

# GEORGIA

## Bacterial Meningitis & Sepsis Investigation & Control Manual

December 2008 | 1st Edition



Acute Disease Epidemiology Section | Georgia Division of Public Health

## **TABLE OF CONTENTS**

<b>Foreword</b>	<b>2</b>
<b>Useful Contact Information</b>	<b>3</b>
<b>Overview</b>	<b>4</b>
<b>Major Bacterial Meningitis/Sepsis Pathogens</b>	<b>6</b>
<b>A. <i>Neisseria meningitidis</i></b>	<b>7</b>
<b>B. <i>Haemophilus influenzae</i> type B</b>	<b>10</b>
<b>C. <i>Streptococcus pneumoniae</i></b>	<b>12</b>
<b>Principles of Diagnosis, Prevention, &amp; Control of Bacterial Meningitis/Sepsis</b>	<b>14</b>
<b><i>Neisseria meningitidis</i> Chemoprophylaxis &amp; Educational Outreach to Contacts</b>	<b>19</b>
<b><i>H. influenzae</i> type B Chemoprophylaxis &amp; Educational Outreach to Contacts</b>	<b>21</b>
<b>Laboratory Procedures for <i>N. meningitidis</i> and <i>H. influenzae</i> Isolates</b>	<b>22</b>
<b>Laboratory Procedures for Submitting Clinical Specimens for PCR Testing at the CDC</b>	<b>24</b>
<b>Checklist for the Investigation of Possible Bacterial Meningitis/Sepsis</b>	<b>26</b>
<b>Resources</b>	<b>27</b>
<b>References</b>	<b>28</b>

## **FOREWORD**

The purpose of this manual is to provide current information and suggestions for the investigation of proven or suspected bacterial meningitis and sepsis in Georgia. It is designed to be used by public health practitioners. It compiles resources and tools for investigation, communication, and disease control. Additionally, this manual will assist in standardizing public health practices statewide.

This document was prepared in 2008 by Snehal R. Patel, MPH with assistance from Kate E. Arnold, MD. Acknowledgements are also given to work of the Metro Atlanta Surveillance Task Force in 2003, overseen by Heidi Davidson, MPH, and to District Epidemiology Staff reviewers: Debra Abercrombie, BA, Farrah Machida, MSPH, and Helen Ellis, RN.

If you have questions or comments regarding this manual, please contact the Acute Disease Epidemiology Section, Division of Public Health, Georgia Department of Human Resources at 404-657-2588. We appreciate your feedback. Please print and complete the [Feedback Form](#) with your comments and suggestions and fax it to 404-657-9700.

Susan Lance, DVM, PhD  
Senior Director  
Office of Protection & Safety  
Georgia Division of Public Health

Cherie L. Drenzek, DVM, MS  
Director, Acute Disease Epidemiology Section  
Office of Protection & Safety  
Georgia Division of Public Health

## **USEFUL CONTACT INFORMATION**

(For Cases of Suspected Bacterial Meningitis or Sepsis and Meningococcal Disease Consultations)

**NOTE: Meningitis, meningococcal, and invasive disease caused by *Haemophilus influenzae* are immediately notifiable in Georgia.**

### **County & District Health Department Map and Contact Information**

#### **Acute Disease Epidemiology Section**

Georgia Division of Public Health  
2 Peachtree Street, NW, 14<sup>th</sup> Floor  
Atlanta, GA 30303-3142  
404-657-2588

#### **U.S. Centers for Disease Control & Prevention**

Clinician Information Line  
800-CDC-INFO (800-232-4636)

#### **State Public Health Laboratory**

1749 Clairmont Road  
Decatur, GA 30033  
404-327-7900

#### **Georgia Immunization Program**

404-657-3158

Meningococcal Vaccines:

[Sanofi Pasteur, Inc.](#)

800-VACCINE (800-822-2463)

Hib Vaccines:

[Sanofi Pasteur, Inc.](#)

800-VACCINE (800-822-2463)

[Wyeth Vaccines](#)

800-999-9384

[Merck & Co., Inc](#)

800-672-6372

Pneumococcal Vaccines:

[Wyeth Vaccines](#)

800-999-9384

[Merck & Co., Inc](#)

800-672-6372

## **OVERVIEW**

This manual compiles background information and resources for the investigation of suspected or proven bacterial meningitis and sepsis cases, with a focus on bacterial pathogens likely to cause community-onset meningitis after infancy: *Neisseria meningitidis*, *Haemophilus influenzae* type B, and *Streptococcus pneumoniae*. These infections require an urgent public health response, including investigation with risk assessment, communications, and sometimes chemoprophylaxis of close contacts. Forms for reporting cases, gathering epidemiologic information, and submitting isolates and clinical specimens are included, as well as worksheets that help to identify close contacts who may warrant chemoprophylaxis to prevent secondary cases of disease.

Meningitis is inflammation of the fluid and membranes that surround the spinal cord and brain, and has many potential infectious causes including bacterial, fungal, tuberculous, and viral pathogens. Symptoms of meningitis include headache, stiff neck, chills, fever, and may include nausea, vomiting, confusion, sleepiness, and discomfort when looking toward bright lights. Bacteria that cause meningitis may also cause sepsis, pneumonia, and/or purpura fulminans. Symptoms of sepsis may include hypotension or shock, high fever, cough and/or difficulty breathing, and petechial or purpuric rash.

Bacterial meningitis/sepsis is immediately notifiable in Georgia and should be reported whether proven or suspected. Bacterial meningitis can be treated with antibiotics but treatment must be given promptly because illness can progress quickly. Secondary disease prevention requires prompt risk assessment and appropriate public health intervention because the risk of secondary disease is highest immediately following the index case. Although these infections are serious, they are not highly contagious. Bacterial meningitis pathogens are spread through direct and close contact with the discharges of the nose or mouth of an infected person or an asymptomatic carrier.

