Diphtheria

Steve Allen
Director, Field Epidemiology

The term “diphtheria” comes from the Greek term meaning “leather” or “hide” to describe the growth inside the throat. The disease has been recorded in history as early as the 5th century BCE as noted by Hippocrates. It wasn’t until the 1883 that Edwin Klebs described the bacterium. In 1884, Friedrich Loeffler, using Robert Koch rules of linking a disease to a pathogen, first cultivated the bacterium later known as *Corynebacterium diphtheriae*. He also observed that the bacterium produced an exotoxin. In 1888, Emile Rouz and Alzandre Yerson were able to inoculate animals with *C. diphtheriae*. In 1890, Shibasaburo Kitasato and Emil von Behring were first to immunize guinea pigs and in 1891, were first to cure a person with diphtheria. In 1895, horses were found to be suitable animals for making diphtheria antitoxin. Horse serum is still used today to make the antitoxin. For the next 20 years, science was able to make safer antitoxins and toxoids. In 1924, Ramon demonstrated using formaldehyde to render the diphtheria toxin to a non-toxic substance thus creating a safe vaccine. Since that time, the diphtheria toxoid has been refined to produce a very safe and effective vaccine. Diphtheria is rarely seen in industrialized nations because of high vaccination rates.

Humans are the only known reservoir for *C. diphtheriae*, which can cause respiratory or cutaneous infections. Different strains of *C. diphtheriae* can produce toxins. Diphtheria is extremely rare in the US, and all cases are related to travel to countries where diphtheria is still common.

Cutaneous diphtheria is generally mild and produces sores or ulcers on the skin. The sores or lesions may be indistinguishable from impetigo.. If left untreated, symptoms may last from 2-6 weeks. The disease rarely causes complications and only 1%-2% infections are toxigenic. It is a common disease in the tropics but in the temperate climates it is generally seen during the cold season. Outbreaks may occur in persons with poor hygiene and in populations that live in crowded conditions. Normal treatment includes antibiotics to eliminate the bacterium and a dose of diphtheria toxoid. With rare cutaneous toxigenic species, diphtheria antitoxin (DAT) is used.

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Respiratory diphtheria is more serious than cutaneous disease. Respiratory diphtheria is generally spread by airborne droplets from coughing and sneezing but cases can occur from contact with respiratory secretions, contaminated personal items, and household items.

The incubation period is 2-5 days with a range 1-10 days. Initial symptoms include sore throat, difficulty swallowing, low-grade fever, and malaise. In severe cases, generally within 3-5 days, a tough, grayish-white pseudomembrane develops on the tonsils, pharynx, and/or larynx. This is caused from the surrounding dead tissue affected by the toxin. Diphtheria should be considered when the appearance of the pseudomembrane is present. Other diseases that have similar symptoms are streptococcal throat infection, Epstein-Barr virus, and cytomegalovirus

(both of which cause infectious mononucleosis syndrome). The appearance of the pseudomembrane is an indication of moderate or severe disease. The pseudomembrane is difficult to surgically remove and patients may need intubation or tracheotomy. Suffocation can occur without medical intervention. Another symptom is the appearance of throat swelling, otherwise known as the "bull neck." The toxin causes the inflammation of the cervical lymph nodes and soft tissue. Left untreated, the toxin spreads and may cause myocarditis within 1-2 weeks and neuritis within 2-8 weeks after the onset. If myocarditis occurs early in the illness stage, death becomes a high probability. Neurologic complications similar to Guillain-Barre syndrome may occur two weeks after illness. The nervous system may resolve itself months from the onset of the disease but myocarditis symptoms may last a lifetime. Kidney damage may also result from the effects of the toxin. Without treatment, most symptoms last two weeks but complications may last for months. Other lesser known symptoms are pneumonia, otitis media, and paralysis.

Diphtheria antitoxin (DAT) is used to neutralize the toxin. Additional treatment includes antibiotics, supportive care, and immunization with a diphtheria toxoid. At the first signs of possible diphtheria, the physician must notify the Centers for Disease Control and Prevention (CDC) Emergency Operation Center at 770-488-7100. A diphtheria duty officer will discuss the case and determine if DAT is recommended. If required, DAT will be sent from one of the U.S. Public Health Service quarantine stations. It is important to administer DAT as soon as possible: if DAT is administered within 24-48 hours, the mortality rate is 4%. After day 3, it increases to 16.1% and the rises to 29.9% by day 7. DAT neutralizes toxin that has not attached to the cells. As time progresses, more toxin is produced, which damages additional cells. Once the cell has absorbed the toxin, DAT is ineffective in preventing cellular damage. Dosage and sensitivity for DAT can be found on the CDC web site. DAT does not eliminate the bacterium, so the patient must be given antibiotics to prevent further spread of the organism. Procaine penicillin G and erythromycin are recommended antibiotics. Generally the first 48-hour regiment of antibiotics will render the patient non-communicable. Laboratory testing must confirm the patient is no longer communicable.

