ASHP Therapeutic Position Statement on Strategies for Identifying and Preventing Pneumococcal Resistance

Position

The American Society of Health-System Pharmacists (ASHP) supports the establishment of state and national surveillance systems to track the prevalence of drug-resistant *Streptococcus pneumoniae* so that appropriate antimicrobial regimens can be used to treat infections caused by this common community-acquired pathogen.

ASHP supports continued educational efforts to promote the rational use of antimicrobials as a strategy for preventing the development of drug-resistant bacteria.

ASHP supports pharmacist leadership and involvement on antimicrobial stewardship teams and the addition of antimicrobial stewardship as a core component of pharmacy services.

ASHP supports the pharmacist in administration of vaccines for all persons at risk for acquiring pneumococcal disease. ASHP encourages the development of pharmacy-based programs to increase pneumonia vaccination rates of at-risk patients. Use of pneumococcal vaccines is a reliable strategy to decrease the morbidity and mortality associated with invasive infections due to *S. pneumoniae*.

Background

S. pneumoniae, also known as pneumococcus, is the most common cause of community-acquired, bacterial, respiratory-tract infections. It is a frequent cause of meningitis, otitis media, and community-acquired pneumonia. Infections caused by *S. pneumoniae* have been associated with increased morbidity and mortality, especially in children under two years of age and elderly adults. Infections caused by *S. pneumoniae* have historically been successfully treated with a variety of antimicrobials, including penicillin, cephalosporins, and erythromycin. In the early 1990s, the first reports of penicillin-nonsusceptible *S. pneumoniae* (PNSP) began to appear in the United States; these strains include both intermediately resistant and resistant strains of *S. pneumoniae*. To date, reports of increasing resistance of *S. pneumoniae* to penicillin and cephalosporins continue. In the late 1990s, reports of increasing resistance to trimethoprim–sulfamethoxazole, macrolides, and fluoroquinolones began to appear. Many isolates developed resistance to multiple classes of drugs and became known as multidrug-resistant *S. pneumoniae* (MDRSP). The increasing prevalence of MDRSP has created a challenge for health care providers in treating this common community-acquired pathogen.

The clinical significance of drug-resistant *S. pneumoniae* on treatment outcomes is unclear. Most of the available data on clinical outcomes are from retrospective reviews, case–control studies, and case reports. There is evidence that meningitis due to PNSP does not respond to treatment with either penicillin or standard doses of cephalosporins, leading to poor clinical outcomes.[1] In contrast, there does not appear to be a significant difference in clinical outcome, primarily mortality, when pneumonia or other nonmeningeal infections due to PNSP are treated with penicillin or cephalosporins. On the contrary, macrolides and fluoroquinolones with poor in vitro activity against *S. pneumoniae* have been associated with poor clinical outcomes and even treatment failures. It is likely that clinical outcomes are dependent on the mechanism and degree of resistance, the site of infection, and the pharmacokinetic and pharmacodynamic characteristics of the antimicrobial agents used in treatment.

Definitions. The Clinical and Laboratory Standards Institute (CLSI), previously known as the National Committee for Clinical Laboratory Standards, revised the definitions of *S. pneumoniae* susceptibility to several antimicrobials in its 2002 standards. Since that time, there have been two sets of interpretive criteria for *S. pneumoniae* isolates for i.v. penicillin and i.v. cephalosporins, depending on whether meningeal disease is present. *S. pneumoniae* resistant to penicillin is defined in terms of the minimum inhibitory concentration (MIC) of penicillin. Strains in a patient with meningeal disease may be distinguished as susceptible (MIC < 0.06 μg/mL) or resistant (MIC ≥ 0.12 μg/mL). Strains in a patient with nonmeningeal disease may be characterized as susceptible (MIC ≤ 2 μg/mL), intermediately resistant (MIC $= 4$ μg/mL), or highly resistant (MIC ≥ 8 μg/mL).[2] CLSI accounted for the pharmacokinetic and pharmacodynamic factors of a drug in redefining susceptibility breakpoints. The definition of MDRSP is a strain resistant to three or more classes of antibacterials (where those antibacterials may have activity).