The Georgia Division of Public Health conducts active and passive surveillance for bacterial meningitis pathogens. Passive surveillance refers to the routine responsibility of medical and public health officials to monitor and report the occurrence of new meningitis cases on a daily basis. Active surveillance is built upon resources and protocols from the CDC Emerging Infections Program [Active Bacterial Core surveillance](#) (ABCs) to routinely contact all microbiology laboratories in Georgia to identify culture-confirmed cases of meningitis or sepsis. Standardized ABCs case report forms that include demographic characteristics, clinical symptoms, underlying illness, outcome, serogroup, school or daycare attendance and vaccine history are completed. Isolates of *Neisseria meningitidis* and *Haemophilus influenzae* are sent to the Georgia Public Health Laboratory for serotyping and to the CDC for further molecular analysis. In the 20-county Atlanta Metropolitan Statistical Area, pneumococcal isolates are collected by EIP representatives and forwarded directly to CDC for additional testing. Regular laboratory audits assess completeness of routine surveillance and detect unreported cases.

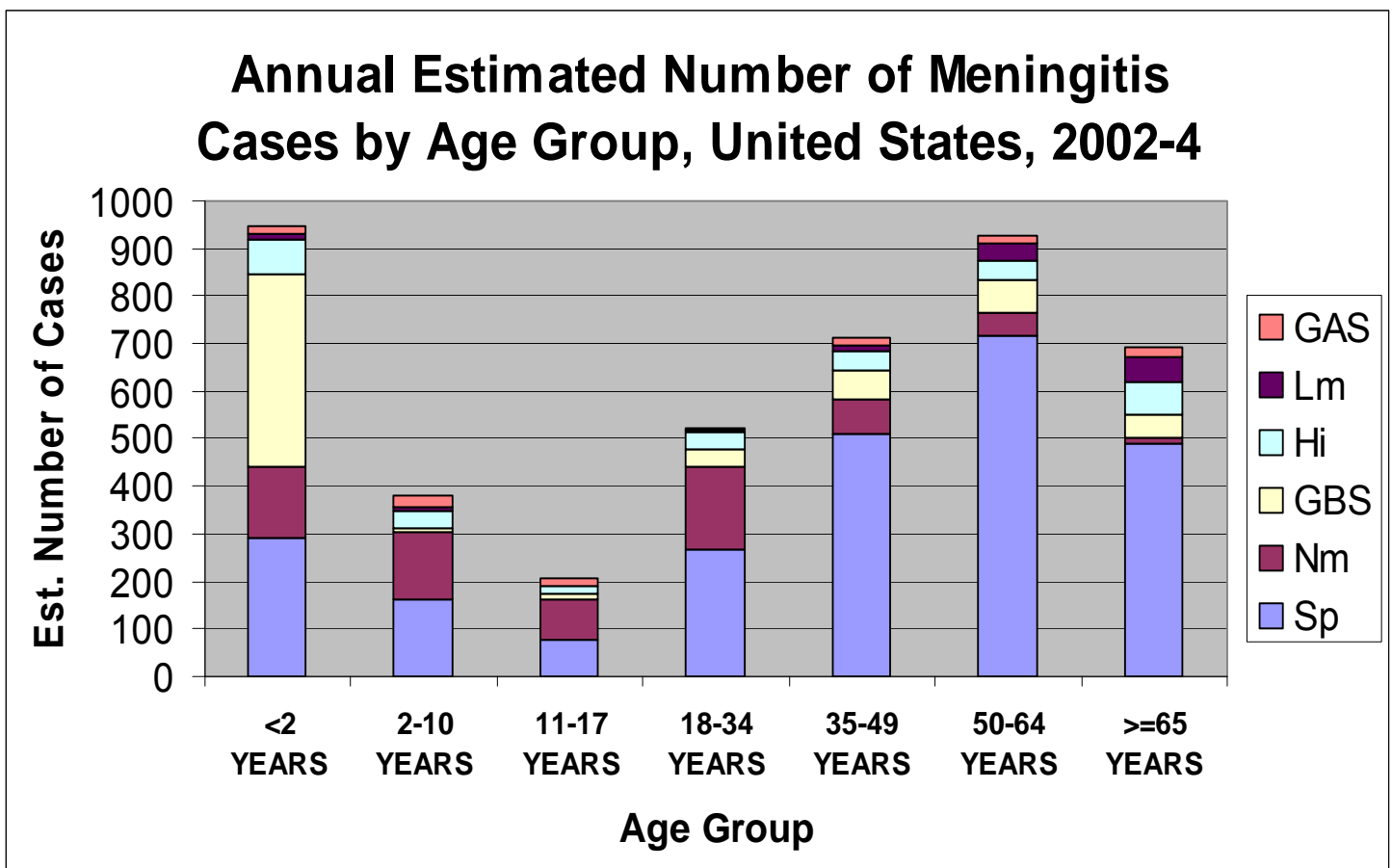
In addition to culture-confirmed cases, molecular testing (PCR, immunohistochemical staining) may be requested from CDC in selected highly suspect cases of meningitis. All reports of cases identified through passive and active surveillance are compiled in the State Electronic Notifiable Disease Surveillance System ([SendSS](#)). Information collected in SendSS and through ABCs is analyzed and used to project annual trends in bacterial meningitis occurrence in Georgia and the U.S. Surveillance isolates are used to monitor disease-causing strains, antibiotic resistance, and for vaccine development and vaccine efficacy purposes.

Additional information or consultations while investigating bacterial meningitis/sepsis are available by contacting the Acute Disease Epidemiology Section, Division of Public Health, Georgia Department of Human Resources at 404-657-2588.

## MAJOR BACTERIAL MENINGITIS/SEPSIS PATHOGENS

After infancy, community-onset bacterial meningitis is primarily caused by three pathogens: *Neisseria meningitidis*, *Haemophilus influenzae* and *Streptococcus pneumoniae*. The relative likelihood of infection with each pathogen is affected at a population level by vaccination rates (which may affect bacterial transmission and “herd immunity”) and by fluctuations in meningococcal disease activity in a community, and at an individual patient level by vaccination history, age and underlying health. Figure 1 shows the annual estimated number of meningitis cases by pathogen and age group for the U.S., during a period 2002 to 2004 when meningococcal disease occurred at a historically low rate.

Figure 1 (Courtesy of M. Thigpen, CDC)



GAS – Group A *Streptococcus*  
 Lm – *Listeria monocytogenes*  
 Hi – *Haemophilus influenzae*  
 GBS – Group B *Streptococcus*  
 Nm – *Neisseria meningitidis*  
 Sp – *Streptococcus pneumoniae*

In addition to meningitis, other serious invasive infections are also caused by these pathogens.

