IDAHO DEPARTMENT OF HEALTH & WELFARE

Disease Bulletin

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Influenza Surveillance in Idaho

The 2012–2013 United States influenza season was considered moderately severe. In Idaho, influenza activity peaked in December, the influenza A (H3N2) subtype predominated, and 35 influenza-associated deaths were reported. Influenza infections, with the exception of novel influenza or those that are part of an outbreak, are not reportable in Idaho; however, comprehensive year-round surveillance is important to provide situational awareness for seasonal, "variant" (the term for flu viruses normally seen in pigs, when the virus infects people), novel, and pandemic influenza detection.

Influenza surveillance at the Idaho Department of Health and Welfare (IDHW) falls into three broad categories: human morbidity, human mortality, and laboratory-based virus testing. These categories provide information on the burden of disease on the population, severity of disease, and types of circulating viruses, respectively.

Human morbidity surveillance

The Centers for Disease Control and Prevention (CDC) maintains a web-based monitoring platform (ILINet) to collect weekly counts of sentinel healthcare provider patient encounters for influenza-like illness (ILI). For ILINet, ILI is defined as fever (temperature ≥100°F [≥37.8°C]), and cough and/or a sore throat without a known cause other than influenza. ILINet reports provide morbidity data by age group, week of report, and geographic location. The Bureau of Communicable Disease Prevention (BCDP) reviews the weekly ILINet reports from participating Idaho ILINet providers to monitor disease activity in the state. If you are interested in participating as an ILINet sentinel site and you see a variety of age groups in your practice, please contact an epidemiologist within BCDP at 208-334-5939. To learn more about ILINet, visit the CDC website www.cdc.gov/flu/weekly/fluviewinteractive.htm.

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2013–2014 Seasonal Influenza Vaccine Scramble

New influenza vaccine products for the 2013–2014 influenza season include quadrivalent vaccine, cell culture-based vaccine, and recombinant vaccine. Patients may be confused by the widening selection of vaccine options to choose from.

Quadrivalent vaccine (several products) include influenza B Victoria lineage virus in addition to an influenza A California 2009 (H1N1)-like virus, influenza A (H3N2) virus of the Victoria lineage, and influenza B Yamagata lineage virus included or incorporated in trivalent vaccines. It is hoped that including two B viruses will improve the performance of this influenza vaccine during each season, since there are often two strains of influenza B circulating.

A cell culture-based, trivalent vaccine (FLUCELVAX®), which is grown on a canine kidney cell line, was approved for use in persons aged >18 years by the Food and Drug Administration (FDA) in November 2012. It contains less than 50 femtograms ($5x10^{-8}$ ug) of egg protein. Persons with severe egg allergies have received egg-based influenza vaccines containing up to 1.4 ug ovalbumin per dose of vaccine administered without occurrence of anaphylaxis. This canine kidney cell line does not express known major canine allergens, but minor canine allergens could be present. Hypersensitivity reactions among persons self-reported to be allergic to dogs have not been documented; however, few reported dog-allergic persons received vaccine in clinical trials.[1] Bioassay performed with serum from 30 docu-

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Human mortality surveillance

The IDHW Bureau of Vital Records and Health Statistics reviews death certificate data weekly and contributes to national mortality surveillance by participating in the 122 Cities Mortality Reporting System (http://wonder.cdc.gov/mmwr/mmwrmort.asp). Because influenza may not always be explicitly mentioned on a death certificate, CDC applies statistical models to underlying cause of death data reported as pneumonia and influenza or respiratory and circulatory to estimate the number of nationwide seasonal influenza-associated deaths. Influenza-associated death data in Idaho, where influenza is explicitly mentioned on the death certificate, are tabulated by week of report, number of deaths, geographic location, and age group(s) affected, and provided to the BCDP; this number is likely an underestimate of influenza associated mortality. During the 2005–06 through 2012–13 influenza seasons, an average of 15 influenza-associated deaths were reported annually (range: 5–35).

