Chapter 11: Pneumococcal Disease

Tamara Pilishvili, MPH; Brendan Noggle, BS; Matthew R. Moore, MD, MPH

I. Disease Description

Streptococcus pneumoniae is a leading cause worldwide of illness and death for young children, persons with underlying medical conditions, and the elderly. The pneumococcus is the most commonly identified cause of bacterial pneumonia; since the widespread use of vaccines against *Haemophilus influenzae* type b, it has become the most common cause of bacterial meningitis in the United States.[1] CDC's Active Bacterial Core Surveillance (ABCs) system has tracked invasive pneumococcal disease (IPD) in selected regions of the United States since 1994. ABCs data suggest that rates of invasive disease are highest among persons younger than 2 years of age and those 65 years of age or older.[2, 3]

Pneumococci can be found in the upper respiratory tract of 15% of well adults; in child care settings, up to 65% of children are colonized.

Cross-sectional studies suggest that pneumococci can be found in the upper respiratory tract of 15% of well adults; in child care settings, up to 65% of children are colonized. Although pneumococcal carriage can lead to invasive disease (e.g., meningitis or bacteremia), acute otitis media (AOM) is the most common clinical manifestation of pneumococcal infection among children and the most common outpatient diagnosis resulting in antibiotic prescriptions in that group.[4]

Each year in the United States, pneumococcal disease accounts for a substantial number of cases of meningitis, bacteremia, pneumonia, and AOM (Table 1).[2, 5–11] Approximately 12% of all patients with invasive pneumococcal disease die of their illness, but case-fatality rates are higher for the elderly and patients with certain underlying illnesses.[2, 6–8]

Table 1: Incidence of pneumococcal infections in the United States

Type of bacterial infection	# cases/ year
Meningitis*	2,000
Bloodstream infection†	8,000
Pneumonia (hospitalized)§	106,000–175,000
Acute otitis media in children <5 yrs¶	3,100,000

* S. pneumoniae *isolated from cerebrospinal fluid or clinical diagnosis of meningitis with pneumococcus isolated from another sterile site*[2]

† *Bacteremia without focus*[2]

§ *Estimates before introduction of pneumococcal conjugate vaccine for children in 2000.*[12]

¶ *The number of doctor visits per year for acute otitis media in children younger than 5 years is estimated to be 14,106,159.*[8] *Approximately 30% of these visits probably represent otitis media with effusion and do not require antibiotics.*[9] *Recent data from etiologic studies of otitis media in two different areas of the United States suggest that approximately 31% of acute otitis media episodes are caused by* S. pneumoniae.[10, 11] *[14.1 million x 70% x 31% = 3.1 million]*

II. Background

Pneumococcal vaccines

A pneumococcal polysaccharide vaccine (PPV) targeting 23 of the most common serotypes of *S. pneumoniae* has been available since 1983. The Advisory Committee on Immunization Practices (ACIP) recommends that it be administered to persons 2 years of age or older who have any of several underlying medical conditions, and to all persons 65 years of age or older.[5] Despite its availability and payment provided under Medicare, current vaccination rates remain below the *Healthy People 2010* national objectives of 90% coverage among persons 65 years of age or older, and 60% coverage among persons 18–64 years of age with underlying medical conditions.[13] In 2003, the median proportion of persons aged 65 years or older who reported ever having received PPV was 64%; the PPV vaccination rate was only 37% among persons 18–64 year of age with diabetes, a group at increased risk for pneumococcal disease.[14, 15] Methods such as the use of standing orders in clinics and hospitals, physician reminder systems, and simultaneous administration of pneumococcal vaccine with influenza vaccine have been shown to improve vaccine utilization.[5]

In February 2000, a 7-valent pneumococcal polysaccharide–protein conjugate vaccine (PCV7) (Prevnar®, manufactured by Wyeth Pharmaceuticals) was licensed for use in infants and young children. PCV7 offers protection against the seven serotypes (PCV7-types) that most commonly cause IPD in children in the United States.[4] In a study conducted among Northern California Kaiser Permanente members, the efficacy of PCV7 was 97% for IPD caused by PCV7 types and 89% for all serotypes.[16] Among Navajo children younger than 2 years of age, efficacy was 76.8% in the per protocol analysis, and 82.6% in the intent-to-treat analysis.[17] Although the efficacy of PCV7 against all AOM episodes is 6%–7%, the efficacy against AOM caused by serotypes included in PCV7 is 57%.[16, 18] In a large clinical trial, radiograph-positive pneumonia episodes were reduced 24.3% in the first year of life, 22.7% in the first 2 years, and 9.0% among children aged 2 years and older.[19]

Since 2000, PCV7 has been recommended for all children younger than 2 years and children 2–4 years of age with certain high-risk conditions.[4] Beginning in August 2001, delays in delivery of PCV7 to some health departments and healthcare providers occurred, with intermittent shortages continuing through September 2004. The ACIP issued updated recommendations to healthcare providers during the shortage, advising them to fully vaccinate high-risk children younger than 5 years and decrease the number of doses administered to healthy infants in lieu of leaving some infants unvaccinated.[20] PCV7 coverage with three or more doses among all U.S. children 19–35 months of age was estimated to be 11% in 2002, and increased to 73% in 2004.[21]

