1 component of this season's Northern Hemisphere vaccine. One influenza A/H3N2 has been characterized as A/Brisbane/10/2007-like, which matches the A/H3N2 component of this season's vaccine.

At this time, 3 influenza B isolates have been antigenically characterized by the CDC. One influenza B isolate has been characterized as B/Florida/4/2006-like, which matches the influenza B component of this season's vaccine. Two influenza B isolates have been characterized as B/Brisbane/60/2008-like, which does not match this season's vaccine, but is a recommended component of the 2009-2010 vaccine.

Michigan Antiviral Resistance Data (as of March 25): 24 influenza A/H1N1 viruses from the MDCH Bureau of Laboratories have been tested for antiviral resistance at CDC for the 2008-2009 season. All 24 viruses were resistant to oseltamivir (Tamiflu®) and sensitive to zanamivir, amantadine and rimantadine. These viruses were collected in the SE(11), SW(12) and N(1) Influenza Surveillance Regions. One influenza A/H3N2, collected in the C Region, has been tested for antiviral resistance; that virus was resistant to the adamantanes (amantadine and rimantadine) and sensitive to oseltamivir and zanamivir. Two influenza B isolates, collected in the SW Region, have been tested for antiviral resistance; these viruses were sensitive to oseltamivir and zanamivir (the adamantanes are not effective against B viruses).

Antiviral resistance testing often takes several weeks to complete, and thus cannot be used to guide treatment of individual patients. However, CDC has made interim recommendations regarding the use of antiviral medications for the treatment of influenza and for prophylaxis. This guidance is available at <http://www2a.cdc.gov/HAN/ArchiveSys/ViewMsgV.asp?AlertNum=00279>.

Influenza-Associated Pediatric Mortality (as of March 25): One influenza-associated pediatric mortality due to influenza A (SW) has been reported to MDCH for the 2008-2009 influenza season.

***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. Please immediately call MDCH to ensure that proper clinical specimens are obtained. View the complete MDCH protocol online at http://www.michigan.gov/documents/mdch/ME_pediatric_influenza_guidance_v2_214270_7.pdf.

Congregate Settings Outbreaks (as of March 25): Three congregate setting outbreaks (1C, 2N) due to influenza (1 influenza A, 1 influenza B, 1 unsubtype) have been reported to MDCH for the 2008-09 influenza season.

National (CDC [edited], March 20): During week 10 (March 8-14, 2009), influenza activity decreased slightly in the United States. One thousand one hundred two (21.7%) specimens tested by U.S. World Health Organization (WHO) and National Respiratory and Enteric Virus Surveillance System (NREVSS) collaborating laboratories and reported to CDC/Influenza Division were positive for influenza. The proportion of deaths attributed to pneumonia and influenza (P&I) was below the epidemic threshold. Six influenza-associated pediatric deaths were reported. The proportion of outpatient visits for influenza-like illness (ILI) was above the national baseline. ILI decreased nationally and in eight of the nine regions compared to the previous week. Eight of nine surveillance regions reported ILI above their region-specific baselines. Thirty states reported widespread influenza activity, 18 states reported regional activity; two states reported local influenza activity; and Puerto Rico and the District of Columbia reported sporadic influenza activity.

Since week 2 (the week ending January 17, 2009), when influenza activity increased nationally, influenza A (H1) viruses have predominated during the season overall. However, the relative proportion of influenza B viruses is increasing nationally and regionally. While influenza activity slightly decreased nationally, several surveillance regions reported an increase in influenza virus circulation, and six regions (East North Central, Mid-Atlantic, New England, Pacific, South Atlantic, and West South Central) reported an equal or higher proportion of influenza B viruses compared to influenza A viruses this week.