Epidemiology. Numerous national and international surveillance studies have been conducted to determine the prevalence of *S. pneumoniae* resistance.[3–7] Although many of these surveillance studies have discontinued the annual collection of data, the Active Bacterial Core Surveillance, known as the ABCs, remains active in the United States.[8] These networks used similar methodologies and specimens: clinical isolates of *S. pneumoniae* from sterile body sites or the respiratory tract, with susceptibility testing in accordance with CLSI standards. Although these studies showed differing resistance rates to the antimicrobials tested, some common trends emerged. The incidence of strains highly resistant to penicillin has surpassed that of intermediately resistant strains. The rates of resistance to non-β-lactams have also increased: the prevalence of macrolide resistance is 20–30%, and trimethoprim–sulfamethoxazole resistance ranges between 24% and 38%. *S. pneumoniae* resistance to levofloxacin is hovering around less than 1%. ABCs personnel evaluate the incidence and susceptibility of invasive *S. pneumoniae* infections in the United States.[8] This surveillance group does not distinguish resistance based on location of disease (i.e., meningeal versus nonmeningeal). For the 2010 isolates, the rates of strains intermediately resistant and highly resistant to penicillin were similar (5.5% and

5.1%, respectively).[8] Resistance to macrolides was 25.7%, which greatly surpassed the intermediately resistant strains (0.5%), leaving 73.8% of strains susceptible. Trimethoprim–sulfamethoxazole susceptibility was slightly higher than the macrolides, at 77.6%, and tetracycline susceptibility was higher at 84.9%. Fluoroquinolone (levofloxacin specifically) resistance remained low at 0.3%, and vancomycin remained universally susceptible (100%). Previously, there were reports from Canada[9] and the Centers for Disease Control and Prevention (CDC)[10] of increasing resistance of *S. pneumoniae* to fluoroquinolones. Most fluoroquinolone-resistant isolates are resistant to other antimicrobials. Fluoroquinolone-resistant organisms are more likely to be found in persons over age 65 years, as this population has the highest usage rate of fluoroquinolones.

Persons at Risk. The greatest risk factor for becoming infected with a drug-resistant strain of *S. pneumoniae* is prior antimicrobial use. Other risk factors include carriage of *S. pneumoniae*, daycare attendance, exposure to children who attend daycare, severe medical comorbidities, immunosuppression, and high alcohol intake.[1] Smoking has been identified as a risk factor for developing invasive *S. pneumoniae* infections.[11] The risk of invasive *S. pneumoniae* infections is 4-fold if the patient is a smoker and 2.5-fold if the patient is exposed to secondhand smoke.[11] The risk of invasive disease declines over time for persons who have stopped smoking.

Mechanisms of Resistance. Resistance of *S. pneumoniae* to β-lactams is due to genetic mutations leading to alterations in three or four of the five high-molecular-weight penicillin-binding proteins (PBPs).[12] The degree of *S. pneumoniae* resistance is dependent on which PBPs are involved and the affinity of the β-lactam agent to the PBP. The differences in expression of these PBPs explain the differences in susceptibility to a variety of β-lactams.

S. pneumoniae resistance to macrolides occurs primarily through two mechanisms: active drug efflux (M phenotype) or ribosomal modification (MLS_β phenotype).[13] Active drug efflux confers resistance to all macrolide agents, whereas ribosomal modification confers resistance not only to the macrolides but also to lincosamides (e.g., clindamycin) and streptogramins. Almost 100% of macrolide-resistant *S. pneumoniae* found in the United States is attributable to ribosomal modification via methylation.[13]

Resistance of *S. pneumoniae* to fluoroquinolones is primarily a result of the mutations of the *parC* and *gyrA* genes, though efflux pumps may also play a role.[14] Alterations in the *parC* subunit of topoisomerase IV result in the reduced susceptibility of *S. pneumoniae* to gatifloxacin, levofloxacin, and moxifloxacin. This single-step mutation is difficult to detect clinically because isolates with a *parC* mutation are reported as susceptible using standard laboratory testing. This is concerning because isolates with single-step mutations are the progenitors for fully drug-resistant strains of *S. pneumoniae*, which have additional mutations in the *gyrA* subunit of DNA gyrase.

Establishment of Surveillance Systems

Surveillance systems are an integral component of combating bacterial resistance. The data gathered from surveillance systems can be used for many purposes, including identifying and tracking global outbreaks, identifying new strains and resistance profiles, setting public health policy, heightening awareness of health care providers to local resistance patterns that may affect the routine care of patients, and determining appropriate treatment for infections.

Health systems should develop a mechanism for the local surveillance of bacterial resistance and participate in state and national surveillance programs when available. Ideally, the surveillance system should identify trends in bacterial susceptibility patterns and correlate them with antimicrobial use in both health systems and communities.[15] The clinical microbiology laboratory, pharmacy, infection prevention, and information technology departments play important roles in maintaining an active surveillance system.