Laboratory-based viral surveillance

The Idaho Bureau of Laboratories (IBL) conducts sub-typing of viruses isolated from clinical samples year-round, with particular focus on testing during the beginning, middle, and end of the influenza season. Viral surveillance is key to determining circulating subtypes and detection of sporadic cases or outbreaks of novel or variant viruses. Viral surveillance also contributes to detection of antiviral resistance and evaluation of vaccine effectiveness. This information informs public health policy recommendations and future vaccine component selection. Rapid influenza diagnostic test kits are useful, but do not provide subtype or drug sensitivity information. Healthcare providers are encouraged to submit samples to IBL year-round for viral surveillance. Currently, surveillance has been enhanced to detect an influenza variant circulating in the United States in the summer months, swine-associated influenza A (H3N2v). IBL may employ everse transcriptase polymerase chain reaction (RT-PCR) and culture techniques to further evaluate respiratory samples for pathogens.

During the influenza season, each state evaluates data from their influenza surveillance system, including reports such as influenza clusters in long term care facilities and school closures, to provide a simple weekly report to CDC (see www.cdc.gov/flu/weekly/usmap.htm) on the estimated level of statewide geographic spread (no activity, sporadic, local, regional, or widespread). Please remember to report any unusual ILI activity to your public health district.

To learn more about seasonal and unique enhanced surveillance efforts to track the emergence of influenza subtypes visit the CDC website: www.cdc.gov/flu/weekly/overview.htm. To learn more about influenza activity in the United States during the 2012–13 season and the composition of the 2013–14 influenza vaccine, see www.cdc.gov/mmwr/pdf/wk/mm6223.pdf. For national surveillance summaries, see Flu View at www.cdc.gov/flu/weekly/.

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mented dog-allergic persons was negative for response to this vaccine.[2]

Recombinant trivalent vaccine (Flublok®) is produced by incorporating influenza hemagglutinin gene into a baculovirus, infecting a fall armyworm Sf9 cell line with the engineered virus, and formulating the expressed and purified protein into vaccine. It was approved by the FDA in January 2013 for use in adults aged 18–49 years. Recombinant vaccine contains no egg protein and can be produced in 21 days. Providers purchasing Flublok® should be aware that it has a shorter shelf life than other inactivated influenza vaccines, with an expiration period of 16 weeks from the production date.

Changes in influenza vaccine production methods and composition required changes in vaccine categories and abbreviations for 2013–14. The acronym TIV (trivalent influenza vaccine) has been retired. IIV will be used for inactivated influenza vaccine, RIV for recombinant hemagglutinin influenza vaccine, and LAIV will continue to be used for live, attenuated influenza vaccine. A numeric suffix (e.g., LAIV4) specifies the number of influenza virus antigens contained in the vaccine. A prefix "cc" indicates cell culture-based vaccine when appropriate. Seasonal influenza vaccines available during 2013–14 include IIV3 (egg-based and cell culture-based), IIV4 (egg-based), RIV3, and LAIV4. IIV3 will be available in both standard and high dose formulations.

Routine influenza vaccination continues to be recommended for all persons aged ≥6 months. See www.cdc.gov/flu/professionals/acip/2013-interim-recommendations.htm for interim/current ACIP recommendations on seasonal influenza vaccine.

H, 5, 7, N, 1, 9: Update on vaccines for non-seasonal influenza

In light of over 130 cases of influenza with a high mortality rate due to H7N9 reported from China in the past year, U.S. public health officials are preparing in case this virus should begin circulating in the human population. At least one vaccine company began clinical trials with influenza A (H7N9) (see page 3) vaccine this summer. Nine different seed strains have been developed, but antigen yields using egg-based production methods are lower than expected. A recombinant oral influenza A (H7N9) vaccine is reported to have induced robust titers in preclinical testing. Vaccine trials with an influenza A (H7N1) vaccine began in July. H7N1 is one of the flu viruses considered to have pandemic potential. Early trials of inactivated subunit H7 vaccines with and without adjuvant haven't shown a strong immune response. A two-dose series might be necessary to produce an adequate immune response (*e.g.*, priming with LAIV H7 vaccine followed by IIV H7 vaccine). Avian influenza A (H5N1), first detected in humans in

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Another Bird Flu Makes the News: novel influenza A (H7N9)