## **Neisseria meningitidis**

### **About**

*Neisseria meningitidis* (or meningococcus) is a “biscuit” or “kidney bean” -shaped gram-negative diplococcus hosted only by humans, naturally carried in the nasopharynx, and spread through droplets of saliva.

Meningococcal disease can manifest as meningitis (infection of the fluid surrounding the brain and spinal cord) and/or meningococcal sepsis (severe illness with presence of the bacteria in the blood). The disease can be characterized by a combination of symptoms including headache, stiff neck, fever, nausea/vomiting, photosensitivity, confusion/altered consciousness, severe malaise, and in cases of sepsis, purpuric (bruise-like areas) or petechial (pinpoint red spots) rashes.

This pathogen is feared because of its propensity to cause fulminant overwhelming infections, sometimes affecting otherwise healthy adolescents and young adults. Rarely, clusters and outbreaks may also occur. Such events create community-wide concerns, and communication challenges. Approximately 10-14% of cases of meningococcal disease are fatal. Of patients who do recover from the disease, approximately 11-19% are left with permanent hearing loss, mental retardation, loss of limbs, or other severe sequelae.

Although rates of disease are currently low in the U.S., the meningococcus remains a leading cause of sporadic bacterial meningitis cases in the U.S. after dramatic reductions in the incidence of meningitis caused by *Streptococcus pneumoniae* and *Haemophilus influenzae* type B due to successful vaccination programs. Pathogenic meningococci are typically surrounded by a capsule which is a virulence factor and target for antibodies. Meningococcal serogroups (capsular types) B, C, and Y are common in the U.S., and serogroups A and W-135 are important for travelers.

Invasive meningococcal isolates should always be referred to the Georgia Public Health Laboratory for serogrouping to monitor for disease clusters and trends in serogroup distribution, and to guide disease prevention efforts.

### **Disease Risk**

Risk of meningococcal disease is age-dependent—highest in children younger than 2 years of age, elevated in the elderly, and also elevated among adolescents and young adults. Risk categories for meningococcal disease include household and close (“kissing”) contacts of case patients, travelers to or residents of countries in which meningococcal disease is hyperendemic, military recruits, college freshmen living in dormitories, microbiologists who work with *Neisseria meningitidis* isolates, and patients with anatomic or functional asplenia or with terminal complement deficiencies. Exposure to active or passive tobacco smoke also elevates risk.



Risk for disease is highest in infants because they lack specific or cross-protective immunity, which tends to develop over time through carriage of various, often benign, *Neisseria* species (e.g. *Neisseria lactamica*). Meningococcal bacteria are commonly carried in the nasopharynx, and carriage is usually not associated with increased risk for disease. Increased risk for disease is thought to be associated with acquisition of a new and virulent meningococcal strain to which pre-existing immunity does not exist. This is one reason for chemoprophylaxis of close contacts to cases. Carriage of a meningococcal strain for more than a few days normally results in an immunologic response and reduction in risk for disease.

### **Vaccination & Primary Prevention**

Currently, there are two vaccines against *N. meningitidis* available in the United States. Meningococcal polysaccharide vaccine (MPSV4 or Menomune<sup>®</sup>) has been available since 1981 for persons aged at least 2 years. Meningococcal conjugate vaccine (MCV4 or Menactra<sup>®</sup>) was licensed in 2005, and is currently licensed for persons aged 2 to 55 years. Both vaccines are designed to prevent serogroups A, C, Y, and W-135 meningococcal disease, but are lacking serogroup B antigen, which is not vaccine preventable in the U.S. at this time. MCV4 is generally preferred over MPSV4 because it is likely to trigger a more robust and long-term immune response.

The Advisory Committee on Immunization Practices (ACIP) recommends routine vaccination of all persons aged 11 to 18 years with 1 dose of MCV4 at the earliest opportunity, because the incidence of meningococcal disease increases during adolescence. Other persons at risk for meningococcal disease (see above) should also be vaccinated. For a detailed schedule of vaccination recommendations, refer to recommendations published by the Advisory Committee on Immunization Practices (ACIP) or consult the [Georgia Immunization Program Manual](#).

Additional prevention advice includes maintaining good overall health, avoiding first and second-hand tobacco smoke, using cough etiquette, and minimizing shared saliva.

### **Secondary Disease Prevention**

Secondary prevention of meningococcal disease includes antibiotic prophylaxis for close contacts of a case.

### **Surveillance Definitions for Meningococcal Disease**

The Council of State and Territorial Epidemiologists (CSTE) and the Centers for Disease Control and Prevention (CDC) have established definitions for cases of meningococcal disease that are used for surveillance purposes.

Confirmed Case: Isolation of *N. meningitidis* from a normally sterile body site (culture) or skin scrapings from purpuric lesions of a person with clinically compatible illness.

Probable Case: A clinically compatible case with:

- Evidence of *N. meningitidis* DNA using a validated PCR, in a specimen obtained from a normally sterile body site,

OR

- Evidence of *N. meningitidis* antigen by positive immunohistochemistry (IHC) on formalin-fixed tissue

OR

- Positive latex agglutination in CSF.

Suspect Case: Clinical purpura fulminans in the absence of a positive blood culture or gram negative diplococci from a normally sterile body site (e.g. blood or CSF).

Purpura: Hemorrhage into the skin, resulting in areas of purplish discoloration

Purpura fulminans: A severe and fatal form of immune thrombocytopenic purpura (a blood disorder characterized by the destruction of blood platelets due to the presence of antiplatelet autoantibodies; purpura pertains to the visible hallmarks: purplish areas in the skin and mucous membranes where bleeding has occurred as a result of decreased platelets). Other evidence of low platelets includes easy bruising ("ecchymosis") and tiny red dots on the skin or mucous membranes ("petechiae").

Primary or Index Case: A case that occurs in the absence of a close contact with a patient infected with *N. meningitidis*.

Co-Primary cases: Co-primary cases are two or more cases that occur among a group of close contacts with onset of illness separated by <24 hours.

Secondary Case: A case that occurs among close contacts of a primary patient  $\geq$  24 hours after onset of illness in the primary patient.

Close Contacts: Household members, child-care center contacts, and persons directly exposed to the patient's oral secretions (e.g. by kissing, mouth-to-mouth resuscitation, endotracheal intubation, or endotracheal tube management).