At a national level, data acquired through surveillance systems such as those used by CDC and the World Health Organization (WHO) can aid in the research and development of policies and treatment guidelines for pneumococcal disease. State and local surveillance is also essential, as national trends may not reflect trends within specific regions. On a local level, surveillance programs can help raise provider and public awareness of drug-resistant *S. pneumoniae* and direct patient care on an institutional level and potentially on the unit level. Institutional antibiograms should be updated annually, and microbiological data used for diagnosis should be stored in a way that will facilitate resistance surveillance.[16,17] Surveillance data may also be useful for tracking the impact of interventions, such as formulary changes and antimicrobial stewardship interventions, targeting the inappropriate or unnecessary use of antibiotics.

Rational Use of Antimicrobials

There is an abundance of literature showing the relationship between antimicrobial-use patterns and the development of bacterial resistance.[18–21] However, the bulk of this literature thus far has been generated from hospital or institutional studies and has little bearing on PNSP. Since *S. pneumoniae* is primarily a community-acquired pathogen, antimicrobial use in the outpatient setting has the greatest influence on its susceptibility profile. Few studies have shown a relationship between outpatient prescription use or antimicrobial stewardship interventions and *S. pneumoniae* susceptibility patterns. In the United States, Diekema and colleagues[22] found a positive correlation between high usage rates of outpatient β-lactam agents and the decreased penicillin susceptibility of *S. pneumoniae*. No correlation was found between the use of other antimicrobial classes (e.g., macrolides, tetracyclines, fluoroquinolones) and the decreased penicillin susceptibility of *S. pneumoniae*. More recently, Hicks et al.[23] reviewed outpatient antimicrobial prescription data (penicillins, cephalosporins, macrolides, and trimethoprim–sulfamethoxazole) and found a consistent relationship between higher prescription rates and increased rates of *S. pneumoniae* nonsusceptibility to the respective antimicrobial class. This study also found that when comparing sites with high versus low antimicrobial prescription rates for the same class of antimicrobials, macrolide and cephalosporin prescriptions were both associated with serotype 19A, despite yearly decreases in outpatient antimicrobial prescribing rates. Both of these studies were large, retrospective database studies and did not account for patient adherence to antimicrobial regimens. However, these studies demonstrated that antimi-

crobial use in the community is substantial and plays a role in the development of microbial resistance.

Approximately 50% of prescriptions for antimicrobials are unnecessary or inappropriate.[24] These agents are usually prescribed for treatment of the common cold, upper-respiratory-tract infections, acute rhinosinusitis, and bronchitis, ailments often caused by viruses that do not respond to antibacterials. Recent clinical practice guidelines from the Infectious Diseases Society of America for acute bacterial rhinosinusitis in children and adults acknowledged the difficulty in distinguishing between viral and bacterial etiologies. To decrease inappropriate antibacterial use, the guidelines recommend initiating antibacterials only if the patient has symptoms that are persistent and not improving (duration of ≥10 days), severe (≥3–4 days), or worsening or "double sickening" (subsequent worsening of symptoms or additional symptoms after earlier improvement). Prescribers for patients who do not yet meet the criteria for antibacterial treatment of rhinosinusitis will occasionally give a prescription for antibacterials with the instructions to fill and take the medication if symptoms are persistent. Pharmacists can assist patients in making appropriate decisions on antimicrobial use by counseling patients on the appropriate timing of initiating antibacterials as well as the importance of completing the prescribed treatment course. In addition, empirical antibacterial selection should not include amoxicillin, macrolides, trimethoprim–sulfamethoxazole, or monotherapy with second- or third-generation cephalosporins due to high rates of resistance in *S. pneumoniae*. Finally, a shorter course of antibacterial treatment (5–7 days) is recommended for adults, compared with the 10–14 days recommended for children. Several national organizations,[15,24] CDC, and WHO have advocated antimicrobial stewardship as a mechanism to limit the development of bacterial resistance.[25,26] One of the cornerstones of antimicrobial stewardship is the appropriate use of antimicrobials. Pharmacists should take active roles in antimicrobial stewardship programs, and the infectious diseases pharmacist is considered a core member of the antimicrobial stewardship team.[24,27]

In 1995, CDC launched the National Campaign for Appropriate Antibiotic Use in the Community, which, in 2003, was renamed Get Smart: Know When Antibiotics Work campaign.[28] This campaign was launched in response to growing antimicrobial resistance with respiratory pathogens and aims to reduce the rise of antimicrobial resistance through the promotion of appropriate prescribing, decrease the demand for antimicrobials to treat viral respiratory infections, and increase patient adherence with antimicrobials prescribed for upper-respiratory-tract infections. This program provides a wealth of information for the antimicrobial stewards and the public to help increase awareness at their facilities and includes promotional material for inpatient, outpatient, and long-term-care settings.