Epidemiology and characteristics

A novel strain of influenza A (H7N9) was first reported in Eastern China on February 19, 2013. This particular strain has a high case fatality rate: deaths occurred in 44 (32.6%) of 135 cases reported as of August 12. Deaths have been associated with severe pneumonia, acute respiratory distress syndrome (ARDS), sepsis, and septic shock. This strain is believed to be derived from at least four different avian influenza viruses and has been isolated from ducks, chickens, and captive-bred pigeons at live animal markets in China. A history of exposure to birds, mostly chickens, has been reported in 77% human cases. Influenza A (H7N9) is notable for its low pathogenicity in avian species. Low pathogenicity in the avian reservoir implies this virus could spread insidiously in poultry and result in sporadic infections in humans, in contrast to the influenza A (H5N1) strain still circulating in many countries, which causes severe disease in avian species. China and Taiwan are the only two nations which have reported cases of H7N9 as of mid-July.

This H7N9 strain has demonstrated two mutations resulting in increased affinity for human type receptors. The virus has infected individuals of all ages, but has a predilection for middle-aged or older men. As of July 2013, the median age of cases is 61 years, in contrast to the persons reported with the avian influenza H5N1 strain circulating in other countries since 1997, in which the median age of cases is 26 years.

Clinical manifestations of H7N9 have largely been described in persons with severe illness, including persons with severe pneumonia and ARDS. Currently, evidence does not support sustained human-to-human transmission: only 6 cases of H7N9 were confirmed among a sample of 20,000 people with influenza-like-illness during a study in China in March and April 2013. These data suggest that milder cases of H7N9 are not prevalent and the virus is not spreading in the human population.

Diagnosis and treatment

Laboratory diagnosis of H7N9 is accomplished on clinical specimens through real time (RT-PCR) from nasopharyngeal swabs or aspirates. CDC currently recommends testing for H7N9 in individuals requiring hospitalization due to new-onset severe acute respiratory infection for which no alternative infectious etiology is identified, and who have recently (within 10 days of illness onset) traveled to China or Taiwan or had recent close contact with a confirmed case of H7N9. To test for H7N9 in Idaho, providers are asked to contact the Idaho Bureau of Laboratories to discuss sample submission for testing. Nasopharyngeal swabs or nasal aspirates or wash in viral transport medium are preferred unless lower respiratory tract illness is present, in which case endotracheal aspirate or bronchoalveolar lavage is preferred. Of note, rapid flu tests are often unable to detect avian or variant influenza A viruses; consequently, negative rapid tests should not discourage further testing if suspicion is high for these influenza viruses.

To date, H7N9 has been susceptible to the neuraminidase inhibitors oseltamivir and zanamivir. A mutation in the neuraminidase (NA) protein associated with in vitro resistance to neuraminidase inhibitors has been detected in only one clinical isolate to date. Because of the potential severity of illness associated with H7N9 infection, CDC recommends that all confirmed, probable, and suspected cases be treated immediately with oseltamivir 75mg BID for 5 days (patients of any age), or zanamivir 10mg (2 inhalations of 5 mg each) BID for 5 days (patients aged ≥ 7 years), even if onset of symptoms was greater than 48 hours prior to presentation to medical care. A 10-day course of neuraminidase inhibitor therapy is suggested in cases of severe illness. If a patient is so severely ill that oral medication cannot be tolerated, an intravenous zanamivir formulation may be available through compassionate use or emergency investigational new drug request (see www.cdc.gov/flu/avianflu/h7n9-antiviral-treatment.htm).

Provider precautions

CDC is recommending that healthcare providers take additional precautions when caring for patients with confirmed or suspected H7N9, including wearing N95 respirators and eye protection. Asymptomatic healthcare providers who have had unprotected exposure to a patient who meets the case definition may be recommended to take prophylactic antivirals and wear a facemask if necessary to allow them to keep working and ensure adequate staffing of the facility. There is no vaccine available to prevent H7N9 at this time. The World Health Organization is providing coordination and guidance regarding possible vaccine candidates, and clinical trials are slated to begin this month.

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1997, has caused cases and clusters of illness in several countries, but has not achieved pandemic potential. An influenza A (H5N1) vaccine was first licensed in the United States in 2007 for intramuscular use in persons aged 18–64 years who are at increased risk of exposure to the subtype in the vaccine. This vaccine is in the National Stockpile, but is not available commercially.