Trends in invasive pneumococcal disease

Despite the vaccine shortages following PCV7 introduction, dramatic declines in invasive pneumococcal disease were reported as early as 2001. Among children younger than 2 years of age, the overall incidence of invasive disease declined by 69%, and the incidence of PCV7-type disease declined by 78% compared with prevaccine rates in 1998–1999.[22] As of 2004, the rate of vaccine-type invasive disease has continued to decline among children in the target age group to 2.5 cases per 100,000, a 93% reduction compared with 1998–1999.[23] The use of PCV7 has also reduced the burden of invasive pneumococcal disease among older children and adults through reduced transmission of vaccine-serotype pneumococci (i.e., herd effect). Declines in the incidence of PCV7-type invasive disease among adults were observed first in 2001 and have continued through 2004, reducing the incidence to 64%–77% below the 1998–1999 baseline, depending on age.[24, 25] Increases in disease caused by serotypes not included in PCV7 (i.e., replacement disease) are evident in children and certain adult populations with underlying illnesses but are small in magnitude compared with the overall reduction in disease.[26, 27]

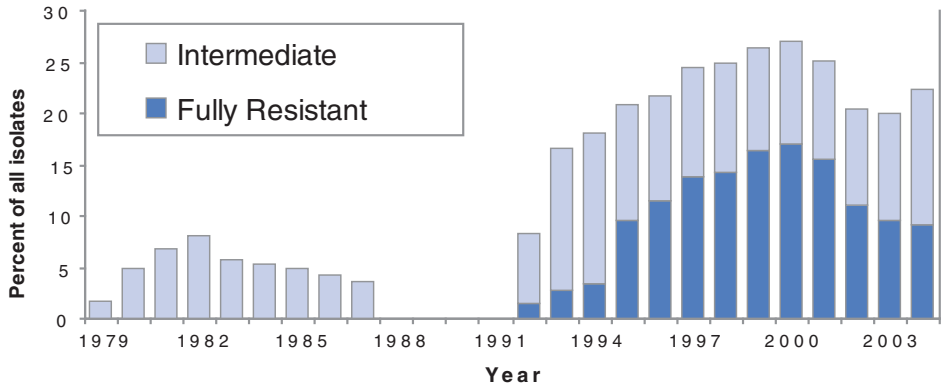
Antimicrobial resistance trends

Before 1990, *S. pneumoniae* was almost uniformly susceptible to penicillin, allowing most physicians to treat persons with severe infections with penicillin alone. However, during the 1990s, resistance to penicillin and to multiple classes of antimicrobial agents spread rapidly in the United States, with an increasing trend of invasive pneumococci resistant to three or more drug classes.[28–31] In 1998, 24% of invasive pneumococcal isolates were nonsusceptible to penicillin, and 78% of these strains belonged to five of the seven serotypes included in PCV7 (types 6B, 9V, 14, 19F, and 23F).[28] Outbreaks due to both susceptible *S. pneumoniae* and drug-resistant *S. pneumoniae* (DRSP) have been reported in child care centers and among residents of long-term care facilities in which pneumococcal vaccine coverage was low.[32–34]

Following the introduction of PCV7 into the routine childhood immunization program in 2000, the incidence of antibiotic-resistant invasive disease declined substantially among both young children and older persons.[22, 35–38] In 2004, the rate of penicillin-nonsusceptible invasive disease caused by serotypes included in PCV7 had declined by 98% among children younger than 2 years of age and by 79% among adults 65 years or older. In contrast, an increase in penicillin-nonsusceptible disease caused by serotypes not included in PCV7 was identified in 2004, although the magnitude of this effect remains small.[35] Before the introduction of PCV7, the proportion of pneumococcal illnesses caused by DRSP among children was higher than that among adults.[28] In 2004, children younger than 2 years of age and adults 65 years of age

and older had similar rates of antibiotic-nonsusceptible invasive disease.[35] The prevalence of resistance varied by geographic area both before and after PCV7 was introduced, with higher prevalence noted for the southeastern United States.[28]

Figure 1. Penicillin resistance in *Streptococcus pneumoniae*, United States, 1979–2004



1979–1994: CDC Sentinel Surveillance System
1995–2004: CDC Active Bacterial Core Surveillance (ABCs) System, Emerging Infections Program[28]

Inappropriate antimicrobial use contributes to the development of DRSP.

The emergence of DRSP has made treatment of pneumococcal disease more difficult. Because of a lack of rapid, sensitive, and specific diagnostic tests, therapy for pneumonia and milder illnesses such as otitis media remains empiric. The increasing prevalence of DRSP has prompted groups of experts to provide national guidance for treating infections commonly caused by pneumococcus, such as otitis media and pneumonia.[39–41] Few communities remain in which resistance is uncommon, and even in these communities, resistant infections can occur. For these reasons, clinicians and public health officials should follow national guidelines rather than attempt to create local treatment recommendations based on local resistance data.

Because of the limitations of current diagnostic testing, clinicians often prescribe empiric antibacterial therapy that is not indicated or is unnecessarily broad. Inappropriate antimicrobial use contributes to the development of DRSP. Principles have been developed to encourage appropriate use of antimicrobial agents for adults and children with upper respiratory infections.[9, 42–45]

III. Importance of Surveillance

Goals of surveillance

Surveillance for invasive pneumococcal disease has several goals: to observe national and local trends, to detect geographic and temporal changes in the prevalence of DRSP, to monitor the impact of PPV and PCV7 vaccines on disease, and to inform future vaccine development.

With the recent introduction of PCV7, surveillance for invasive pneumococcal disease among children younger than 5 years of age is particularly important for identifying populations that may not be receiving vaccination and for monitoring the incidence of disease caused by non-vaccine serotypes, i.e., replacement disease. Surveillance of invasive disease in persons 5 years of age and older is useful for monitoring the impact of PPV vaccination, the indirect effects of PCV7, and replacement disease.