According to the Communicable Disease Reporting Rule for Physicians, Hospitals, and laboratories, 410 IAC 1-2.3, cases of diphtheria are required to be reported immediately to the ISDH in collaboration with the local health department to confirm the case and follow-up testing and identify contacts of cases for testing, prophylaxis, immunization, and surveillance for symptoms.

Upon notification of a diphtheria case, laboratory samples (blood, throat swab) will be sent to the CDC for confirmation. The provider may send samples of nasopharyngeal and throat culture to the ISDH laboratory rule out possible cases. The ISDH laboratory or the Epidemiology Resource Center must be notified prior to any submission. It is important to obtain samples before starting antibiotics to prevent false negative results.

The diphtheria toxoid was developed around 1921 but not widely used until the early 1930's. Today it is part of the routine immunization given to children and adults. Past infection of diphtheria disease does not confer lifelong immunity. Immunizations for children are three or four primary doses, depending upon their age, and a booster dose every 10 years thereafter. All adults should get a booster every 10 years. Although the World Health Organization reported that the last known case in the U.S. occurred in 2012, it is important to remain current with vaccination, since diphtheria still commonly occurs in other parts of the world.

An unusual case occurred in Indiana in 1996. On October 24, a patient reported having symptoms of fever, sore throat, and difficulty swallowing. On October 26, she went to an outpatient clinic with more severe symptoms and a swollen neck. She tested negative for streptococcal disease and was diagnosed with acute pharyngitis. She was giving an injection of antibiotic and prescribed oral antibiotics. On the morning of October 27, she was hospitalized with vomiting, difficult breathing, and inability to swallow. Her temperature

was normal but she had mild tachycardia, swelling of the uvula with membranous exudates covering the uvula and both tonsils, bilateral cervical lymphadenopathy, and soft tissue swelling. Based on the patient's history of never receiving any vaccinations, doctors suspected respiratory diphtheria. After consulting with the CDC, DAT was shipped and administered on October 27 along with continued antibiotics. The patient started to improve on October 28 and was discharged on November 1. The patient was given a dose of diphtheria vaccine and instructed to finish the series.

The patient reported never traveling outside the U.S. and had no known contacts with international travelers during the previous month. She attended a folk art festival on October 20 but had not consumed any unpasteurized milk products nor had she had any contact with any farm animals. Laboratory results from throat and membrane fragments were sent to a private laboratory and the CDC. Results from both laboratories were negative. On October 31, the CDC reported the PCR test for toxin production was positive for *C. ulcerans*. Subsequence testing by the CDC confirmed this agent as the cause of the woman's illness. *C. ulcerans* is one of the species of diphtheria that is found in humans and animals, especially cattle. It was critical to treat this patient with DAT prior to laboratory confirmation because toxigenic *C. ulcerans* has been known to cause human deaths.

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Lassa Fever Exposure Aboard a Commercial Flight

Stephanie English
Field 6 Epidemiologist

The CDC contacted the ISDH in early April about four Indiana residents who had traveled to Liberia and had been exposed to a case of Lassa Fever, a type of viral hemorrhagic fever, during their return flight to the US on March 31. The CDC issued messaging to flight passengers regarding the case, disease transmission, risk of exposure (direct contact with blood or body fluids), symptom monitoring, and where to find additional information. The CDC categorized travelers on the flight into the following risk groups:

- High Risk: Exposed to body fluids of index case (direct skin contact or mucous membrane exposure)
- Low Risk: Sat near index case, but no contact with bodily fluids
- No Risk: Did not sit near index case and did not have contact with bodily fluids

Using the information provided by the CDC, the District 6 Field Epidemiologist quickly contacted the Indiana travelers who were on the same flight as the infected patient. Only one traveler was reported as being in the coughing radius and needed to be interviewed and monitored. However, all four Indiana travelers were members of a larger group, which included five individuals from other states, who taught children in Liberia to read and use laptop computers. This tightly-knit group had significant concern about only one person being interviewed.

