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IDAHO DISEASE Bulletin

IDAHO DEPARTMENT OF HEALTH & WELFARE

Office of Epidemiology, Food Protection, and Immunization

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Influenza Update: Surveillance, Testing, and Vaccine Safety Monitoring

Providers seeing patients with suspected influenza this fall may ask themselves whether testing for H1N1 is necessary for clinical purposes, desired from a public health standpoint, or even required under certain circumstances. Clinical decision-making is left up to the provider, but in general it is likely that in most circumstances, a positive rapid test might be helpful, but a negative test is not sufficient to rule out influenza disease, and treatment and prophylaxis decisions will need to be made prior to any culture or H1N1 confirmatory results being available. The public health surveillance strategy for this influenza season is outlined on this page and the next page. In no circumstances is testing required, although providers are now required to report patients with probable and confirmed novel H1N1 infection if hospitalized (see next page). As always, feel free to call Dr. Christine Hahn at the Office of Epidemiology, Food Protection, and Immunization (208-334-5939) if you have any clinical questions; Dr. Leslie Tengelsen and Dr. Kris Carter are also available at the same number to answer questions about testing, surveillance, vaccination, or other issues surrounding H1N1.

Tracking influenza in Idaho

Influenza surveillance is a year-round activity designed to monitor illness severity and characterize circulating strains. The emergence of the 2009 H1N1 influenza virus (aka swine flu, pandemic flu) in April and subsequent designation as a pandemic virus prompted heightened influenza surveillance efforts. To that end, regular influenza surveillance activities have been enhanced with 2009 H1N1 influenza-specific surveillance methods.

Regular influenza surveillance

1. **ILI sentinel surveillance.** Influenza-like illness (ILI) surveillance is designed to monitor the relative level of influenza activity. Eighteen sentinel healthcare provider sites across the state are reporting weekly the proportion of visits for ILI among all visits and participating in virologic surveillance.
2. **Virologic surveillance.** The Idaho Bureau of Laboratories (IBL) has specific laboratory surveillance protocols for ILI sites and hospital clinical laboratories in order to characterize circulating strains. ILI sites routinely submit a sample of respiratory specimens for viral sub-typing year-round; with particular focus on sampling early, middle, and late in the influenza season. Many samples are routinely forwarded to the Centers for Disease Control and Prevention (CDC) for additional antiviral drug resistance testing and monitoring.
3. **Mortality tracking.** The Idaho Department of Health and Welfare (DHW) receives and reviews cause of death data daily. Influenza-associated death data are tabulated by number, seasonality, and age and reported to the CDC.
4. **State influenza activity code.** A weekly review of influenza surveillance is used to determine relative statewide influenza activity levels. The

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weekly state activity code, which is an assessment of overall influenza activity based on the data above and other reports such as media reports, school closures, *etc*., is reported to the CDC and available at **www.cdc.gov/flu/weekly/.**

Enhanced influenza surveillance activities

Novel influenza A reporting rules went into effect on September 1, 2009.

1. **2009 H1N1 influenza reporting.** As of September 1, 2009 all laboratories confirming the presence of 2009 H1N1 influenza (currently limited to Quest Diagnostics, LabCorp, and IBL) are required to report to Idaho local or state public health officials. Additionally, physicians and hospitals must report hospitalized probable or confirmed cases of novel H1N1. Local public health district staff may investigate any probable or confirmed case of novel influenza A. A tabulation of reported counts by county of residence is updated each Wednesday and available at **www.panflu.idaho.gov.**
2. **Tracking severity.** All hospitals are now required to report all hospitalized laboratory-confirmed and probable cases (those individuals with a positive influenza test of any sort) to IDHW. Among these cases, extended chart reviews will take place for Ada, Bingham, and Kootenai County residents to evaluate risk factors for severe disease.
3. **Aggregate reporting to CDC.** Currently CDC is asking all states to report the cumulative number of hospitalizations for flu-like illness and the cumulative number of deaths associated with influenza and pneumonia weekly by age group.

Laboratory testing

Many preliminary influenza tests, which identify the presence of influenza A but do not indicate the subtype, may be done within the office or hospital clinical laboratory. They include rapid influenza diagnostic tests, which may differentiate between influenza A and B, and other tests such as DFA, IFA, or culture. Two commercial laboratories (Quest Diagnostics [**www.questdiagnostics.com/**] and LabCorp [**www.labcorp.com/wps/portal/**]) are offering confirmatory laboratory testing for the 2009 H1N1 influenza virus. They use an FDA-authorized real-time RT-PCR technique under an emergency use authorization.

The IBL offers confirmatory testing for the 2009 H1N1 influenza virus and circulating seasonal viruses under the following circumstances:

1. a person hospitalized with suspected influenza, or
2. a person with a fever AND either cough or a sore throat who:
   - works in a hospital setting, or
   - is pregnant (regardless of hospitalization status), or
   - is part of a possible outbreak being investigated by public health officials.