Community-Based Outbreak: Involves the occurrence of three or more confirmed or probable cases of meningococcal disease in less than or equal to three months among persons residing in the same area who are not close contacts of each other and who do not share a common affiliation.

Organization-Based Outbreak: Involves the occurrence of three or more confirmed or probable cases of meningococcal disease of the same serogroup in less than or equal to three months among persons who have a common affiliation but no close contact with each other.

## **Haemophilus influenzae type B**

### **About**

*Haemophilus influenzae* is a small pleomorphic gram-negative bacterium that is found only in humans, carried naturally in the upper airways, and spread through droplets of saliva. *H. influenzae* is not related to the viruses that cause influenza or parainfluenza. *H. influenzae* may be encapsulated (and typeable) or unencapsulated (and non-typeable). The capsule is a virulence factor, and associated with invasive disease, although even non-typeable *H. influenzae* can cause serious respiratory infections.

*H. influenzae* type B (Hib) is one serotype of *H. influenzae* that is well known for its virulence and propensity to cause severe disease in young healthy children. Until the introduction of the Hib conjugate vaccine, over one-half of infections caused by Hib included meningitis. Hib can also cause sepsis, epiglottitis, pneumonia, arthritis, and cellulitis. The case-fatality rate is 2 to 5% despite appropriate antimicrobial therapy, and hearing impairment or other neurologic sequelae occur in 15 to 30% of survivors. Children younger than age 5 years are most susceptible and should be vaccinated against Hib beginning at age 2 months.

Because of widespread vaccination, Hib is now rare in the U.S., but invasive *H. influenzae* disease continues to occur. Invasive *H. influenzae* isolates should always be referred to the Georgia Public Health Laboratory for serotyping to monitor the effectiveness of Hib prevention efforts.

### **Disease Risk**

Unvaccinated children, including those younger than age 2 months (who cannot be vaccinated yet) remain at elevated risk for Hib disease. Other encapsulated and non-typeable *H. influenzae* strains occasionally cause invasive disease in children and regularly cause serious respiratory infections or invasive disease in persons with Chronic Obstructive Pulmonary Disease (COPD), but these infections are not vaccine preventable.

### **Vaccination & Primary Prevention**

The Hib polysaccharide vaccine first became available in 1985 for children aged 18 months and older, followed by several types of Hib conjugate vaccine series which have been available since 1990 for children beginning at age 2 months since. Hib vaccines have profoundly affected the incidence of Hib disease, which was reduced by 98% during the 1990s. Hib vaccines are available as single antigens but are commonly given as combination vaccines. For a detailed schedule of vaccination recommendations, refer to recommendations published by the Advisory Committee on Immunization Practices (ACIP) or consult the [Georgia Immunization Program Manual](#).

### **Secondary Disease Prevention**

Secondary prevention of invasive Hib Disease (but not infection caused by other *H. influenzae* organisms) may include antibiotic prophylaxis of family members

when the household of a case includes unimmunized or under-immunized children.

**Surveillance Definitions for Invasive *Haemophilus influenzae* Disease**

Confirmed case of *H. influenzae*: A clinically compatible case with isolation of *H. influenzae* from a normally sterile site.

Confirmed case of Hib: As defined above, plus confirmation of isolate as type B. Only isolates that have been serotyped as Hib by GPLH are included in the surveillance case definition for Hib disease in Georgia, because problems with slide agglutination serotyping of *H. influenzae* isolates have been well documented in non-reference laboratories.

Probable case of Hib: A clinically compatible case with *H. influenzae* type B antigen in CSF.

## **Streptococcus pneumoniae**

### **About**

*Streptococcus pneumoniae* (or pneumococcus) is a lancet-shaped gram-positive bacterium that is commonly carried in the nasopharynx and can be transmitted through coughing, sneezing and saliva contact. There are over 90 pneumococcal serotypes (based on the capsule coating the bacterial cell wall), some of which can be prevented with vaccines.

*S. pneumoniae* is a major cause of pneumonia, meningitis, sinusitis, and otitis media. Pneumococcal pneumonia is a common infectious cause of death in the elderly, and sequelae of pneumococcal meningitis, including deafness, paralysis, and mental retardation may affect half of survivors.

### **Disease Risk**

Risk for invasive pneumococcal disease is age dependent, affecting healthy persons primarily between ages 6 and 23 months, and those older than age 50 years. Numerous underlying disease conditions also increase risk, including those associated with deficient antibody production, polymorphonuclear leukocyte chemotaxis and phagocytic function, or splenic function such as multiple myeloma, lymphoma, chronic lymphocytic leukemia, HIV, neutropenia, asplenia, sickle cell disease, diabetes mellitus, and terminal complement deficiency. Persons prone to aspiration of pneumococci are at risk for pneumococcal pneumonia and bacteremia, including those with general debilitation, malnutrition, stroke, and alcoholism. Persons with chronic lung disease, cigarette smoke exposure, and viral infections may also develop pneumococcal lung disease and bacteremia. Those with cochlear implants are at increased risk for pneumococcal meningitis, probably by direct extension from the middle ear.

### **Vaccination & Primary Prevention**

Primary prevention of pneumococcal disease by vaccination of persons at risk is essential, because no specific form of secondary prevention is available.

Currently, two vaccines are available in the U.S. to prevent pneumococcal disease.

A 7-valent pneumococcal conjugate vaccine (PCV7) series was introduced in 2001 and is recommended for all children beginning at age 2 months and up to 23 months. This vaccine was designed to prevent infection with pneumococcal serotypes prevalent among U.S. children. The advent of widespread PCV7 administration profoundly affected serotype-specific disease rates among children who received the vaccine and also among adults (through herd immunity, whereby nasopharyngeal carriage and transmission to adults was reduced). Replacement disease, particularly with serotype 19A (which is not in PCV7) has slowly eroded some of the disease reduction over time.

The current 23-valent pneumococcal polysaccharide vaccine (PPV23) replaced the 14-valent pneumococcal vaccine (introduced in 1977) in 1983.

Polysaccharide vaccines are not effective in children younger than age 2 years, and PPV23 is primarily used for adults at risk for pneumococcal disease (persons older than 65 years of age), though children with high risk medical conditions should also receive this vaccine in addition to PCV7.

For a detailed schedule of vaccination recommendations, refer to recommendations published by the Advisory Committee on Immunization Practices (ACIP) or consult the [Georgia Immunization Program Manual](#).