To allay the concerns of the returning travelers, the group's director and the Field Epidemiologist decided to interview the entire group. A group interview also ensured that everyone was asked the same questions and would also decrease the amount of time required to conduct. The group interview proved fun and challenging as it was difficult to keep up with paperwork and documentation. The Field Epidemiologist explained the purpose and content of the interview and ensured that all participants understood. None of the participants reported having contact with anyone's blood or body fluids from the flight, assisting any sick passengers on the flight, or having any current fever or other symptoms at the time of the interview.

All nine travelers were assessed in the low risk category and asked to monitor their fever until April 21, 2014. If they developed a fever they were instructed to seek care immediately and inform the health care provider of their exposure and travel. The Field Epidemiologist maintained contact with all nine travelers, who completed monitoring without incident and remained symptom-free, and sent all information to the CDC for distribution to the appropriate states of jurisdiction.

This experience provided several lessons. It was important to understand the facts about this particular disease, because it is not a common disease in Indiana or the US. Research from reliable and credible sources was needed before calling travelers. The Field Epidemiologist utilized an effective interview method that to gain solid information in a short amount of time and also allay concerns of the travelers. Although Lassa Fever is not common in Indiana or the US, it is important to remain vigilant and respond quickly to infectious disease threats that may present via international travel.

Health Care Access and Chronic Disease

Linda Stemnock
BRFSS Coordinator

The Indiana State Department of Health received 2012 Prevention and Public Health Funds through the Centers for Disease Control and Prevention (CDC) to include the Health Care Access Module in the 2013 Indiana Behavioral Risk Factor Surveillance System (BRFSS) survey. The BRFSS is an annual random digit-dial telephone (landline and cell) survey of non-institutionalized adults ages 18 years and older. The survey is conducted through a cooperative agreement between state departments of health and the CDC, and all states and the District of Columbia participate.

The Health Care Access Module obtained information on health insurance coverage, doctor visits, not being able to take medication as prescribed due to cost, satisfaction with care received, and if any medical bills were being paid off over time. The July 2014 BRFSS newsletter provided an overview of the results from the Health Care Access Module.

According to Healthy People 2020, access to health care impacts:

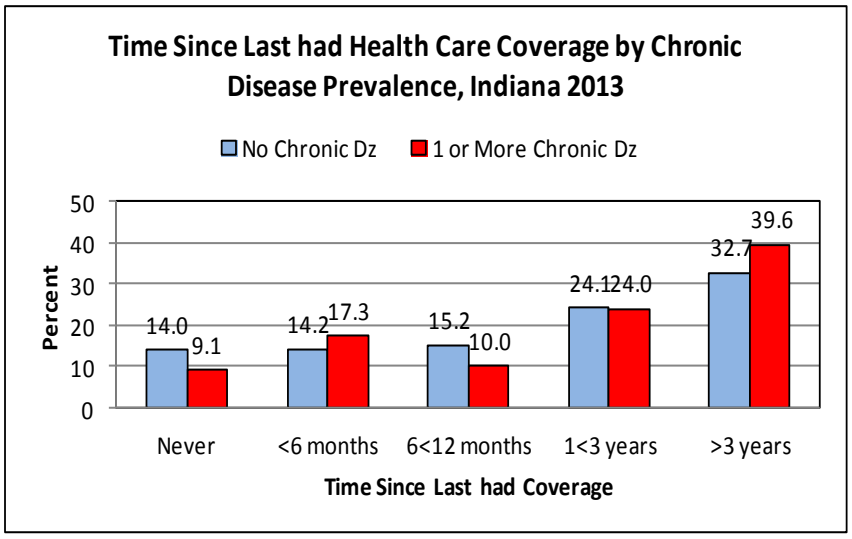
- Overall physical, social, and mental health status
- Prevention of disease and disability
- Detection and treatment of health conditions
- Quality of life
- Preventable death
- Life expectancy

Adequate access to medical care, including preventive services, can reduce premature morbidity and mortality, as well as enhance overall quality of life. Delays in health care can lead to poorer health outcomes and higher medical costs over time. Since more than 96% of adults age 65 years and older reported having Medicare, this newsletter focuses on adults ages 18-64 years.

Chronic diseases and conditions are among the most common, costly, and preventable of all health problems (CDC). Deaths from cancer and heart disease made up 46% of deaths among Indiana residents in 2012. Almost 50% (47.3%) of adults ages 18-64 years of age reported they had at least one chronic disease (heart, hypertension, stroke, cancer, arthritis, kidney, diabetes, asthma or chronic obstructive pulmonary disease), corresponding to an estimated 1.9 million Indiana adults.