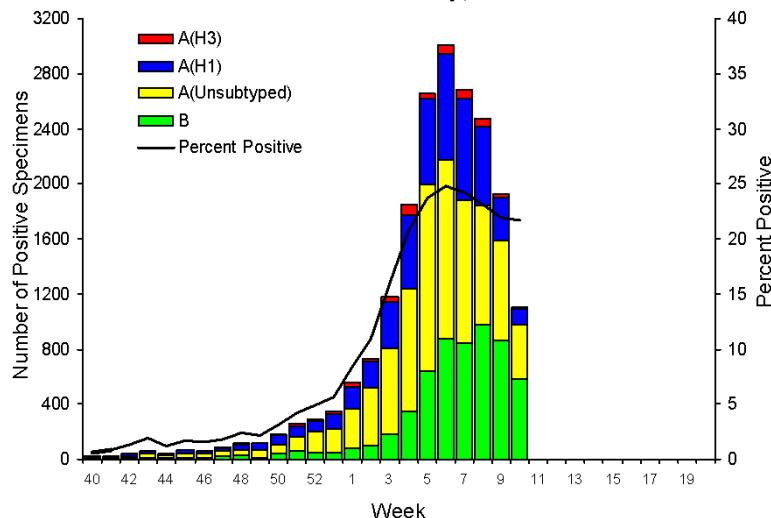
Since October 1, 2008, 474 influenza A (H1N1), 77 influenza A (H3N2), and 227 influenza B viruses have been tested for resistance to the neuraminidase inhibitors (oseltamivir and zanamivir). Four hundred seventy-six influenza A (H1N1) and 77 influenza A (H3N2) viruses have been tested for resistance to the adamantanes (amantadine and rimantadine). The results of antiviral resistance testing performed on these viruses are summarized in the table below.

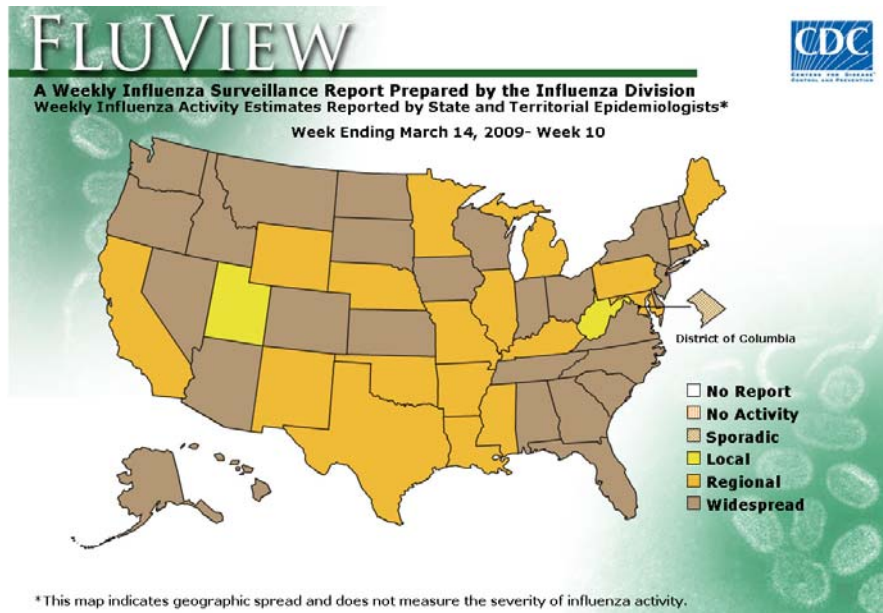
	Isolates tested (n)	Resistant Viruses, Number (%)		Isolates tested (n)	Resistant Viruses, Number (%)
		Oseltamivir	Zanamivir		
Influenza A (H1N1)	474	469 (98.9%)	0 (0)	476	3 (0.6%)
Influenza A (H3N2)	77	0 (0)	0 (0)	77	77 (100%)
Influenza B	227	0 (0)	0 (0)	N/A*	N/A*

*The adamantanes (amantadine and rimantadine) are not effective against influenza B viruses.

To access the entire CDC weekly surveillance report throughout the influenza season, visit <http://www.cdc.gov/flu/weekly/fluactivity.htm>

Influenza Positive Tests Reported to CDC by U.S. WHO/NREVSS Collaborating Laboratories, National Summary, 2008-09





International (WHO [edited], March 19): During the weeks 9-10, the level of influenza activity increased in some parts of the world while it declined in other countries. Influenza activity has continued to decline in western Europe and is below baseline levels in most countries. For many of the remaining countries activity has shown relatively little change compared to the previous fortnight although increased activity has been reported in some central and eastern European countries as well as in a large part of the Russian Federation. While influenza A (H3) continues to be the dominant influenza virus circulating in Europe, an increasing number of countries reported influenza B as the dominant or co-dominant virus type. In Canada and the United States of America, influenza activity continued to increase with both influenza A and B viruses circulating.

Sporadic influenza activity was observed in Austria (H3,B), Denmark (H1,H3,B), China (H1,H3,B), Kazakhstan (A,B), Mongolia (H1), Poland (B), Portugal (H3), Spain (B), Sri Lanka, Tunisia (H3,B), and United Kingdom of Great Britain and Northern Ireland (H1,H3,B).