### **Secondary Disease Prevention**

Antibiotic prophylaxis of close contacts of cases of invasive pneumococcal disease is not recommended.

### **Surveillance Definitions for Invasive Pneumococcal Disease**

Invasive pneumococcal disease: a clinically compatible case with isolation of *S. pneumoniae* from a normally sterile site

Drug-resistant invasive pneumococcal disease: As defined above, plus isolate is “non-susceptible” (i.e., intermediate- or high-level resistance of the *S. pneumoniae* isolate to at least one antimicrobial agent currently approved for use in treating pneumococcal infection).

## **PRINCIPLES OF DIAGNOSIS, PREVENTION AND CONTROL OF BACTERIAL MENINGITIS/SEPSIS**

### **Case Investigation Protocol**

1) Notification to Public Health of a possible or confirmed bacterial meningitis or sepsis case. Sources of information include hospital infection control practitioners (ICPs), clinicians, school nurses, press, & the public.

- a) Request or ensure entry of case report into SendSS
- b) Notify state and local Public Health

**NOTE:** For cases where viral meningitis is considered likely, detailed public health investigation is rarely necessary. However, etiology is unclear for many cases early on.

2) Collection of initial information from the medical record of the case, laboratory, and ICP using the **Possible Bacterial Meningitis/Sepsis Case Investigation Worksheet** ([Worksheet A](#))

- a) Request information from hospital ICP and/or microbiology laboratory that confirms or supports presumptive etiologic diagnosis. Faxed copies of medical records and laboratory values are often helpful. Most valuable is a positive sterile-site culture, followed by other confirmatory tests (latex agglutination, gram stain, or PCR). Even in bacterial meningitis or sepsis, cultures can be negative, especially (but not exclusively) if the patient has been pre-treated with antibiotics.

#### **Test methods used in hospitals for diagnostic purposes:**

- i) Gram Stain: Standard method for staining bacteria on a microscopy slide; performed on clinical specimens and on early growth of cultures.
- ii) Culture: Growth of the organism on laboratory media.
- iii) Latex Agglutination: Occasionally used commercially available rapid test for detecting bacterial antigens in CSF or serum. It may be useful for antibiotic pre-treated patients where culture is negative, but sensitivity (ability to detect the pathogen) is limited. This method of testing is performed by some hospitals in the state. However, it is not clinically available at the Georgia Public Health Laboratory or at the CDC.

#### **Test methods used for research purposes:**

- i) PCR: A research test (not meant for diagnostic purposes) that detects bacterial DNA and can be performed on CSF or blood, available by

permission at CDC and in some academic laboratories, the test is not clinically available at this time.

- ii) **IHC:** Immunohistochemical staining of tissue, ordinarily conducted post-mortem; available upon request from the CDC infectious diseases pathology laboratory.
- b) If the pathogen is unknown, determine what the infectious diseases consultant or attending clinician thinks is the likely cause of illness (bacterial/viral/other). A review of the patient's medical record or discussion with the ICP may provide this information, but if warranted, a senior epidemiologist can assist with contacting the attending physician for further inquiry. Clinicians are generally in the best position to make this judgment since they have all the facts at hand.
- i) Clinical information that supports a presumptive bacterial etiology includes presence of a petechial or purpuric rash or increased severity of illness (e.g.: shock, need for pressors and/or ventilator).
  - ii) Laboratory values may also suggest a presumptive etiology (see below).
- c) Consider consultation with the state Acute Disease Epidemiology Section regarding the decision to provide prophylaxis to close contacts based on preliminary information collected in Worksheet A.

**Characteristic Laboratory Values for Differentiating Etiology of Acute Meningitis/Sepsis:**

Serum C-Reactive Protein (CRP): An acute phase reactant or inflammatory marker where normal values are <8 mg/dL. Highest values occur in acute bacterial infections (>30 mg/dL) and typically lower (<20 mg/dL) in viral infections, but may be high in both. Normal values are unlikely in bacterial infections after 24 hours duration. It may also be elevated by chronic inflammatory disorders (rheumatoid conditions, inflammatory bowel disease), tissue injury or necrosis (surgery, trauma).



CSF Profiles suggestive of Acute Meningitis\*:

Pathogen	CSF Appearance	CSF WBC Count	CSF Protein	CSF Glucose	CSF Gram Stain**
Virus	Cloudy	6-100 cells	Slightly Elevated (45-150)	Normal	WBCs, No Bacterial Organisms
Bacteria	Cloudy	100-1000 cells	Elevated (50-1000)	Below Normal (< 40)	WBCs +/- Bacterial Organisms
Normal value	Clear, colorless	< 8 cells	≤ 40	40 to 80	No cells/organisms

\*Many cases are atypical

\*\*Appearance of Pathogens on Gram Stain:

Pathogen	Appearance
<i>Neisseria meningitidis</i>	Gram-negative “biscuit” shaped or “kidney-bean” shaped diplococci (cocci in pairs)
<i>Haemophilus influenzae</i>	Small Gram-negative rods or coccobacilli
<i>Streptococcus pneumoniae</i>	Gram-positive lancet shaped diplococci (cocci in pairs)

Click for a printer-friendly chart of [Suggestive Patterns for Discerning the Etiology of Meningitis Cases](#) using lab results.

**NOTE:** Pre-treatment with antibiotics is likely to reduce the yield of culture results particularly if exposure to antibiotics is prolonged prior to culture.

- 3) If invasive meningococcal disease or Hib is culture-confirmed, Public Health epidemiologists should:
  - a) Ensure that the hospital/lab promptly submits the isolate of the pathogen to the Georgia Public Health Laboratory. Isolates may be picked up by EIP (in the 20-county MSA) or shipped (in GOA). Instructions on isolate submission are further described on page 22.