Appropriate clinical specimens

Specimens acceptable for testing include the following: nasopharyngeal swabs, nasal aspirate or swab, or a combined nasopharyngeal/oropharyngeal swab. For patients who are intubated, an endotracheal aspirate should also be collected. Specimens collected by other methods, such as a bronchoalveolar lavage should be accompanied if possible by an approved specimen listed above. All specimens must be accompanied by the appropriate laboratory submission form which can be found on "For Providers" page of **www.panflu.idaho.gov** under "Testing and Surveillance Information: Laboratory Testing."

H1N1 vaccine safety monitoring

On September 15, 2009 the FDA approved four vaccines against the 2009 H1N1 influenza virus: three injectable products containing inactivated virus and one intranasal product containing live attenuated virus. Because clinical trials use relatively small numbers of subjects, very rare adverse events and delayed reactions associated with a vaccine might not be detected until the vaccine is given to millions of people. Health care providers are encouraged to report any clinically significant or unexpected event (even if uncertain that vaccine caused the event) for any vaccine through the Vaccine Adverse Event Reporting System (VAERS) at **www.vaers.hhs.gov**. In addition, a severe reaction known or suspected to be due to any vaccine is a reportable condition in Idaho and must be reported to the Idaho DHW or your local public health district within one working day of identification. If you have any questions about adverse event reporting, you may contact the Idaho Immunization Program's Vaccine Safety Coordinator, Jeff Kingsbury, at 208-334-5967.

In addition to monitoring VAERS data in collaboration with the Food and Drug Administration (FDA), CDC will monitor Influenza A (H1N1) 2009 Monovalent Vaccine safety through:

1. the Vaccine Safety Datalink (a collaborative effort between CDC and eight large managed care organizations),
2. the Vaccine Analytic Unit (a collaboration among the Department of Defense, the CDC, and the FDA),
3. the Clinical Immunization Safety Assessment (a collaboration between CDC and six academic centers with expertise in immunization safety), and
4. active case-finding for Guillain-Barré syndrome (GBS) through CDC's Emerging Infections Program, a population-based collaboration between CDC and partners in ten states. The provisional case definition from the Brighton Collaboration (see **www.brighton-collaboration.org**) will be used for GBS surveillance.

Your patients may be particularly concerned about the safety of Influenza A (H1N1) 2009 Monovalent Vaccine because of the association between the 1976 swine flu vaccine and GBS in adults (see the Institute of Medicine's Immunization Safety Review: Influenza Vaccines and Neurological Complications at **www.nap.edu/catalog.php?record_**

id=10822. The CDC has developed a frequently asked question webpage (see **www.cdc.gov/h1n1flu/**) for patients who have concerns about Influenza A (H1N1) 2009 Monovalent Vaccine safety. In addition, rumors have circulated that this vaccine will be mandatory. Patients should be informed that the Advisory Committee on Immunization Practices makes recommendations on who should receive vaccine, but that vaccine is not mandatory in Idaho.

Infant Botulism: Recognition and Resources

Infant botulism investigations in Idaho suggest that clinicians might have a low index of suspicion for infant botulism. Infant botulism is a rare disease that primarily affects infants aged 1–50 weeks (median 15 weeks). Although rare, infant botulism is the most common form of human botulism in Idaho and the United States. During 2004–2008, all three reported cases of botulism in Idaho were infant botulism. In the United States, approximately 65% of reported, laboratory-confirmed botulism cases are infant botulism.

Unlike classic foodborne botulism, infant botulism occurs when ingested spores of *Clostridium botulinum* colonize, grow, and produce botulinum neurotoxin in the infant's large intestine. The only spore-containing food associated with infant botulism is honey; in most cases, the source of the spores is unknown and thought to be environmental as *C. botulinum* spores are ubiquitous in soil worldwide. Infant botulism caused by toxins produced by other clostridia (*i.e., C. butyricum, C. baratii*) has also been reported. Breastfeeding is not protective, but infant botulism tends to occur in formula-fed infants at a younger age.

Botulinum toxin binds at the neuromuscular junction; prevents release of acetylcholine; and produces a symmetrical, descending, flaccid motor paralysis.

The first indication of illness is usually a decreased frequency of defecation, or constipation (three or more days without defecation in a previously regular infant), but this sign is frequently overlooked. Typically, caregivers first notice that the infant is feeding poorly and breast-feeding mothers may experience breast engorgement because the baby's suck is weak. The infant appears listless, breathing might become shallow, and the cry is feeble. Drooling may become more noticeable, but is sometimes attributed to teething rather than dysphagia.

On clinical presentation, in mild cases or in the early stages of illness, signs may be subtle and easily overlooked. The first signs of illness are related to the cranial nerves. Careful examination can elicit cranial nerve palsies and muscle fatigability (see Table).

On initial presentation, the patient typically has some or all of the following findings: weak cry, diminished suck and gag, drooling and/or pooling of saliva, ptosis (which may not be evident until the infant's head is held erect), dilated and/or sluggishly reactive pupils, disconjugate gaze, blunted facial expression, poor head control, decreased anal sphincter tone, hypotonia, and generalized weakness ("floppy baby"). Deep tendon reflexes may be normal or decreased. Sensation remains intact, but may be difficult to demonstrate because of the motor paralysis. Rarely death without preceding signs, resembling sudden infant death syndrome, can occur. Suspected sepsis is the most common admission diagnosis for patients with infant botulism.