Argentina, Bulgaria, Cameroon and Malta reported no activity.

To access the entire report, visit <http://www.who.int/csr/disease/influenza/update/en/>

MDCH reported **LOCAL INFLUENZA ACTIVITY** to the CDC for the week ending March 21, 2009.

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 weekly during the influenza season.

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, Human (WHO, March 23): The Ministry of Health and Population, Egypt has reported a new confirmed human case of Avian Influenza. The case is a 38-year old female from Elfath District, Assiut Governorate. Her symptoms started with a fever and headache on March 14. She was admitted to Assiut Fever Hospital on March 14 where she was started on oseltamivir the same day (March 14) and remains in a stable condition. Infection with H5N1 avian influenza was confirmed on 18 March by the Egyptian Central Public Health Laboratory.

Investigations into the source of her infection indicate a history of close contact with dead and sick poultry prior to becoming ill. Of the 59 cases confirmed to date in Egypt, 23 have been fatal.

International, Poultry (HT Syndication [edited], March 19): A total of 1595 chicken and 205 eggs were culled in a farm at Kendua Upazila [Bangladesh] in the district on Friday last due to detection of bird-flu virus.

Netrakona District Livestock Office sources said, an incident of detection of Bird Flu virus in a poultry farm of one Rasel Ahmed at village Rampur under Kendua Upazila of Netrakona district was reported.

International, Poultry (DEFRA Global Animal Health, March 19): 1) Disease Report: France has reported an outbreak of H5N1 LPAI in decoy ducks on a premises in Calvados and a 2nd outbreak of H5 (not N1) in decoy ducks in Pas-de Calais. The site in Calvados contains 45 ducks in 2 aviaries covered with fencing and kept by one hunter. Two of 10 ducks tested positive for H5N1 LPAI. The 2nd premises in Pas-de-Calais contained 563 ducks in 32 adjacent aviaries owned by a hunter cooperative.

During routine surveillance, 5 ducks each from 3 of the 32 aviaries were tested for avian influenza. Two ducks from one aviary were positive, while the other 10 ducks from the 2 aviaries were negative. Both the infected premises have been placed under surveillance, and biosecurity has been increased, but other disease controls have not been applied, and the affected birds were not culled (European Commission 2009).

2) Situation Assessment: Decoy ducks are used as captive birds to lure wild birds to a shooting area for hunting. They are kept tethered when they are taken out to water and have little direct contact with wild birds. The French authorities will continue to conduct surveillance for the time being. As there are no commercial poultry premises within a one-km radius of the 2 premises, no restriction zones have been imposed.

According to EU rules, immediate culling of birds infected with LPAI is not required, but they must be kept under restrictions.

There have been previous reports of LPAI H5N1 being detected in wild birds in Italy and France. Laboratory tests of these viruses suggested there was no relationship to Asian HPAI H5N1 strains. There may be some limited wild bird movements between North France and South East England at this time of year.

International, Research (CIDRAP [edited], March 19): Scientists who analyzed 67 H5N1 avian influenza viruses from across Africa report that the viruses fall into three distinct sublineages, or families, and that some have mutations that make them resistant to antiviral drugs.

The scientists also found that some of the African viruses have genetic markers that are characteristic of human flu viruses rather than avian strains, according to their report, published yesterday in the online journal *PLoS One*.

"These findings raise concern for the possible human health risk presented by viruses with these genetic properties and highlight the need for increased efforts to monitor the evolution of A/H5N1 viruses across the African continent," says the report by a large international team of scientists. The group includes several from African countries and the UN Food and Agriculture Organization.

Lethal H5N1 viruses made their African debut on Nigerian poultry farms in January 2006, the report notes. Soon afterward the virus cropped up in Egypt, Niger, and Cameroon, and in April 2006 it was found in Sudan, Burkina Faso, Djibouti, and Ivory Coast. The virus surfaced in Ghana and Togo in mid-2007 and in Benin in December 2007. All but two human cases of H5N1 disease in Africa have occurred in Egypt, whose official case count is 58, with 23 deaths. Nigeria and Djibouti have each had one human case.

The researchers determined that all the African viruses belong to clade 2.2 and are related to the H5N1 viruses that have been circulating throughout Europe, Russia, and the Middle East since late 2005. Clade 2.2 traces back to the outbreak of avian flu in thousands of migratory birds at China's Qinghai Lake in the spring of 2005, the article notes.