- b) For cases of meningococcal disease, complete the CDC [ABCs Case Report Form](#) and fax it to the Georgia Division of Public Health at 404-657-9700.
  - c) As a courtesy, the state Meningitis Coordinator should notify the Georgia Immunization Program of the case, including serogroup when available (particularly if affecting adolescent or resulting in death). The District may also wish to notify the local Immunization Coordinator.
  - d) Ensure that the patient's vaccine history is complete in SendSS.
- 4) If invasive Hib or meningococcal disease is culture-confirmed or presumptive (see 4b), Public Health should:
- a) Ensure prophylaxis for close contacts. See page 19-22 for detailed information on providing prophylaxis to contacts. Note that for Hib cases, only cases that are confirmed as serotype B at the Georgia Public Health Laboratory may require prophylaxis of close contacts.
    - i) In the case of meningococcal disease, use the **Worksheet for Prevention of Secondary Meningococcal Disease Cases** ([Worksheet B](#)) to identify all possible contacts.
    - ii) Verify contact list and obtain estimated age, weight (for dosage calculation), and telephone numbers/addresses using the **Contact Exposure Follow-up Worksheet** ([Worksheet C](#)).
  - b) The criteria for presumptive or confirmed invasive meningococcal disease include clinically compatible illness (sepsis or meningitis syndrome) and at least one of the following:
    - i) Latex agglutination, PCR, IHC or positive culture for *Neisseria meningitidis*.
    - ii) Gram-negative diplococci on the gram stain of a specimen from a sterile site.
    - iii) Presence of clinical purpura fulminans.
    - iv) Epidemiologic link to a known case.
  - c) In the absence of such evidence, prophylaxis may still be considered, for example, in settings with high risk populations. District epidemiology staff may want to consider consulting with the state Meningitis Coordinator for assistance in making this decision.
  - d) In presumptive but culture-negative cases, clinical specimens from sterile body sites should also be forwarded to CDC for PCR testing, and/or post-

mortem tissues should be forwarded to the CDC special pathology laboratory for IHC staining to document the pathogen and the serogroup, if possible. Instructions for clinical specimen submission can be found in the *Laboratory Procedures* section on page 24.

- e) In addition to offering chemoprophylaxis, Public Health staff (usually District Health Staff) should interview the patient and/or family, and educate close contacts about disease and prevention.
  - i) Educate close contacts about signs and symptoms of meningitis/bacterial sepsis, advising them to seek early medical attention if illness occurs. [The Meningococcal Disease Fact Sheet](#) and [The Hib Fact Sheet](#) can be used for this purpose.
  - ii) If chemoprophylaxis will be recommended, stress the need to fill the prescription promptly and to take all doses as recommended.
  - iii) Follow up on any close contacts with suggestive symptoms to rapidly identify a possible cluster or outbreak.
- 5) When appropriate, educational outreach may require a letter to schools or other community partners.
  - o Click to view a [Sample Letter to a School/Daycare](#) for distribution to parents where prophylaxis is arranged through Public Health.
  - o Click to view a [Sample Letter to a Physician](#) to alert of disease in the community and possibility of need to provide prophylaxis.
  - o Click to view a [Sample Letter to School](#) for distribution to parents where the case is one of bacterial meningitis but prophylaxis is unnecessary.
- 6) Epidemiologic follow-up includes:
  - a) Determining the serogroup (from GPHL results) and mapping the case to monitor clustering in time and space.
  - b) Determining the disease outcome and sequelae and updating this information in SendSS and in the ABCs case report form.

## **N. meningitidis CHEMOPROPHYLAXIS AND EDUCATIONAL OUTREACH TO CONTACTS**

Prophylaxis for meningococcal exposures should be accomplished as early as possible after recognition of a presumptive or confirmed case (defined above), because secondary cases usually occur soon after the index case, and disease risk falls back to baseline after 14 days.

Close contact identification should focus on identifying all persons who meet criteria for prophylaxis and ensuring access to medication and education for them. In principle, however, Public Health should strive to limit recommended prophylaxis to only those for whom evidence supports the need for prophylaxis (outlined in worksheets B and C). Meningococcal disease can be frightening and often results in overuse of antibiotics in persons who are not actually at increased risk, particularly healthcare workers with no exposure to respiratory droplets. This cannot always be avoided, but overuse of antibiotic prophylaxis results in a perception of risk for others who are not at increased risk, adds unnecessary costs, and puts pressure on the healthcare system and may lead to antibiotic resistance.

As early as possible after a meningococcal case is recognized, District Epidemiology staff should interview the patient, if possible, or a patient surrogate (family or friends) using worksheets B and C. Bring educational materials including fact sheets about meningococcal disease and advice for taking and completing antibiotic treatment.

- 1) Worksheets B & C: Focusing on the 7 days preceding onset of illness until effective treatment is given, list contact names, estimated age, weight (for children) and phone numbers. Focus on persons likely to have shared saliva, beverages, eating utensils, sleeping quarters, etc. but not casual contacts (office co-workers). Determine which persons or social groups meet the criteria for chemoprophylaxis. A patient is no longer considered infectious after 24 hours of antibiotic therapy.
- 2) Determine if a patient's physician will treat close contact family members, who are often at the bedside and most easily addressed this way. If not, arrange for urgent prophylaxis by Public Health staff. This is done under the [Public Health Nurse Protocol Manual 2008](#) (found in the *Other Infectious Diseases* section) but each District may use different methods to implement prophylaxis and obtain medications.
- 3) Health Districts should be prepared to supply prophylaxis without the assistance of the patient's physician, and should be prepared to write physician-authorized prescriptions (under the Nurse Protocol), and to provide medication or refer to a pharmacy (including a compounding pharmacy for children) that can do so if necessary.

- 4) Prophylaxis in daycare settings serving toddlers is recommended for all adults and children when a child or adult with meningococcal disease attends for 4 or more hours per week. This is because the risk of exposure to uncontained saliva is high in this setting. Challenges include risk communications, the need for weight-based dosing of antibiotics in children, and the need for a compounding pharmacy to prepare liquid formulations of recommended antibiotics. Health Districts should know where such a pharmacy is available.
- 5) If the case resides in another Health District, the appropriate Health District should be notified. This can be facilitated by the state Meningitis Coordinator.
- 6) If the case occurs in an out-of-state resident, the appropriate state Health Department should be notified. This can be facilitated by the state Meningitis Coordinator.
- 7) For cases from institutional settings (prisons, long-term care facilities, mental hospitals, etc.), Health District staff should work closely with the nursing staff of the institution to identify close contacts. It is important to provide educational outreach and emphasize the mechanisms of spread.
- 8) If the case has traveled by air prior to onset of meningococcal disease, Health Districts should refer to the CDC's [Guidelines for the Management of Airline Passengers Exposed to Meningococcal Disease](#). Please consult the state Meningitis Coordinator for further guidance.
- 9) Prophylaxis is recommended for health care workers exposed to the oral secretions of a meningococcal case (through mouth-to-mouth resuscitation, endotracheal intubation, or endotracheal tube management). Prophylaxis is not recommended for health care workers who have had casual contact with the case or by being in the same room or breathing the same air, unless exposed to droplet spray within 3 feet, before completion of the first 24 hours of antibiotic therapy.
- 10) Antibiotic prophylaxis is not recommended for the control of meningococcal disease outbreaks.