Serotyping of pneumococcal isolates is useful for understanding vaccine effects. However, serotyping is expensive and requires specialized reagents and extensive technical training; therefore, serotyping capacity is not widely available. The use of polymerase chain reaction (PCR) to identify pneumococcal capsular genes specific for individual capsular serotypes may be feasible for state public health and academic research centers in the near future.[46, 47]

Pneumococcal surveillance enables recognition of new or rare resistance patterns. Surveillance information can be used on the national level for research and policy development and at the state or local level to raise awareness of DRSP among clinicians and the general public. Surveillance data also may be useful for tracking the impact of interventions aimed at reducing unnecessary use of antimicrobial agents.

Reportable conditions

In 1994, the Council of State and Territorial Epidemiologists (CSTE) recommended that states adopt mandatory reporting of invasive infections caused by DRSP.[48] In 2000, the CSTE recommended national reporting of all invasive pneumococcal disease in children younger than 5 years of age.[49] It also suggested surveillance of disease in all age groups, especially by making laboratory reporting mandatory. Surveillance including all age groups would enable more complete analysis of the impact of the new PCV7 vaccine and of campaigns to increase the use of the 23-valent pneumococcal polysaccharide vaccine. In addition, surveillance in all age groups is desirable to calculate the prevalence of DRSP among all pneumococci causing invasive disease.

Between September 2001 and March 2005, the Respiratory Diseases Branch of CDC tracked reports from state health departments of cases of invasive pneumococcal disease among infants and young children who had received at least one dose of PCV7. Data from this surveillance project suggest that children who develop invasive pneumococcal disease following PCV7 vaccination tend to have been incompletely vaccinated or vaccinated late (CDC, unpublished data). Data from ABCs suggest that most cases of invasive pneumococcal disease among vaccinated children are caused by serotypes not covered by the vaccine.[26] True PCV7 failures—defined as PCV7-type invasive disease among fully vaccinated children—occur but are uncommon; therefore, collection of isolates from vaccinated children is no longer routinely recommended.

IV. Disease Reduction Goals

Since the introduction of PCV7 into the childhood immunization schedule in 2000, a significant decrease in invasive pneumococcal disease among infants and young children in the age groups targeted for vaccination has been observed.[22, 23] The *Healthy People 2010* goals for children under 5 years are to reduce the annual rate of invasive pneumococcal disease to 46 cases per 100,000 population from a baseline of 76 cases per 100,000 population in 1997, and to reduce the annual rate of penicillin-resistant invasive pneumococcal disease to 6 cases per 100,000 population from a baseline of 16 cases per 100,000 population in 1997.[13] The overall incidence of invasive disease among children younger than 5 years of age declined to 24 cases per 100,000 population in 2003, exceeding the *Healthy People 2010* objective for this age group.[26] Rates of penicillin-nonsusceptible invasive disease in children younger than 5 years ranged from 25.9 to 33.8 per 100,000 between 1996 and 1999, before the introduction of conjugate vaccine, and declined to 7.5 per 100,000 in 2004, thereby exceeding this *Healthy People 2010* objective as well.[35]

The *Healthy People 2010* goal for overall disease reduction for adults 65 years of age or older is 42 cases per 100,000 population compared with a baseline of 62 cases per 100,000 in 1997.[13] In 2003, the overall incidence of invasive disease declined to 42 cases per 100,000 population, meeting the *Healthy People 2010* objective for this age group.[26] The *Healthy People 2010* target for reduction of invasive pneumococcal disease due to penicillin-nonsusceptible strains is 7 cases per 100,000 persons 65 years and older. In this group, the rate of penicillin-nonsusceptible disease decreased from 16.4 per 100,000 in 1999 to 8.4 per 100,000 in 2004, a 49% reduction.[35] Continuous surveillance is important to evaluate whether reductions in invasive pneumococcal disease incidence will be sustained and whether increases in disease caused by pneumococcal serotypes not included in PCV7 (i.e., replacement disease) will reduce the overall benefit of PCV7.

Disease reduction goals also focus on minimizing complications of DRSP infections through prevention and control measures. In 1995, CDC launched a national campaign to reduce antimicrobial resistance through promotion of appropriate antibiotic use. The control efforts initially targeted the pediatric population and later expanded to include adults.[42, 44]

V. Case Definition

The following case definitions are used for national surveillance of pneumococcal disease in the United States. They were approved by the Council of State and Territorial Epidemiologists (CSTE) for drug-resistant *S. pneumoniae* (DRSP) invasive disease in 1994, and for invasive pneumococcal disease in children younger than 5 years of age in 2000.[48, 49] They were modified in 2006 to prevent duplicate reporting of individual cases.[50]

Drug-resistant *S. pneumoniae* (DRSP) invasive disease

Clinical description

Pneumococci may cause a wide variety of clinical syndromes depending on the site of infection (e.g., otitis media, pneumonia, bacteremia, meningitis). For purposes of national surveillance, "invasive" pneumococcal disease shall refer only to bacteremia and/or meningitis. Although *S. pneumoniae* infections involving other normally sterile sites such as joint, pleural, or peritoneal fluid are sometimes considered invasive, these infections are not intended for inclusion under this surveillance system.