Vaccination

Pneumococcal infection has been associated with 2.4 million days of hospitalization and approximately 5000 deaths annually in the United States.[29] As vaccination may contribute to a reduction in these numbers and because hospitalization is an underutilized opportunity for vaccination, the Joint Commission (in collaboration with the Centers for Medicare and Medicaid Services) in January 2012 expanded the pneumococcal vaccination process measure to include all patients regardless of diagnosis. This measure evaluates if, before hospital discharge, patients age 6 years or older were screened for pneumococcal vaccine status and received the pneumococcal vaccine if appropriate. Infections caused by *S. pneumoniae* continue to cause significant morbidity and mortality despite the availability of effective vaccines.

The 23-valent pneumococcal polysaccharide vaccine (PPSV23), the 13-valent pneumococcal conjugate vaccine (PCV13), and the 7-valent pneumococcal conjugate vaccine (PCV7) have been shown to be highly effective in providing protection against the most commonly isolated pneumococcal serotypes that cause human disease, including those serotypes known to be antimicrobial resistant. While the use of these vaccines will not prevent the development of drug-resistant *S. pneumoniae*, they will likely prevent invasive infection caused by a drug-resistant organism. PPSV23 is recommended for all adults age 65 years or older and other adults with certain comorbid conditions.[30] It may also be

Table 1.

Patients Who Should Receive the 13-Valent Pneumococcal Conjugate Vaccine (PCV13)

Risk Group	Underlying Medical Condition
Immunocompetent persons	Cerebrospinal fluid leak Cochlear implant
Immunocompromised persons	Congenital or acquired immune deficiency Human immunodeficiency virus infection Chronic renal failure Nephrotic syndrome Leukemia Lymphoma Hodgkin disease Generalized malignancy Iatrogenic immunosuppression (diseases requiring treatment with immunosuppressive drugs, including long-term systemic corticosteroids and radiation therapy) Solid organ transplant Multiple myeloma
Persons with functional or anatomical asplenia	Sickle cell disease or other hemaglobinopathy Congenital or acquired asplenia

given to select groups of high-risk patients over 2 years of age (such as those with cochlear implants) as long as it is administered at least eight weeks after administration of the last dose of PCV7 or PCV13. This PPSV23 vaccine does not produce an adequate immunologic response in children under 2 years old and should not be used in that population. PCV7 was added to the standard recommended pediatric vaccines in October 2000.[31] PCV13 was added in 2010. The PCV series should be given to all children beginning at age 2 months. A single supplemental dose of PCV13 is recommended for all children age 14–59 months and for children age 60–71 months with certain underlying medical conditions who have already received an age-appropriate PCV7 series.[32] The CDC National Immunization Program has established recommendations for pneumococcal vaccine administration.[30,32]

PPSV23 was licensed in the early 1980s and has demonstrated good immunogenicity in both young and older adults; however, an individual will not develop an immune response to all 23 pneumococcal serotypes.[33] The reason for

Table 2.

Medical Conditions or Other Indications for Administration of 13-Valent Pneumococcal Conjugate Vaccine (PCV13), and Indications for 23-Valent Pneumococcal Polysaccharide Vaccine (PPSV23) Administration and Revaccination for Adults Age 19 Years or Older[24,a]

	PCV13	PPSV23	
Risk Group and Underlying Medical Condition	**Recommended**	**Recommended**	**Revaccination 5 Years After First Dose**
Immunocompetent persons			
Chronic heart disease[b]		X	
Chronic lung disease[c]		X	
Diabetes mellitus		X	
Cerebrospinal fluid leak	X	X	
Cochlear implant	X	X	
Alcoholism		X	
Chronic liver disease, cirrhosis		X	
Cigarette smoking		X	
Persons with functional or anatomic asplenia			
Sickle cell disease or other hemaglobinopathy	X	X	X
Congenital or acquired asplenia	X	X	X
Immunocompromised persons			
Congenital or acquired immunodeficiency[d]	X	X	X
Human immunodeficiency virus infection	X	X	X
Chronic renal failure	X	X	X
Nephrotic syndrome	X	X	X
Leukemia	X	X	X
Lymphoma	X	X	X
Hodgkin disease	X	X	X
Generalized malignancy	X	X	X
Iatrogenic immunosuppression[e]	X	X	X
Solid organ transplant	X	X	X
Multiple myeloma	X	X	X