### **H. influenzae type B CHEMOPROPHYLAXIS AND EDUCATIONAL OUTREACH TO CONTACTS**

Identification, education, and prophylaxis of close contacts to confirmed Hib cases should be conducted in a manner similar to those for meningococcal disease investigations. However, prophylaxis for Hib exposures should be accomplished only after confirmation of serotype B. Secondary cases are rare and only likely among unvaccinated or immuno-compromised household contacts.

Prophylaxis of Hib is done under the [Public Health Nurse Protocol Manual 2008](#) (*Other Infectious Diseases* section) but each District may use different methods to implement prophylaxis and obtain medications.

## **LABORATORY PROCEDURES for *N. meningitidis* and *H. influenzae* Isolates**

### **Introduction**

All isolates of *N. meningitidis* and *H. influenzae* recovered from sterile sites should be forwarded to the Georgia Public Health Laboratory (GPHL), Bacteriology Unit, either directly or through the Emerging Infections Program (EIP). Isolates should be submitted as pure cultures. *N. meningitidis* grouping and *H. influenzae* typing are provided by the GPHL at no charge. Antimicrobial susceptibilities are not routinely performed. Selected isolates of *S. pneumoniae* (from the Atlanta Metropolitan Statistical Area or MSA) are also collected by the EIP and forwarded to the CDC for serotyping and antimicrobial susceptibility testing.

### **Specimen Submission**

- A. Submit referred cultures of *H. influenzae* or *N. meningitidis* as actively growing, pure 18-24 hour subcultures on chocolate slants (slants may be obtained from the GPHL).
- B. Clearly label referred cultures with the patient's name or other unique identifier. Unlabeled specimens or cultures will not be tested.
- C. Complete the GPHL [Bacteriology Submission Form #3410](#) to include the following information:
  1. Unique patient identifier (name or number). The patient identifier (name or number) indicated on the requisition form should match that written on the specimen or culture
  2. Agent suspected or test requested
  3. Submitter's name and address
  4. Name and telephone number of contact person
  5. Date of specimen collection
  6. Source of specimen
  7. Date of transplant (if applicable)
  8. Brief clinical history
  9. Patient's race, sex, age, and occupation, if available
- D. Submit through the EIP, by mail, or by courier.
- E. The mailing address for the Georgia Public Health Laboratory can be found in the *Useful Contact Information* section on page 3.
- F. For more information on specimen submission, refer to the [GDPH Laboratory Services Manual](#)

### **Unacceptable Specimens**

- Cultures broken in transit.
- Non-viable cultures: all cultures received will be sub-cultured upon receipt. Every attempt will be made to obtain viable growth. If no growth occurs, the submitter will be notified by telephone and a report will be issued immediately. Another subculture will be requested, if available.
- Cultures grossly overgrown with contaminants.
- No patient identifier on the specimen or culture.
- Specimens improperly collected or submitted (see section on specimen collection and shipment).

**Reporting of Results**

Results of serogrouping for *Neisseria meningitidis* usually require 1-3 working days and 2-3 working days for *H. influenzae*.



## **LABORATORY PROCEDURES for Submitting Clinical Specimens for PCR Testing at the CDC**

### **Introduction**

In cases of culture-negative meningitis or sepsis where *N. meningitidis* remains highly suspect, clinical specimens may be submitted through the Georgia Public Health Laboratory for PCR testing subsequently performed at the CDC. PCR testing can also be used to characterize the serogroup of non-viable meningococcal isolates.

### **Permission**

The state Meningitis Coordinator should obtain clinical and laboratory details about the case from the District. Subsequently, the State Meningitis coordinator will contact the GPHL and the CDC to arrange for PCR testing. The State Meningitis coordinator will call the epidemiologist on call at the Meningitis & Vaccine Preventable Disease Branch at the CDC to request permission to submit the specimen. Upon receipt of permission, the state Meningitis Coordinator should call the GPHL to clear submission of the specimen with either Dr. Mahin Park or Lynett Poventud.

### **Specimen Submission**

- A. Appropriate clinical specimens for meningococcal PCR include body fluids from sterile sites, such as cerebrospinal fluid (CSF), blood, and/or serum, or non-viable meningococcal isolates.
- B. Send at least 0.2 ml of each clinical specimen, frozen on dry ice, if possible; if not, then on cold packs. Clearly label referred specimens with the patient's name or other unique identifier. Unlabeled specimens will not be tested.
- C. A completed GPHL [Bacteriology Submission Form #3410](#) should accompany each specimen and include the following information:
  1. Unique patient identifier (name or number). The patient identifier (name or number) indicated on the requisition form should match that written on the specimen or culture
  2. Test requested (specify PCR for bacterial meningitis pathogens)
  3. Submitter's name and address
  4. Name and telephone number of contact person
  5. Date of specimen collection
  6. Source of specimen
  7. Brief clinical history
  8. Patient's race, sex, age, and occupation, if available
- D. The mailing address for the Georgia Public Health Laboratory can be found in the Useful Contact Information section on page 3.
- E. For more information on specimen submission, refer to the [GDPH Laboratory Services Manual](#).

**Reporting of Results**

PCR is not made available as a clinical diagnostic tool, but is being evaluated at CDC for epidemiologic purposes. Reporting delays may be anticipated, but results will be shared with submitters as quickly as they become available.