Laboratory criteria for diagnosis

1. Isolation of *S. pneumoniae* from blood or cerebrospinal fluid.

2. Intermediate and high-level resistance* (defined by NCCLS-approved methods and interpretive MIC breakpoints) of the *S. pneumoniae* isolate to at least one antimicrobial agent currently approved for use in treating pneumococcal.

**Resistance defined by Clinical and Laboratory Standards Institute (CLSI [formerly National Committee for Clinical Laboratory Standards, NCCLS])–approved methods and CLSI-approved interpretive minimum inhibitory concentration (MIC) standards (µg/ml) for* S. pneumoniae *(NCCLS Guidelines, 1994). CLSI recommends that all* S. pneumoniae *isolates from patients with life-threatening infections undergo susceptibility testing by using a quantitative MIC method acceptable for penicillin, extended-spectrum cephalosporins, and other drugs as clinically indicated.*[51]

Case classification

Probable: A clinically compatible case due to laboratory-confirmed culture of *S. pneumoniae* identified as "nonsusceptible" (i.e., oxacillin zone size <20 mm) when oxacillin screening is the only method of antimicrobial susceptibility testing performed.

Confirmed: A clinically compatible case due to laboratory-confirmed *S. pneumoniae* identified as "nonsusceptible" according to MIC interpretive breakpoints as outlined in CLSI guidelines for susceptibility testing to any antimicrobial agent currently approved for use in treating pneumococcal infections.

Comment: A variety of methods are available for determining the antimicrobial susceptibility of *S. pneumoniae*; these commonly include disk diffusion, testing by agar dilution or broth microdilution, and testing by antimicrobial gradient agar diffusion (E-test® method). When oxacillin disk screening is the only antimicrobial susceptibility method used, the antimicrobial susceptibility profile cannot be definitively determined. Oxacillin screening is highly sensitive and somewhat specific for detecting beta-lactam–resistant *S. pneumoniae*; however, resistance to non–beta-lactam antibiotics is not detected with this screening method (see Section VI, "Laboratory testing").

Invasive *S. pneumoniae* (Children younger than 5 years)

Case definition

For purposes of this surveillance recommendation, invasive pneumococcal disease is defined as isolation of *S. pneumoniae* from a normally sterile site (e.g., CSF, blood, joint fluid, pleural fluid, pericardial fluid, other).[52]

Modification of case classifications for DRSP and IPD

Case classifications for DRSP and IPD have been modified as follows:

- Isolates causing IPD from children younger than 5 years of age and which antimicrobial susceptibility testing has determined to be DRSP should be reported ONLY as DRSP (event code 11720).
- Isolates causing IPD from children younger than 5 years of age that are susceptible, or for which susceptibility results are not available, should be reported ONLY as IPD (11717).
- All other components of the case definitions remain as referenced.[48, 49]

VI. Laboratory Testing

Definitive diagnosis of pneumococcal infection is confirmed by the recovery of *S. pneumoniae* from a normally sterile body site (e.g., blood, CSF, pleural fluid, or peritoneal fluid). Because pneumococci frequently colonize the upper respiratory tract in the absence of disease, the clinical significance of recovering the organism from nonsterile body sites (e.g., expectorated sputum, conjunctiva) is less certain. Gram strain may be helpful in interpreting cultures of expectorated sputum; finding a predominance of gram-positive diplococci and more than 25 leukocytes with fewer than 10 epithelial cells per high power field on microscopic examination supports the diagnosis of pneumococcal pneumonia.

Recommendations from CLSI state that clinical laboratories should test all isolates of *S. pneumoniae* from CSF for resistance to penicillin, cefotaxime or ceftriaxone, meropenem, and vancomycin.[51] Recently, susceptibility breakpoints have been changed for isolates from sites other than CSF, resulting in somewhat lower proportions of nonmeningeal isolates characterized as nonsusceptible to third-generation cephalosporins.[53] For organisms from other sources, laboratories should consider testing for resistance to erythromycin, penicillin, trimethoprim–sulfamethoxazole, clindamycin, cefotaxime or ceftriaxone, meropenem, tetracycline, vancomycin, and a fluoroquinolone such as levofloxacin. Pneumococci resistant to vancomycin have never been described; a strain with a vancomycin minimum inhibitory concentration of 2 µg/ml or greater or zone diameter less than 17 mm should be submitted to a reference laboratory for confirmatory testing, and if resistant, reported to the state health department. Because pneumococci are fastidious organisms, some susceptibility testing methods used for other organisms are not appropriate for pneumococci; CLSI's Performance Standards for Antimicrobial Susceptibility Testing should be consulted for testing recommendations.[51]

Currently licensed vaccines target a limited number of pneumococcal polysaccharide capsule serotypes. Identifying the serotypes of pneumococcal strains can be useful for evaluating outbreaks of pneumococcal disease such as those that occur in institutional settings. Serotyping is currently performed in only a limited number of state public health laboratories, academic centers, or at CDC. CDC's Streptococcal Reference Laboratory will serotype pneumococcal isolates from blood, CSF or other sterile sites in outbreak settings. The recent development of a PCR-based technique for determining capsular serotypes could broaden the capacity for state health departments and other countries to perform pneumococcal serotyping.[46, 47]

VII. Reporting

Each state and territory has regulations and laws governing the reporting of diseases and conditions of public health importance.[54] These regulations and laws list the diseases that are to be reported, and describe those persons or institutions responsible for reporting, such as healthcare providers, hospitals, laboratories, schools, daycare and child care facilities, and other institutions. Persons reporting should contact the state health department for state-specific reporting requirements.[52]