Detailed analysis of the hemagglutinin genes showed that the viruses fall into three sublineages (labeled I, II, and IV). All three groups "had been co-circulating since the beginning of the epidemic in Africa,"

suggesting that all three had been introduced into Africa separately, as reported in previous studies, the report says.

Just how the three groups entered Africa and spread so rapidly is still unclear. But the viruses emerged in Africa when related strains were present in European migratory birds, "and such birds may have played a significant role in the introduction of the virus," the scientists write.

The three sublineages had geographic dimensions, but the patterns were complex. All the Egyptian isolates were in sublineage IV, which they shared with isolates from Gaza and Israel. Strains from Burkina Faso, Ivory Coast, Ghana, and Cameroon formed a single cluster in sublineage I. However, the authors found all three groups in Nigeria, a finding that agreed with an earlier study.

Viruses collected in Sudan were in sublineage I and closely related to those from Nigeria, Burkina Faso, and Ivory Coast, rather than to those from nearby Egypt and Djibouti. Overall, the findings "may suggest that a certain degree of geographical segregation has occurred in Africa" since the initial viral introductions, the report states.

In searching signs of antiviral resistance, the team found four bird isolates from Egypt carrying a mutation linked with resistance to the older class of flu drugs, the adamantanes (amantadine and rimantadine). They also found viruses from two human cases in Egypt that had a mutation (known as N294S) that confers resistance to oseltamivir (Tamiflu) and slightly reduced sensitivity to zanamivir (Relenza).

However, no mutations conferring resistance to oseltamivir or zanamivir were found in any of the African viruses from birds.

The authors also found a number of isolates with genetic markers usually found in human flu viruses rather than avian strains. In particular, they checked the African viruses for 13 genetic markers consistently found in the flu viruses that caused the pandemics of 1918, 1957, and 1968. They found two, both in the PB2 gene. One of these, known as E627K and associated with increased H5N1 virulence in mice, was found in all the African isolates. Another was found in just two bird viruses from Egypt.

In other findings, the report says that two different reassortant viruses representing combinations of two of the three sublineages were found in Nigeria in 2006 and 2007. One of these became the predominant strain in Nigeria's poultry in 2007.

David A. Halvorson, DVM, an avian flu expert at the University of Minnesota in St. Paul, said the report appears to confirm that there were three separate introductions of H5N1 into Africa and that those strains continue to circulate.

Halvorson also commented that the findings regarding antiviral resistance are not surprising: "These mutations are typical of viruses as they circulate in a host. It seems they can mutate to resistance without any antiviral compound present."

Michigan Wild Bird Surveillance (USDA, as of March 25): For the 2008 testing season, 2105 Michigan samples have been taken so far, comprised of 327 live birds, 1218 hunter-killed birds, 35 morbidity or mortality samples and 525 environmental samples.

HPAI subtype H5N1 has not been recovered from any Michigan samples tested to date, or from the 77,769 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.nbio.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.

