State of Alaska Epidemiology Bulletin

Department of Health and Social Services
William J. Streur, Commissioner
Ward B. Hurlburt, MD, MPH, CMO

3601 C Street, Suite 540
Anchorage, Alaska 99503 http://www.epi.Alaska.gov

Division of Public Health
Kerre Shelton, Director

Local (907) 269-8000
24 Hour Emergency (800) 478-0084

Editors:
Joe McLaughlin, MD, MPH
Louisa Castrodale, DVM, MPH

Bulletin No. 15 August 19, 2014

Non-toxigenic Diphtheria Cases — Alaska, 2012–2013

Introduction

Diphtheria is an acute, toxin-mediated disease caused by the *Corynebacterium diphtheriae* bacterium. With respiratory diphtheria, the toxin can cause local tissue destruction, myocarditis, neuritis, and extensive membrane formation in the upper airway, which can lead to life-threatening airway obstruction. Clinical disease with non-toxin producing diphtheria strains is generally milder, often causing a minor sore throat; however, non-toxigenic strains of *C. diphtheriae* may also cause invasive illness. Cutaneous diphtheria, caused by either toxigenic or non-toxigenic strains of *C. diphtheriae*, usually manifests as non-distinctive sores or ulcers.[1]

In the 1920s in the United States, up to 200,000 cases of diphtheria and 15,000 deaths were reported each year. Diphtheria became an integral part of Alaska history in 1925 when an outbreak in Nome was mitigated by dog mushers who raced antitoxin from Nenana to Nome. Their heroic efforts inspired the Iditarod Trail Sled Dog Race. Diphtheria toxoid was developed in 1921, but was not routinely used until the late 1940s. Nationally, the last major diphtheria outbreak occurred among homeless persons living in Seattle during 1972–1975, resulting in 558 cases and five deaths. Beginning in 1980, non-toxigenic diphtheria cases were excluded from reporting.[1] During 1980–2004, 57 diphtheria cases were reported in the United States; only 2 cases were reported during 2009–2014.[2,3]

Diphtheria is a public health emergency requiring immediate reporting to state public health officials. State and local health departments are, in turn, expected to promptly notify the Centers for Disease Control and Prevention (CDC) of all diphtheria cases. Diphtheria antitoxin (DAT) is indicated for treatment of suspected or confirmed toxigenic diphtheria, but is not recommended for prophylaxis of contacts or treatment of non-toxigenic diphtheria.[4] This *Bulletin* presents two recent cases of non-toxigenic *C. diphtheriae* in Alaska and provides recommendations for diagnosis, prevention and investigation of suspected toxigenic cases.

Case Series

Patient 1

A 15-year-old female with an 8-year history of halitosis and rhinorrhea, underwent surgery to release fluid from a right maxillary sinus cyst in March 2012. Two months after the procedure, she attended a follow-up appointment with a physician who cultured an infected lesion in her nasal septum. *C. diphtheriae* was isolated from the lesion. The patient was up-to-date on vaccinations, and had never travelled outside of the United States. SOE notified CDC, and the isolate was forwarded to CDC headquarters for further testing. An Elek test confirmed a non-toxigenic strain of *C. diphtheriae*. As a precautionary measure, the patient was started on treatment for possible diphtheria with erythromycin. Asymptomatic household members were swabbed to test for carriage of *C. diphtheriae*; all household members tested negative.

Patient 2

In April 2013, a 49-year-old female sought medical attention after experiencing fever, chills, and abdominal pain. The patient had never traveled outside of Alaska, did not have regular contact with anyone outside of her household, and was up-to-date on her vaccinations. Neither the patient nor her household members exhibited any upper-respiratory symptoms. Two different blood cultures from the patient identified *C. diphtheriae*; she was started on ampicillin and sulbactam and her symptoms resolved shortly thereafter. Isolates were submitted to CDC for further testing. Initial PCR tests did not detect the toxin gene, and an Elek assay confirmed that the cultures were non-toxigenic.

Discussion

Vaccination with diphtheria toxoid has nearly eliminated diphtheria in the United States. After a primary series of four doses in infants, a protective level of antitoxin is achieved in more than 95% of persons. Diphtheria toxoid is available in the following vaccines: Td, DTaP, and Tdap.

Although diphtheria has been well-controlled in the United States since 1980, in the 1990s there was an upsurge of epidemic diphtheria in Eastern Europe with more than 157,000 cases and 5,000 deaths. A subset of non-toxigenic *C. diphtheriae* cases occurred that were *tox* gene-positive, but did not express the protein.[5] Non-toxigenic *C. diphtheriae* strains have become recognized as emerging pathogens across Europe over the past 30 years, with clusters of cases often being associated with homelessness and substance abuse.[6]

While the occurrence of diphtheria cases is currently very rare in the United States, in 2011, 4,887 cases of diphtheria were reported worldwide to the World Health Organization (WHO), and many more cases undoubtedly went unreported. As such, exposure to toxigenic strains of diphtheria is just an airplane ride away, underscoring the need for continued vigilance in maintaining on-time vaccination in children and adults.

Recommendations

1. Health care providers must immediately notify the Section of Epidemiology (SOE) of any suspected or confirmed cases of diphtheria by calling 907-269-8000 during work hours, and 1-800-478-0084 after hours. SOE staff will work to assist with referral for follow-up laboratory testing and acquisition of DAT if indicated.
2. Children should be immunized against diphtheria with a 5-dose DTaP series followed by Tdap at or after age 11 years. See the Alaska childhood vaccine schedule available at: http://www.epi.alaska.gov/id/iz/schedule.pdf
3. Adolescents and adults and should receive a single dose of Tdap followed by Td boosters every 10 years. To decrease the risk of pertussis infection in infants, pregnant women should receive a dose of Tdap during each pregnancy, ideally between 27 and 36 weeks gestation. The Alaska adult vaccine schedule is available at: http://www.epi.alaska.gov/id/iz/schedule/adult.htm
4. When visiting countries with high diphtheria rates, travelers should confirm that they are appropriately vaccinated against diphtheria.

References

1. CDC. Vaccine-Preventable Diseases Surveillance Manual, 5th edition, 2012. Diphtheria. Available at: http://www.cdc.gov/vaccines/pubs/surv-manual/chpt01-dip.pdf
2. CDC. Epidemiology and Prevention of Vaccine-Preventable Diseases, 12th edition, 2012. Chapter 6. Available at: http://www.cdc.gov/vaccines/pubs/pinkbook/downloads/dip.pdf
3. CDC. Notifiable Diseases. *MMWR* 2014;63(25):339-52. Available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6325md.htm?s_cid=mm6325md_w
4. CDC. Use of Diphtheria Antitoxin (DAT) for Suspected Diphtheria Cases. Available at: http://www.cdc.gov/diphtheria/downloads/protocol.pdf
5. Zakikhany K, Neal S, Efstratiou A. Emergence and molecular characterisation of non-toxigenic tox gene-bearing *Corynebacterium diphtheriae* biovar mitis in the United Kingdom, 2003–2012. *Euro Surveill* 2014;19(22).
6. Romney MG, Roscoe DL, Bernard K, Lai S, Efstratiou A, Clarke AM. Emergence of an invasive clone of nontoxigenic *Corynebacterium diphtheriae* in the urban poor population of Vancouver, Canada. *J Clin Microbiol* 2006;44(5):1625-9.

(Contributed by: Thomas Frasene BA, and Rosalyn Singleton, MD, MPH, Alaska Section of Epidemiology.)