Reporting to CDC

Reporting invasive pneumococcal disease in children younger than 5 years of age. Healthcare providers or laboratories should report to their local or state health department all cases of invasive *S. pneumoniae* occurring in children younger than 5 years of age. Some states also require reporting cases among those 5 years and older. The following data are recommended for case investigation and reporting:

- Patient's date of birth or age
- The anatomic site of specimen collection
- Type of infection

Other epidemiologic information that is useful includes patient's sex, race and ethnicity, specimen collection date, whether the patient was hospitalized for the episode, clinical syndrome, antibiotic susceptibility, details of pneumococcal vaccination history, underlying medical conditions, daycare attendance, and outcome. Additional information may be collected at the direction of the state health department. The *S. pneumoniae* Surveillance Worksheet is included as Appendix 13. If the isolate causing IPD from a child younger than 5 years of age is known to be antibiotic susceptible, or if susceptibility results are not available, the case should be reported only as IPD in a child younger than 5 years of age (event code 11717 in the National Electronic Telecommunications System for Surveillance [NETSS]).[50]

Reporting drug-resistant invasive pneumococcal disease. Participating healthcare providers or laboratories should report to their local or state health department all cases of DRSP. The following data are recommended for case investigation and reporting:

- Patient's date of birth or age
- The anatomic site of specimen collection
- Type of infection

Other epidemiologic information that is useful includes patient's sex, race and ethnicity, specimen collection date, whether the patient was hospitalized for the episode, clinical syndrome, antibiotic susceptibility, details of pneumococcal vaccination history, underlying medical conditions, daycare attendance, and outcome. Additional information may be collected at the direction of the state health department. Accurate reporting of all cases of IPD—not only those occurring among children younger than 5 years of age—along with the antibiogram of the *S. pneumoniae* isolate will allow calculation of the prevalence of DRSP. Such a change in the case reporting requirements has been adopted or is under consideration in several states. An additional benefit of conducting surveillance for all invasive pneumococcal disease is the ability to track the progress of vaccine efforts to reduce the incidence of *S. pneumoniae* infections. See Appendix 13 for the *S. pneumoniae* Surveillance Worksheet. If a state is reporting through NETSS, use code 11720. If the DRSP case is in a child younger than 5 years of age, please note the modifications of case classifications for DRSP and IPD (Section V, above) and follow the reporting recommendations from CSTE:[50]

- Isolates causing IPD from children <5 years of age and which antimicrobial susceptibility testing has determined to be DRSP should be reported ONLY as DRSP (event code 11720).
- Isolates causing IPD from children <5 years of age which are susceptible, or for which susceptibility results are not available, should be reported ONLY as IPD in children <5 years of age (11717).
- All other components of the case definitions remain as referenced.[48, 49]

VIII. Vaccination

The Advisory Committee on Immunization Practices (ACIP) recommends that the pneumococcal conjugate vaccine (PCV7) be used for all children 23 months of age or younger and for children ages 24–59 months who are at increased risk for pneumococcal disease (e.g., children with sickle cell disease, CSF leak, human immunodeficiency virus infection, and other immunocompromising or chronic medical conditions).[4] ACIP also recommends that the vaccine be considered for all other children ages 24–59 months, with priority given to the following groups:

- Children ages 24–35 months
- Children who are of Alaska Native, American Indian, and African-American descent
- Children who attend group daycare centers

The conjugate vaccine has not been studied sufficiently with older children or adults to make recommendations for its use for persons 5 years old or older who are at increased risk for serious pneumococcal disease. These persons should continue to receive 23-valent polysaccharide vaccine in accordance with previous ACIP recommendations.

The 23-valent pneumococcal polysaccharide vaccine (PPV) is approximately 56%–75% efficacious for the prevention of invasive pneumococcal infection caused by vaccine serotypes.[55, 56] Children 2–4 years of age with high-risk medical conditions should receive PPV at least 2 months after receiving recommended PCV7 doses. A dose of vaccine should be administered to all persons 5–64 years of age who are at increased risk of serious pneumococcal infection because of underlying medical conditions and to all persons 65 years of age and older.[5] A single revaccination after at least 3–5 years (3 years for persons younger than 10 years of age, 5 years for persons 10 or years of age or older) should be considered for persons ages 2 to 64 years who are at highest risk or likely to have rapid declines in antibody levels. This includes those with functional or anatomic asplenia, HIV infection, leukemia, lymphoma, Hodgkin disease, multiple myeloma, generalized malignancy, chronic renal failure, nephrotic syndrome or immunosuppression (e.g., organ transplants or receiving chemotherapy). Previously vaccinated persons should be revaccinated at 65 years of age or older, providing at least 5 years has passed since the first dose. Pneumococcal vaccine may be administered

It is important to educate providers about which events should be reported and about how accurate reporting is critical to control of communicable diseases.

IX. Enhancing Surveillance

Several surveillance activities may improve the detection and reporting of pneumococcal disease and the quality of the reports.

Establishing reporting of all invasive pneumococcal disease in children younger than 5 years

CSTE has recommended reporting of all invasive pneumococcal disease in children younger than 5 years of age to monitor the impact of the pneumococcal conjugate vaccine for this age group; to track progress toward *Healthy People 2010* objectives; and, in conjunction with reporting of drug-resistant strains, to determine the burden of DRSP.