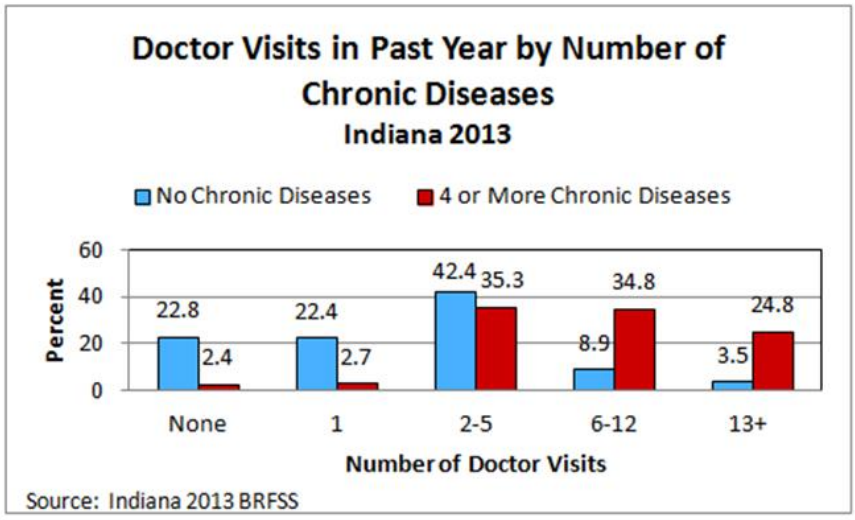
Respondents were asked if they were currently covered by health insurance or health coverage plans. Overall, 20.7% of respondents reported not being currently covered, and for those with one or more chronic disease, the prevalence of not being currently covered ranged from 9.3% (skin cancer) to 28.0% (chronic obstructive pulmonary disease). Respondents who had coverage were also asked if there was any time in the past 12 months that they did not have any health insurance or coverage, and if they responded “yes”, they were asked how long it had been since they last had health care coverage. For those who had no health care coverage any time in the past 12 months, there were no significant differences between those without a chronic disease and those with more than one in the time since they last had health care coverage (Figure 1).

Figure 1



Doctor visits are important, especially when managing a chronic disease. Respondents with four or more chronic diseases were less likely than those without a chronic disease to have one or no visits in the past year, and more likely to have six or more visits (Figure 2). However, respondents with two or more visits were more likely than those with one or no visits to report they were paying off bills over time.

Figure 2

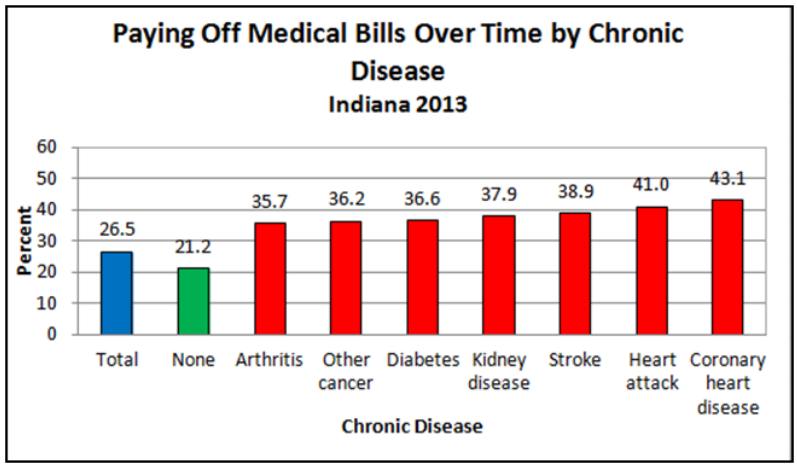


Prescription medication may be prescribed for a chronic disease. Overall, those who did not have health care coverage in the past 12 months were more likely than those with health care coverage to report not being able to take their medication as prescribed because of cost (19.5% vs. 7.3% respectively). Respondents with one or more chronic diseases were more likely than those without chronic disease to report not being able to take their medication as prescribed because of cost (16.3% vs 5.1%, respectively).

Approximately 4% of respondents with at least one chronic condition reported that they did not have any prescribed medication, compared with 15.6% of those without a chronic condition.

Respondents were asked if they currently had any medical bills that are being paid off over time. Overall, an estimated 26.5% of adults reported they were paying off medical bills. Adults with a chronic disease were more likely than those without to have medical bills being paid off over time (Figure 3).