Immune globulin (BabyBIG®)

A human-origin botulinum immune globulin (BabyBIG®) for treatment of infant botulism is available from the California Department of Public Health's Infant Botulism Treatment and Prevention Program (IBTPP) at a current cost of $45,300. According to the IBTPP, treatment with BabyBIG® is cost-effective as it reduces the mean hospital stay from approximately 5.7 weeks in untreated patients to approximately 2.3 weeks. To obtain BabyBIG®, the patient's physician must contact the IBTPP on-call physician in California at (510) 231-7600 to review indications for treatment. Treatment should be started as early in the illness as possible. See **http://infantbotulism.org** for more information.

Table. Physical examination signs helpful in the diagnosis of infant botulism

Test 1. Take the patient to a dark room. Shine a bright light into the eye; note the quickness of pupillary constriction. Remove the light when constriction is maximal; let the pupil dilate. Then immediately repeat, continuing for 2–3 minutes. Supportive findings: The initially brisk pupillary constriction may become sluggish and unable to constrict maximally.

Test 2. Shine a bright light onto fovea, keeping it there for 1–3 minutes even if the infant tries to deviate the eyes. Supportive findings: Latent ophthalmoplegia may be elicited, and/or purposeful efforts to avoid the light may diminish, because fatigability with repetitive muscle activity is the clinical hallmark of botulism. Also observe for initial squirming of the extremities that may diminish because of fatigability.

Test 3. Place a clean fifth finger in the infant's mouth, taking care not to obstruct the airway. Note the strength and duration of the reflex sucking. Supportive findings: The suck is weak and poorly sustained. The gag reflex strength also may be quickly checked (if the infant has not been fed recently).

In addition, constrictor muscle fatigability may yield a "pseudo" gibbus.

Source: Adapted from Arnon SS. Infant botulism. pp. 1866 in Feigin RD, Cherry JD, Demmler-Harrison GJ, Kaplan SL, eds. Textbook of Pediatric Infectious Diseases, Sixth Edition. WB Saunders, Philadelphia, 2009 and modification of 2004 table version accessed on 6/15/2009 at **http://infantbotulism.org**

Idaho case study

A previously well 5-month old white male was hospitalized for inability to feed and dehydration. He lived on a dairy farm and was exclusively breastfed. Two days before admission, a throat swab was positive for group A *Streptococcus* on rapid antigen testing, and he started oral amoxicillin. He had not previously taken any medications, and no toxin exposure was suspected. Because he typically had bowel movements every 5–10 days, no change in stooling was noted by his parents.

No growth was seen on culture of blood, urine, and CSF. CBC, chemistries, and CSF findings were normal. He was treated with intravenous ceftriaxone and intravenous hydration, but continued to be unable to feed. He was afebrile with normal vital signs. Intravenous fluconazole was given because of thrush.

After six days, he was transferred to the care of a pediatric gastroenterologist at a children's hospital. Upper gastrointestinal endoscopy was done to rule out esophagitis or esophageal foreign body.

Infantile botulism was considered. Examination at that time included weak cry, ptosis, poor head control, large sluggishly reactive pupils, and absence of suck and gag reflexes. He was able to lift arms or legs against gravity, was alert and attentive to his parents, had conjugate extraocular movements, and had detectable deep tendon reflexes. Stool was submitted through the Idaho Bureau of Laboratories for botulinum toxin assay. He received botulinum immune globulin (BabyBIG®) after the attending physician contacted IBTPP. He was discharged from the hospital receiving nasogastric feedings six days after receiving botulinum immune globulin. He made a complete recovery over several months. This case illustrates the nonspecific symptoms that make infant botulism challenging to diagnose, and serves as a reminder that botulism should be in the differential diagnosis of any infant with poor feeding.

Reporting and testing

Every suspected case of botulism must be reported immediately to your local public health district or the Idaho Department of Health and Welfare (IDHW). Please be aware that contacting California's IBTPP does not constitute a report to Idaho public health officials. In addition, all requests for testing for infant botulism must be approved by the IDHW and coordinated through the Idaho Bureau of Laboratories—the IBTPP does not provide testing for Idaho patients. A stool or enema specimen is required to perform a direct toxin analysis and to isolate *Clostridium botulinum*. See **www.healthandwelfare.idaho.gov/Health/Labs/ClinicalMicrobiology/tabid/190/Default.aspx** for sample submission guidelines and **http://infantbotulism.org** for detailed specimen collection procedures.

CME

The American Academy of Pediatrics offers CME on infant botulism (AAP Grand Rounds 19:30-31, 2008 at **http://aapgrandrounds.aappublications.org/cgi/content/extract/19/3/30**).

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ROUTINE 24-Hour Disease Reporting Line
1.800.632.5927

EMERGENCY 24-Hour Reporting Line
1.800.632.8000

An electronic version of the Rules and Regulations Governing Idaho Reportable Diseases may be found at http://adm.idaho.gov/adminrules/rules/idapa16/0210.pdf.

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