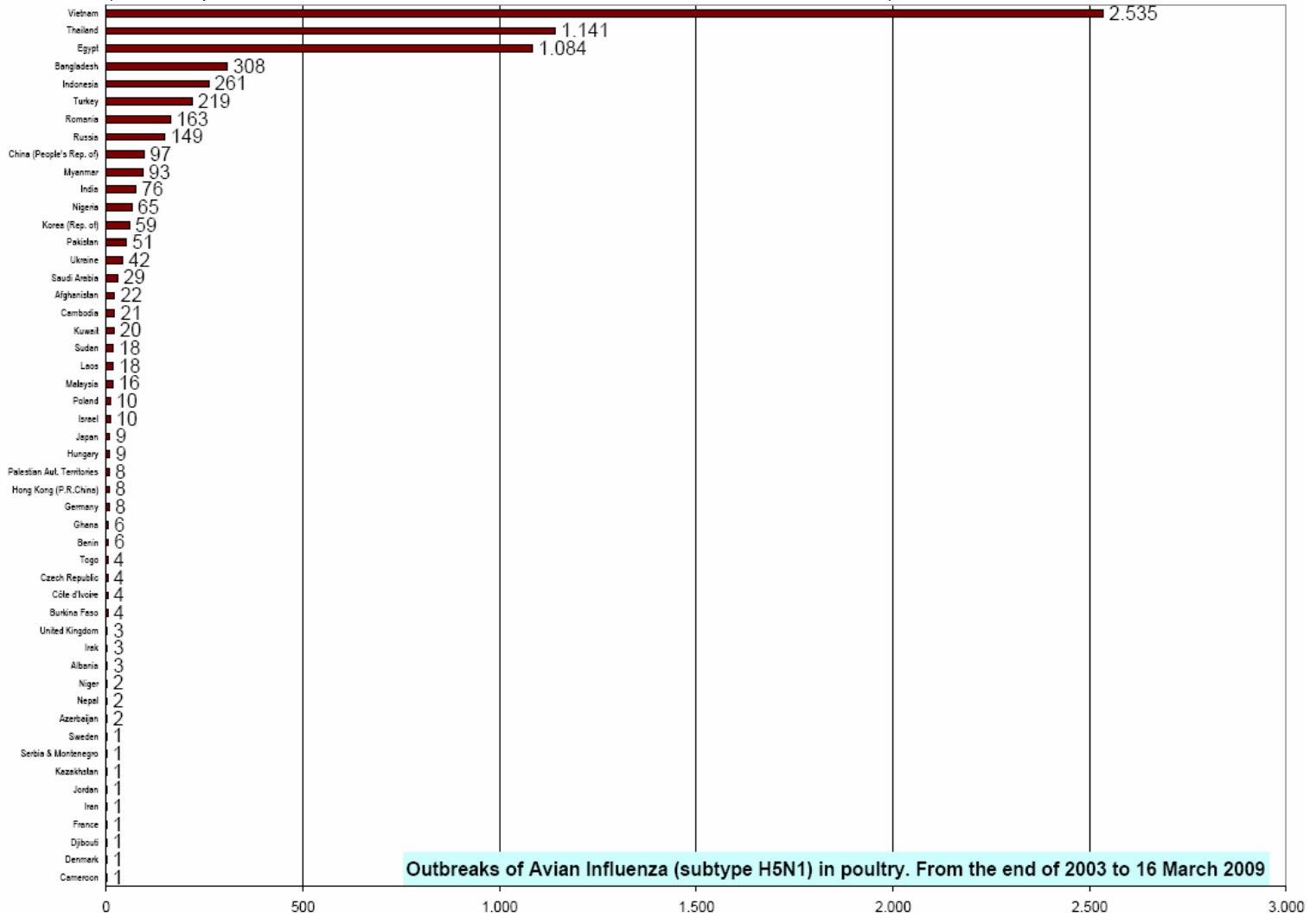
Contributors

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MDCH Bureau of Laboratories – Patricia Clark, MPH

Table 1. H5N1 Influenza in Poultry (Outbreaks up to March 16, 2009)

(Source: http://www.oie.int/downld/AVIAN%20INFLUENZA/A_AI-Asia.htm Downloaded 3/18/09)



Outbreaks of Avian Influenza (subtype H5N1) in poultry. From the end of 2003 to 16 March 2009

Table 2. H5N1 Influenza in Humans (Cases up to March 23, 2009)

(http://www.who.int/csr/disease/avian_influenza/country/cases_table_2009_03_23/en/index.html Downloaded 3/23/2009)

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

Country	2003		2004		2005		2006		2007		2008		2009		Total	
	cases	deaths	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	0	0	8	5
Bangladesh	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0
Cambodia	0	0	0	0	4	4	2	2	1	1	1	0	0	0	8	7
China	1	1	0	0	8	5	13	8	5	3	4	4	7	4	38	25
Djibouti	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1	0
Egypt	0	0	0	0	0	0	18	10	25	9	8	4	8	0	59	23
Indonesia	0	0	0	0	20	13	55	45	42	37	24	20	0	0	141	115
Iraq	0	0	0	0	0	0	3	2	0	0	0	0	0	0	3	2
Lao People's Democratic Republic	0	0	0	0	0	0	0	0	2	2	0	0	0	0	2	2
Myanmar	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	0
Nigeria	0	0	0	0	0	0	0	0	1	1	0	0	0	0	1	1
Pakistan	0	0	0	0	0	0	0	0	3	1	0	0	0	0	3	1
Thailand	0	0	17	12	5	2	3	3	0	0	0	0	0	0	25	17
Turkey	0	0	0	0	0	0	12	4	0	0	0	0	0	0	12	4
Viet Nam	3	3	29	20	61	19	0	0	8	5	6	5	2	2	109	54
Total	4	4	46	32	98	43	115	79	88	59	44	33	17	6	412	256