Phase I clinical trials of an oral recombinant influenza A (H5N1) vaccine for humans are reported to have positive results for safety and immunogenicity. Oral delivery by tablet could greatly simplify logistics of vaccine administration. For a complete list of clinical trials on influenza vaccine, see http://clinicaltrials.gov.

References

[1]Communication from Novartis Vaccines and Diagnostics, Inc.
[2]Wanich N, Bencharitiwong R, Tasi T, et al. In vitro assessment of the allergenicity of a novel influenza vaccine produced in dog kidney cells in individuals with dog allergy. Ann Allergy Asthma Immunol 2010; 104; 426-433.

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Current and past issues are archived online at www.idb.dhw.idaho.gov.

Data Snapshot: Cryptosporidiosis—Idaho, 2007–2012

Idaho's annual rate of reported cryptosporidiosis has been comparable to the national rate since 2001 (Figure). However, during 2007, Idaho experienced a very high rate of 35.4 per 100,000 population; among 513 reported cases, 362 (71%) were attributed to 4 large outbreaks. Annual incidence dropped in 2008, but has been steadily increasing since then. Last year, Idaho's rate of reported cryptosporidiosis more than doubled from the previous year; 5 reported outbreaks accounted for 53% of the reported cases.

During 2007 through 2012, among 1,171 cryptosporidiosis cases, the number reported by month peaked in September, at 29.6 times greater than the lowest number of cases reported by month, which was in February (445 [38%] and 15 [1.3%], respectively). The majority of reported cases per 100,000 population occurred in counties in the Treasure Valley. Age- and gender-specific rates of reported cases per 10,000 population was highest among male (4.0) and female (2.7) children aged <5 years.

Most human cases of cryptosporidiosis are caused by either *Cryptosporidium hominis*, with a primarily human-to-human transmission cycle, or *C. parvum*, which infects both humans and ruminants. Other *Cryptosporidium* species such as *C. felis* and *C. canis* only occasionally cause human infection. Because multiple potential exposures, such as daycare, animal contact, and recreational water are often reported for each case, making the source of infection often unclear, collection and submission of *Cryptosporidium*-positive stool samples from sporadic and outbreak cases to the Idaho Bureau of Laboratories for speciation and genotyping is encouraged to help identify sources of infection.

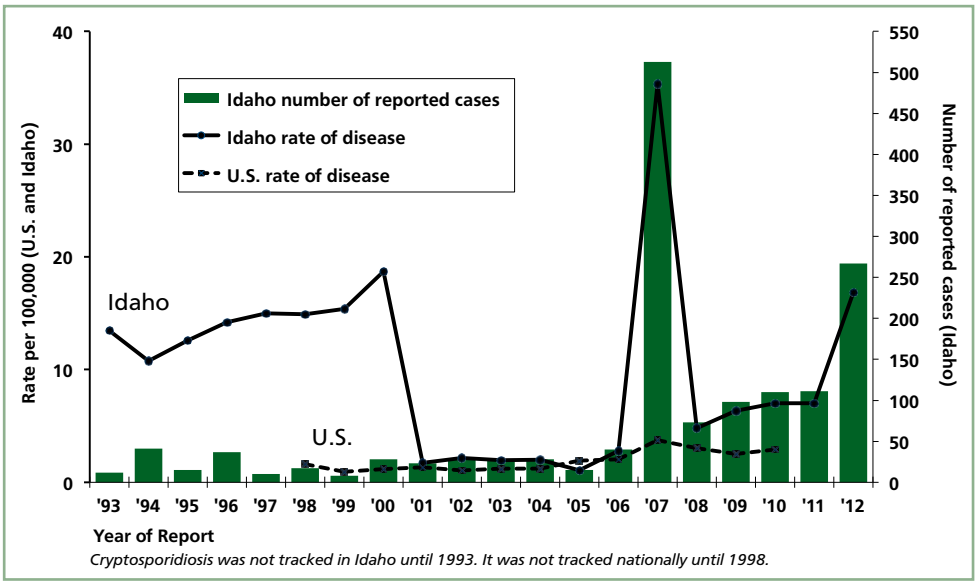

Figure. Number and rate of reported cryptosporidiosis cases, Idaho and U.S., 1993–2012