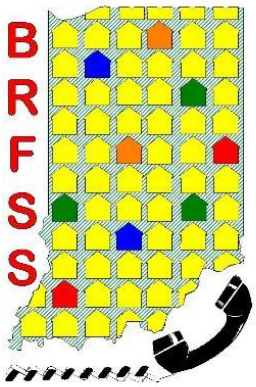
Figure 3



Respondents were also asked if they had delayed getting needed medical care for a reason other than cost in the past 12 months. Those without a chronic condition were more likely than those with one or more to report they did not delay getting medical care or did not need medical care (85.5% vs. 80.3%, respectively). There were no differences between those with and without chronic conditions in the level of satisfaction with the health care they received: very satisfied (63.9% for those with no chronic diseases; 60.1% for those with one or more); somewhat satisfied (30.9% for those with no chronic conditions; 35.1% for those with one or more); and not at all satisfied (5.2% for those with no chronic conditions; 4.9% for those with one or more).

For additional information on finding health care, please visit the Indiana Family and Social Services Administration at http://www.in.gov/fssa/index.htm or the federal Health Resources and Services Administration at http://www.hrsa.gov/gethealthcare/index.html.

The BRFSS survey uses a complex sample design to randomly select respondents with either listed or unlisted landline and cell telephones. State health departments conduct the BRFSS surveys continuously through the year using a standardized core questionnaire and optional modules. The BRFSS is the sole source of state-level health risk factors, behaviors, and prevalence of certain chronic conditions. The BRFSS relies on self-reported data. This type of survey has certain limitations that should be understood when interpreting the data. Respondents have the tendency to underreport behaviors that may be considered socially unacceptable, such as smoking and driving after drinking alcohol. Conversely, respondents may overreport behaviors that are desirable, such as physical activity. The differences reported in this article are statistically significant ($p<0.05$) unless otherwise noted.



Training Room

INDIANA STATE DEPARTMENT OF HEALTH
IMMUNIZATION PROGRAM PRESENTS:
Immunizations from A to Z

Immunization Health Educators offer this FREE, one-day educational course that includes:

- Principles of Vaccination
- Childhood and Adolescent Vaccine—Preventable Diseases
- Adult Immunizations—Pandemic Influenza
- General Recommendations on Immunization
    - Timing and Spacing
    - Indiana Immunization Requirements
    - Administration Recommendations
    - Contraindications and Precautions to Vaccination
- Safe and Effective Vaccine Administration
- Vaccine Storage and Handling
- Vaccine Misconceptions
- Reliable Resources

This course is designed for all immunization providers and staff. Training manual, materials and certificate of attendance are provided to all attendees. Please see the Training Calendar for presentations throughout Indiana. Registration is required. To attend, schedule/host a course in your area or for more information, please visit http://www.in.gov/isdh/17193.htm.

ISDH Data Reports

The following data reports and the *Indiana Epidemiology Newsletter* are available on the ISDH webpage:
http://www.IN.gov/isdh/

HIV/STD/Viral Hepatitis Semi-Annual Report (June 2007 – December 2013)	Indiana Mortality Report (1999-2012)
Indiana Cancer Reports: Incidence; Mortality; Facts & Figures	Indiana Linked Infant Birth/Death Report (1999, 2002, 1990-2003)
Indiana Health Behavior Risk Factors Report (1999–2012)	Indiana Natality Report (1998–2012)
Indiana Health Behavior Risk Factors (BRFSS) Newsletter (2003–2014)	Indiana Induced Termination of Pregnancy Report (1998–2013)
Indiana Hospital Consumer Guide (1996)	Indiana Marriage Report (1995, 1997-2004)
Public Hospital Discharge Data (1999–2013)	Indiana Infectious Disease Report (1997 - 2012)
Assessment of Statewide Health Needs (2007)	Indiana Maternal & Child Health Outcomes & Performance Measures (1989-1998 through 2002–2011)

HIV Disease Summary

Information as of September 30, 2014 based on 2010 population of 6,483,802

HIV - without AIDS:

89	New HIV cases from July 1, 2014 thru September 30, 2014	12-month incidence	1.37 cases/100,000
5,314	Total HIV-positive, alive and without AIDS on September 30, 2014	Point prevalence	81.95 cases/100,000

AIDS cases:

73	New AIDS cases from July 1, 2014 thru September 30, 2014	12-month incidence	1.12 cases/100,000
6,069	Total AIDS cases, alive on June 30, 2014	Point prevalence	93.60 cases/100,000
12,522	Total AIDS cases, cumulative (alive and dead) on September 30, 2014		

Reported cases of selected notifiable diseases		
Disease	**Cases Reported in July - September**	
	2013	**2014**
Animal Bites	1,914	1,739
Brucellosis	1	0
California Serogroup Encephalitis (La Crosse)	1	0
Campylobacteriosis	231	126
Chlamydia*	7,291	7,670
Cryptococcus neoformans	7	4
Cryptosporidiosis	37	23
Dengue Fever	0	0
E. coli, shiga toxin-producing	40	34
Ehrlichiosis	4	9
Giardiasis	57	49
Gonorrhea*	1,915	2,016
Haemophilus influenzae, invasive	31	19
Hemolytic Uremic Syndrome (HUS)	1	0
Hepatitis A	10	2
Hepatitis B (acute)	32	6
Hepatitis B, infant born to HBsAg-positive mother	1	0
Hepatitis C (acute)	47	3
Hepatitis D	1	0
Hepatitis E	0	0
Histoplasmosis	19	24
Influenza-Associated Death	0	0
Influenza, other or unspecified	2	0
Legionellosis	34	44
Listeriosis	2	1
Lyme Disease	49	35
Malaria	8	10
Measles (rubeola)	1	1
Meningitis, other	3	5
Meningococcal, invasive	4	1
Mumps	2	4
Other arboviral		4
Pertussis (Whooping Cough)	208	134
Rabies, Animal	6	4
Rocky Mountain Spotted Fever	1	0
Rubella	0	0
Salmonellosis	244	131

Reported cases of selected notifiable diseases (cont.)		
Disease	**Cases Reported in July – September**	
	2013	**2014**
Shigellosis	31	506
Severe *Staphylococcous aureus* Infection in Previously Healthy Person	7	1
Streptococcus disease, invasive, Group B, Newborn	3	10
Streptococcus Group A, invasive	27	10
Streptococcus Group B, Invasive (All ages)	108	45
Streptococcus pneumoniae (invasive, all ages)	96	62
Streptococcus pneumoniae (invasive, drug resistant)	0	0
Streptococcus pneumoniae (invasive, <5 years of age)	7	3
Syphilis (Primary and Secondary)*	61	36
Toxic Shock Syndrome, streptococcal (STSS)	2	0
Tuberculosis	0	0
Tularemia	0	0
Typhoid Fever (Salmonella Typhi)	0	1
Typhus/Rickettsial disease	0	0
Varicella (Chickenpox, confirmed and probable)	13	18
Varicella (Hospitalization or Death)	1	2
Vibriosis (non-cholera Vibro species infections)	7	4
West Nile Virus neuroinvasive disease	5	1
West Nile Virus non-neuroinvasive disease (aka West Nile Fever)	2	0
Yersiniosis	1	3

***2014 STD data are provisional**

For information on reporting of communicable diseases in Indiana, call the *ERC Surveillance and Investigation Division* at 317.233.7125.

Indiana State Department of Health
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Indianapolis, IN 46204
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epinewsletter@isdh.in.gov

The *Indiana Epidemiology Newsletter* is published quarterly by the Indiana State Department of Health to provide epidemiologic information to Indiana health care professionals, public health officials and communities.

FIND US ON THE WEB

http://www.in.gov/isdh/25154.htm

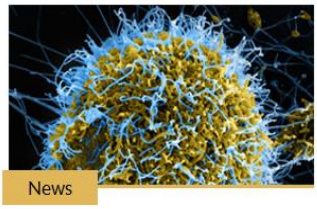
Indiana State Department of Health
Epidemiology Resource Center

Social Media

The Indiana State Health Department is on social media! Check out our social media pages for the latest health information, updates, event information and photos. Like us on Facebook at www.facebook.com/ISDH1. Follow us on Twitter @StateHealthIN. Watch videos on YouTube.

CDC News Updates

What's New



News

Ebola Update

CDC taking active steps related to hospital preparedness for Ebola treatment

News

Passenger Notifications

CDC is expanding its outreach to airline passengers now to include those who flew from Dallas Fort Worth to Cleveland

Feature

EV-D68 and US Children

Parents, take basic steps to protect your child from enterovirus D68.

News

New, Faster EV-D68 Lab Test

CDC Develops a New, Faster Lab Test for Detecting Enterovirus D68 (EV-D68)

http://www.cdc.gov/