Enhancing reporting of DRSP

Concern over increasing resistance to antimicrobial agents has prompted many state health departments to institute reporting of resistant *S. pneumoniae* strains. Health departments are tracking DRSP using a variety of methods, including electronic laboratory-based reporting. CDC is working with state health departments to evaluate different surveillance methods to determine which methods would improve the reliability of surveillance data, given certain goals and resource limitations.[57] Use of aggregated antibiogram data collected from all hospital laboratories in an area has been shown to give a relatively accurate description of the proportion of isolates that are resistant to penicillin and a limited number of other drugs,[58] but such data typically cannot be analyzed by age group or other factors of interest. Sentinel systems, which may collect individual reports with more details from a limited number of laboratories, can provide an accurate view of resistance if designed well.[59]

Encouraging provider reporting

Most states' infectious disease surveillance systems depend upon receipt of case reports from healthcare providers and laboratories. These data are usually incomplete and may not be representative of certain populations; completeness of reporting has been estimated to vary from 6% to 90% for many of the common notifiable diseases.[54] Therefore, it is important to educate providers about which events should be reported and about how accurate reporting is critical to control of communicable diseases. Increasing provider awareness of local rates of DRSP and local reporting requirements could improve surveillance.

Improving detection of DRSP in laboratories by promoting optimal techniques and appropriate interpretive standards

Because pneumococci are fastidious organisms, laboratory methods that are appropriate for some organisms are not appropriate for pneumococci.[51] In addition, many laboratories are not monitoring resistance to some agents that are widely used for suspected pneumococcal infections, such as fluoroquinolone agents.[29] Universal adoption of optimal testing methods and testing for resistance to recommended antibiotics would improve the ability to detect and monitor resistant pathogens.

Streamlining reporting using electronic methods

Most surveillance systems still rely on paper and pencil for data collection; use of electronic data transferred directly from clinical laboratories would significantly improve reporting speed and data quality as well as reduce workload. Efforts are under way to implement electronic reporting.[60]

X. Case Investigations

As with most respiratory pathogens, rapid, sensitive, and specific diagnostic tests for *S. pneumoniae* infection are not available; thus, early in the course of illness, diagnosis is usually presumptive and the choice of antimicrobial therapy is nearly always empiric. However, once *S. pneumoniae* is isolated from a normally sterile body site, antimicrobial susceptibility testing may be necessary for patient management. Case investigations are not usually warranted, except in outbreaks or as determined by the state health department. CDC is available during outbreaks to assist with epidemiologic and laboratory investigations.

References

1. Schuchat A, Robinson K, Wenger JD, Harrison, LH, Farley M, Reingold AL, et al. Bacterial meningitis in the United States in 1995. *N Engl J Med* 1997;337:970–6.
2. CDC. Active Bacterial Core Surveillance (ABCs) Report *Streptococcus pneumoniae*, 2004. Atlanta: Centers for Disease Control and Prevention, 2005. Available at http://www.cdc.gov/ncidod/dbmd/abcs/survreports/spneu04.pdf
3. Thigpen MC, Rosenstein NE, Whitney CG, Lynfield R, Farley M, Craig AS, et al. Bacterial meningitis in the United States—1998–2003. Presented at the Annual Meeting of the Infectious Diseases Society of America, Boston, MA, Sept. 2005.
4. CDC. Preventing pneumococcal disease among infants and young children: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 2000;49(No. RR-9):1–35.
5. CDC. Prevention of pneumococcal disease. *MMWR* 1997;46(No. RR-8):1–20.
6. Robinson KA, Baughman W, Rothrock G, Barrett NL, Pass M, Lexau C, et al. Epidemiology of invasive *Streptococcus pneumoniae* infections in the United States, 1995–1998: opportunities for prevention in the conjugate vaccine era. *JAMA* 2001;285:1729–35.
7. CDC. Unpublished data. 2006.
8. CDC. National Ambulatory Medical Care Survey (NAMCS). Hyattsville, MD: US Department of Health and Human Services, Centers for Disease Control and Prevention, 2003.