## **CHECKLIST for the Investigation of Possible Bacterial Meningitis/Sepsis**

- Health District/State Public Health Notification
- Entry & Completion of Report in SendSS
- Preliminary Investigation (Worksheet A) completed by District
- Contact Investigation completed by District (Worksheets B and C)
- Public Health Decision about Prophylaxis
  - If yes, prophylaxis ensured to closest contacts (Worksheet C)
- Educational outreach to contacts and others (as appropriate) completed
  - Letter to School/Daycare Facility/Physician (if necessary/applicable)
  - Meningococcal Disease Fact Sheet/Hib Fact sheet
  - Press Release
- If Culture-Confirmed Case:
  - Completion of ABCs case-report form (meningococcal disease only)
  - Submission of isolate to GPHL
  - Courtesy Notification of Georgia Immunization Program (particularly if adolescent or resulting in death)
- If not Culture-Confirmed Case:
  - Clinical specimens (CSF, blood or blood components) submitted for PCR at CDC (through GPHL)
- Epidemiologic Follow-up (State):
  - Serogroup Determination (GPHL) and Mapping of Case
  - Cluster analysis

## **RESOURCES**

### **General**

[Georgia Division of Public Health](http://health.state.ga.us)

(<http://health.state.ga.us>)

[Georgia Public Health Laboratory](http://health.state.ga.us/programs/lab/)

(<http://health.state.ga.us/programs/lab/>)

[U.S. Centers for Disease Control & Prevention](http://www.cdc.gov)

([www.cdc.gov](http://www.cdc.gov))

### **Prevention & Vaccination**

[Public Health Nurse Protocol Manual 2008 \(Other Infectious Diseases\)](http://www.health.state.ga.us/pdfs/nursing/Protocol%20Manual/13.0%20Other%20Infectious%20Diseases.pdf)

(<http://www.health.state.ga.us/pdfs/nursing/Protocol%20Manual/13.0%20Other%20Infectious%20Diseases.pdf>)

[Advisory Committee on Immunization Practices](http://www.cdc.gov/vaccines/recs/acip/default.htm)

(<http://www.cdc.gov/vaccines/recs/acip/default.htm>)

[ACIP Recommendations: Prevention and Control of Meningococcal Disease \(May 27, 2005/Vol. 54/No. RR-7\)](http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5407a1.htm)

(<http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5407a1.htm>)

[Revised ACIP Recommendations: Vaccinate All Persons Aged 11-18 Years with Meningococcal Conjugate Vaccine](http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5631a3.htm?s_cid=mm5631a3_e)

([http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5631a3.htm?s\\_cid=mm5631a3\\_e](http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5631a3.htm?s_cid=mm5631a3_e))

[Revised ACIP Recommendations: Use of Quadrivalent Meningococcal Conjugate Vaccine \(MCV4\) in Children Aged 2-10 Years at Increased Risk for Invasive Meningococcal Disease](http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5648a4.htm?s_cid=mm5648a4_e)

([http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5648a4.htm?s\\_cid=mm5648a4\\_e](http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5648a4.htm?s_cid=mm5648a4_e))

[Guidelines for the Management of Airline Passengers Exposed to Meningococcal Disease](http://www.cdc.gov/travel/content/Menin.aspx)

(<http://www.cdc.gov/travel/content/Menin.aspx>)

[Georgia Immunization Program](http://health.state.ga.us/programs/immunization/)

(<http://health.state.ga.us/programs/immunization/>)

[National Network for Immunization Information](http://www.immunizationinfo.org/)

(<http://www.immunizationinfo.org/>)

[Immunization Action Coalition](http://www.immunize.org/)

(<http://www.immunize.org/>)

## REFERENCES

1. CDC. Prevention and Control of Meningococcal Disease: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2005;54(RR07);1-21.
2. CDC. Revised Recommendations of the Advisory Committee on Immunization Practices to Vaccinate All Persons Aged 11-18 Years with Meningococcal Conjugate Vaccine. MMWR 2007; 56(31);794-5.
3. CDC. Notice to Readers: Recommendation from the Advisory Committee on Immunization Practices (ACIP) for Use of Quadrivalent Meningococcal Conjugate Vaccine (MCV4) in Children Aged 2—10 Years at Increased Risk for Invasive Meningococcal Disease. MMWR 2007; 56(48); 1265-6.
4. CDC. Report from the Advisory Committee on Immunization Practices (ACIP): Decision Not to Recommend Routine Vaccination of All Children Aged 2—10 Years with Quadrivalent Meningococcal Conjugate Vaccine (MCV4). MMWR 2008; 57(17):462-5.
5. CDC. Epidemiology and Prevention of Vaccine-Preventable Diseases. Atkinson W, Hamborsky J, McIntyre L, Wolfe S, eds. 10<sup>th</sup> ed. Washington DC: Public Health Foundation, 2007;115-128; 257-270.
6. American Academy of Pediatrics. *Haemophilus influenzae* Infections. In: Pickering LK, Baker CJ, Long SS, McMillan JA, eds. *Red Book: 2006 Report of the Committee on Infectious Diseases*. 27<sup>th</sup> ed. Elk Grove Village, IL: American Academy of Pediatrics; 2006: 310-311.
7. National Network for Immunization Information: *Haemophilus influenzae* type B Vaccine Information. Available at [http://www.immunizationinfo.org/vaccineinfo/vaccine\\_detail.cfv?id=5](http://www.immunizationinfo.org/vaccineinfo/vaccine_detail.cfv?id=5).
8. CDC. Direct and indirect effects of routine vaccination of children with 7-valent pneumococcal conjugate vaccine on incidence of invasive pneumococcal disease, United States, 1998-2003. MMWR Morb Mortal Wkly Rep 2005; 54(36): 893-897.
9. Ray GT, Whitney CG, Fireman BH, Ciruryla V, Black SB. Cost-effectiveness of pneumococcal conjugate vaccine: evidence from the first 5 years of use in the United States incorporating herd effects. *Pediatr Infect Dis J*. 2006; 25(6):494-501.
10. Sanofi Pasteur: Preventable Diseases – *Haemophilus influenzae* Type B (Hib) Infections. Available at [http://www.sanofipasteur.us/sanofi-pasteur/front/index.jsp?codePage=VP\\_PD\\_Haemophilus&codeRubrique=19&lang=EN&siteCode=AVP\\_US](http://www.sanofipasteur.us/sanofi-pasteur/front/index.jsp?codePage=VP_PD_Haemophilus&codeRubrique=19&lang=EN&siteCode=AVP_US)

11. Immunization Action Coalition: Vaccine Policy & Licensure. Available at <http://www.immunize.org/fda/>
12. CDC. Vaccines and Preventable Diseases: Pneumococcal Vaccine. Available at <http://www.cdc.gov/vaccines/vpd-vac/pneumo/default.htm>