9. Dowell SF, Marcy SM, Phillips WR, Gerber MA, Schwartz B. Otitis media—principles of judicious use of antimicrobial agents. *Pediatrics*1998;101:165–71.
10. Block SL, Hedrick J, Harrison CJ, et al. Community-wide vaccination with the heptavalent pneumococcal conjugate significantly alters the microbiology of acute otitis media. *Pediatr Infect Dis J* 2004;23(9):829-33.
11. Casey JR, Pichichero ME. Changes in frequency and pathogens causing acute otitis media in 1995–2003. *Pediatr Infect Dis J* 2004;23:824–8.
12. Feikin DR, Schuchat A, Kolczak M, Barrett NL, Harrison LH, Lefkowitz L, et al. Mortality from invasive pneumococcal pneumonia in the era of antibiotic resistance, 1995–1997. *Am J Public Health* 2000;90:223–9.
13. US Department of Health and Human Services. *Healthy People 2010*. 2nd. ed. With understanding and improving health and objectives for improving health (2 vols.). Washington DC: US Department of Health and Human Services, 2000.
14. CDC. Influenza and pneumococcal vaccination coverage among persons aged >65 years and persons aged 18–64 years with diabetes or asthma—United States, 2003. *MMWR* 2004;53(43):1007–12.
15. Kyaw MH, Rose CE, Jr., Fry AM, Singleton JA, Moore Z, Zell ER, et al. The influence of chronic illnesses on the incidence of invasive pneumococcal disease in adults. *J Infect Dis* 2005;192:377–86.
16. Black S, Shinefield H, Fireman B, Lewis E, Ray P, Hansen J, et al. Efficacy, safety and immunogenicity of heptavalent pneumococcal conjugate vaccine in children. Northern California Kaiser Permanente Vaccine Study Center Group. *Pediatr Infect Dis J* 2000;19:187–95.
17. O'Brien KL, Moulton LH, Reid R, Weatherholtz R, Oski J, Brown L, et al. Efficacy and safety of seven-valent conjugate pneumococcal vaccine in American Indian children: group randomised trial. *Lancet* 2003;362:355–61.
18. Eskola J, Kilpi T, Palmu A, Jokinen J, Haapakoski J, Herva E, et al. Efficacy of a pneumococcal conjugate vaccine against acute otitis media. *N Engl J Med* 2001;344:403–9.
19. Black SB, Shinefield HR, Ling S, Hansen J, Fireman B, Spring D, et al. Effectiveness of heptavalent pneumococcal conjugate vaccine in children younger than 5 years of age for prevention of pneumonia. *Pediatr Infect Dis J* 2002;21:810–5.
20. CDC. Notice to Readers: Updated recommendations on the use of pneumococcal conjugate vaccine in a setting of vaccine shortage—Advisory Committee on Immunization Practices. *MMWR* 2001;50(50):1140–2.
21. CDC. National Immunization Survey. Atlanta, GA: Centers for Disease Control and Prevention, 2004. Available at http://www2a.cdc.gov/nip/coverage/nis/nis_iap.asp?fmt=v&rpt=tab02_antigen_iap&qtr=Q1/2004-Q4/2004
22. Whitney CG, Farley MM, Hadler J, Harrison LH, Bennett NM, Lynfield R, et al. Decline in invasive pneumococcal disease after the introduction of protein-polysaccharide conjugate vaccine. *N Engl J Med* 2003;348:1737–46.
23. Pilishvili T, Moore M, Lynfield R, Hadler J, Reingold A, Farley M, et al. Invasive pneumococcal disease in children four years following the introduction of the conjugate vaccine: an update from Active Bacterial Core Surveillance (ABCs). Presented at the International Conference on Emerging Infectious Diseases, Atlanta, Georgia, March 19–22, 2006.
24. Lexau CA, Lynfield R, Danila R, et al. Changing epidemiology of invasive pneumococcal disease among older adults in the era of pediatric pneumococcal conjugate vaccine. *JAMA* 2005;294(16):2043-51.
25. Moore MR, Pilishvili T, Bennett N, Hadler J, Thomas A, Farley M, et al. Trends in invasive pneumococcal disease among adults, 1998–2004: implications for conjugate vaccine development. Presented at the International Conference on Emerging Infectious Diseases, Atlanta, GA, March 19–22, 2006.

26. 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* 2005;54(36):893–7.
27. Flannery B, Heffernan RT, Harrison LH, Ray SM, Reingold AL, Hadler J, et al. Changes in invasive pneumococcal disease among HIV-infected adults living in the era of childhood pneumococcal immunization. *Ann Intern Med* 2006;144:1–9.
28. Whitney CG, Farley MM, Hadler J, Harrison LH, Lexau C, Reingold A, et al. Increasing prevalence of multidrug-resistant *Streptococcus pneumoniae* in the United States. *N Engl J Med* 2000;343:1917–24.
29. Pletz MW, McGee L, Jorgensen J, Beall B, Facklam RR, Whitney CG, et al. Levofloxacin-resistant invasive *Streptococcus pneumoniae* in the United States: evidence for clonal spread and the impact of conjugate pneumococcal vaccine. *Antimicrob Agents Chemother* 2004;48:3491–7.
30. Butler JC, Hofmann J, Cetron MS, Elliott JA, Facklam RR, Breiman RF. The continued emergence of drug-resistant *Streptococcus pneumoniae* in the United States: an update from the Centers for Disease Control and Prevention's Pneumococcal Sentinel Surveillance System. *J Infect Dis* 1996;174:986–93.
31. Breiman RF, Butler JC, Tenover FC, Elliott JA, Facklam RR. Emergence of drug-resistant pneumococcal infections in the United States. *JAMA* 1994;271:1831–5.
32. CDC. Multidrug-resistant *Streptococcus pneumoniae* in a child care setting in Southwest Georgia, December 2000. *MMWR* 2002;50:1156–8.
33. Nuorti JP, Butler JC, Crutcher JM, Guevara R, Welch D, Holder P, et al. An outbreak of multidrug-resistant pneumococcal pneumonia and bacteremia among unvaccinated nursing home residents. *N Engl J Med* 1998;338:1861–8.
34. Reichler MR, Allphin AA, Breiman RF, Schreiber JR, Arnold JE, McDougal LK, et al. The spread of multiply resistant *Streptococcus pneumoniae* at a day care center in Ohio. *J Infect Dis* 1992;166:1346–53.
35. Kyaw MH, Lynfield R, Schaffner W, Craig AS, Hadler J, Thomas AR, et al. Effect of introduction of the pneumococcal conjugate vaccine on drug-resistant *Streptococcus pneumoniae*. *N Engl J Med* 2006;354:1455–63.
36. Kaplan SL, Mason EO, Jr., Wald ER, Schutze GE, Bradley JS, Tan TO, et al. Decrease of invasive pneumococcal infections in children among 8 children's hospitals in the United States after the introduction of the 7-valent pneumococcal conjugate vaccine. *Pediatrics*2004;113(3 Pt 1):443–9.
37. Stephens DS, Zughaier SM, Whitney CG, Baughman WS, Barker L, Gay K, et al. Incidence of macrolide resistance in *Streptococcus pneumoniae* after introduction of the pneumococcal conjugate vaccine: population-based assessment. *Lancet* 2005;365:855–63.
38. Talbot TR, Poehling KA, Hartert TV, Arbogast PG, Halasa NB, Mitchel E, et al. Reduction in high rates of antibiotic-nonsusceptible invasive pneumococcal disease in Tennessee after introduction of the pneumococcal conjugate vaccine. *Clin Infect Dis* 2004;39:641–8.
39. American Academy of Family Physicians, American Academy of Otolaryngology-Head and Neck Surgery, American Academy of Pediatrics Subcommittee on Otitis Media with Effusion. Otitis media with effusion. *Pediatrics* 2004;113:1412–29.
40. American Academy of Family Physicians, American Academy of Otolaryngology-Head and Neck Surgery, and American Academy of Pediatrics: Subcommittee on Management of Acute Otitis Media. Diagnosis and management of acute otitis media. *Pediatrics* 2004;113:1451–65.
41. Mandell LA, Bartlett JG, Dowell SF, File TM, Jr., Musher DM, Whitney C. Update of practice guidelines for the management of community-acquired pneumonia in immunocompetent adults. *Clin Infect Dis* 2003;37:1405–33.

42. Dowell S, Marcy S, Phillips W, Gerber M, Schwartz B. Principles of judicious use of antimicrobial agents for pediatric upper respiratory tract infections. *Pediatrics* 1998;101:163–5.
43. Gonzales R, Bartlett JG, Besser RE, Cooper RJ, Hickner JM, Hoffman, JR, et al. Principles of appropriate antibiotic use for treatment of uncomplicated acute bronchitis: background. *Ann Intern Med* 2001;134:521–9.
44. Gonzales R, Bartlett JG, Besser RE, Cooper RJ, Hickner JM, Hoffman, JR, et al. Principles of appropriate antibiotic use for treatment of acute respiratory tract infections in adults: background, specific aims, and methods. *Ann Intern Med* 2001;134:479–86.
45. Gonzales R, Bartlett JG, Besser RE, Hickner JM, Hoffman JR, Sande MA. Principles of appropriate antibiotic use for treatment of nonspecific upper respiratory tract infections in adults: background. *Ann Intern Med* 2001;134:490–4.
46. Pai R, Gertz RE, Beall B. Sequential multiplex PCR approach for determining capsular serotypes of *Streptococcus pneumoniae* isolates. *J Clin Microbiol* 2006;44:124–31.
47. Pai R, Limor J, Beall B. Use of pyrosequencing to differentiate *Streptococcus pneumoniae* serotypes 6A and 6B. *J Clin Microbiol* 2005;43:4820–2.
48. Council of State and Territorial Epidemiologists. National surveillance for drug-resistant *Streptococcus pneumoniae* (DRSP) invasive disease. Position Statement 1994-10, 1994. Available at http://www.cste.org/ps/1994/1994-nsc-0.htm
49. Council of State and Territorial Epidemiologists. Surveillance for invasive pneumococcal disease in children less than five years of age. Position Statement 2000-6, 2000. Available at http://www.cste.org/ps/2000/2000-ID-06.htm
50. Council of State and Territorial Epidemiologists. Enhancing local, state and territorial-based surveillance for invasive pneumococcal disease in children less than five years of age. Position Statement 2006-14, 2006. Available at http://www.cste.org/PS/2006pdfs/PSFINAL2006/06-ID-14FINAL.pdf
51. Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing; Fifteenth informational supplement. Approved standard M100-S15. Wayne, PA: Clinical and Laboratory Standards Institute, 2005.
52. CDC. Case definitions for infectious conditions under public health surveillance. *MMWR* 1997;46(No. RR-10):20.
53. CDC. Effect of new susceptibility breakpoints on reporting of resistance in *Streptococcus pneumoniae*—United States, 2003. *MMWR* 2004;53(7):152–4.
54. Roush S, Birkhead G, Koo D, Cobb A, Fleming D. Mandatory reporting of diseases and conditions by health care professionals and laboratories. *JAMA* 1999;282:164–70.
55. Butler JC, Breiman RF, Campbell JF, Lipman HB, Broome CV, Facklam RR. Pneumococcal polysaccharide vaccine efficacy. An evaluation of current recommendations. *JAMA* 1993;270:1826–31.
56. Shapiro ED, Berg AT, Austrian R, Schroeder D, Parcells V, Margolis A, et al. The protective efficacy of polyvalent pneumococcal polysaccharide vaccine. *N Engl J Med* 1991;325:1453–60.
57. Noggle B, Iwamoto M, Chiller T, et al. Tracking resistant organisms: Workshop for improving state-based surveillance programs [conference summary]. International Conference on Emerging Infectious Diseases, Atlanta, GA, March 19–22, 2006.
58. Van Beneden CA, Lexau C, Baughman W, Barnes B, Bennett N, Cassidy PM, et al. Aggregated antibiograms and monitoring of drug-resistant *Streptococcus pneumoniae*. *Emerg Infect Dis* 2003;9:1089–95.
59. Schrag SJ, Zell ER, Schuchat A, Whitney CG. Sentinel surveillance: a reliable way to track antibiotic resistance in communities? *Emerg Infect Dis* 2002;8:496–502.
60. Progress in improving state and local disease surveillance—United States, 2000–2005. *MMWR* 2005;54(33):822–5.