[a]All adults age ≥65 years should receive a dose of PPSV23, regardless of previous history of vaccination with pneumococcal vaccine.
[b]Including congestive heart failure and cardiomyopathies, excluding hypertension.
[c]Including chronic obstructive pulmonary disease, emphysema, and asthma.
[d]Includes B- (humoral) or T-lymphocyte deficiency, complement deficiencies (particularly C1, C2, C3, and C4 deficiencies), and phagocytic disorders (excluding chronic granulomatous disease).
[e]Diseases requiring treatment with immunosuppressive drugs, including long-term systemic corticosteroids and radiation therapy.

this is unclear. Despite the vaccine's long-standing availability and documented effectiveness, approximately 64% of eligible persons actually receive it.[34] One of the Healthy People 2020 goals is for 90% of eligible adults to receive the pneumococcal vaccine.[35] This is an excellent opportunity for pharmacists to improve the vaccination rate of older adult patients and help promote national health care goals.

Revaccination with PPSV23 is recommended for adults over age 65 years if the first dose was administered when they were under 65 years old at the time of vaccination and at least 5 years has elapsed since the first dose.[30] In addition, persons younger than 65 years with immunocompromising conditions may receive a one-time revaccination if 5 years has elapsed since the first dose of PPSV23. Revaccination with PPSV23 results in a somewhat blunted immune response and is associated with increased injection-site reactions.[33]

PCV7 for children has been available since February 2000. Use of this vaccine has been shown to decrease the carriage rate of *S. pneumoniae* and the incidence of invasive pneumococcal disease, acute otitis media, and pneumonia in vaccinated populations.[36,37] The rate of vaccine-specific serotype *S. pneumoniae* carriage in vaccinated children remains below the rate for nonvaccinated children over prolonged periods of time. Widespread vaccination of children with PCV7 has shown a "herd effect" in decreasing the carriage rate of *S. pneumoniae* in children, who are an important vector for the transmission of *S. pneumoniae* to other children and adults.[36] This is similar to what was seen with widespread use of the *Haemophilus influenzae* type B vaccine and the marked decrease in *H. influenzae*-related infections.

PCV13 for children and adults has been available since February 2010 and has taken the place of the discontinued PCV7. All children age 2–59 months should have routine immunization with PCV13.[32] CDC has established routine and catch-up schedules for vaccination. Recommendations by the CDC Advisory Committee on Immunization Practices for the use of PCV13 in adults were established in 2012.[30] Patients who have immunocompromising conditions should receive PCV13 in addition to PPSV23 (Tables 1 and 2). Screening and vaccination should occur in all appropriate adult patients. Timing of PCV13 and PPSV23 administration is important to ensure maximal immune response. If the person has never received a dose of PCV13 or PPSV23, he or she should receive a dose of PCV13 followed by a dose of PPSV23 at least eight weeks later. If the patient has received one or more doses of PPSV23, the patient should receive one dose of PCV13 at least one year after the last dose of PPSV23.

Health care institutions should develop robust programs to increase pneumococcal vaccination rates as pneumococcal disease continues to contribute to a significant amount of morbidity and mortality in the United States. More than 65% of patients with severe pneumococcal disease have been hospitalized in the preceding—three to five years, but few have received vaccine.[34] Most people who succumb to preventable infections have visited a health care provider in the preceding year but were not vaccinated.[38–42] Clinicians should ensure that patients receive proper immunizations,[43,44] and pharmacists can promote vaccination efforts by serving as educators, facilitators, and vaccinators. Currently, all 50 states allow pharmacists to administer vaccines, and 49 states allow pharmacists to administer pneumococcal vaccines.[45] Variability exists among the states regarding patient age limitations and pharmacist-administered vaccines, with 13 states authorizing pharmacists to vaccinate patients of any age.[46] Although vaccinations are typically administered in the ambulatory care setting, clinicians must also seize opportunities to vaccinate hospitalized patients (Figure 1). Pharmacists have demonstrated that they can increase the number of persons receiving needed vaccines in both inpatient and ambulatory care settings.[47]

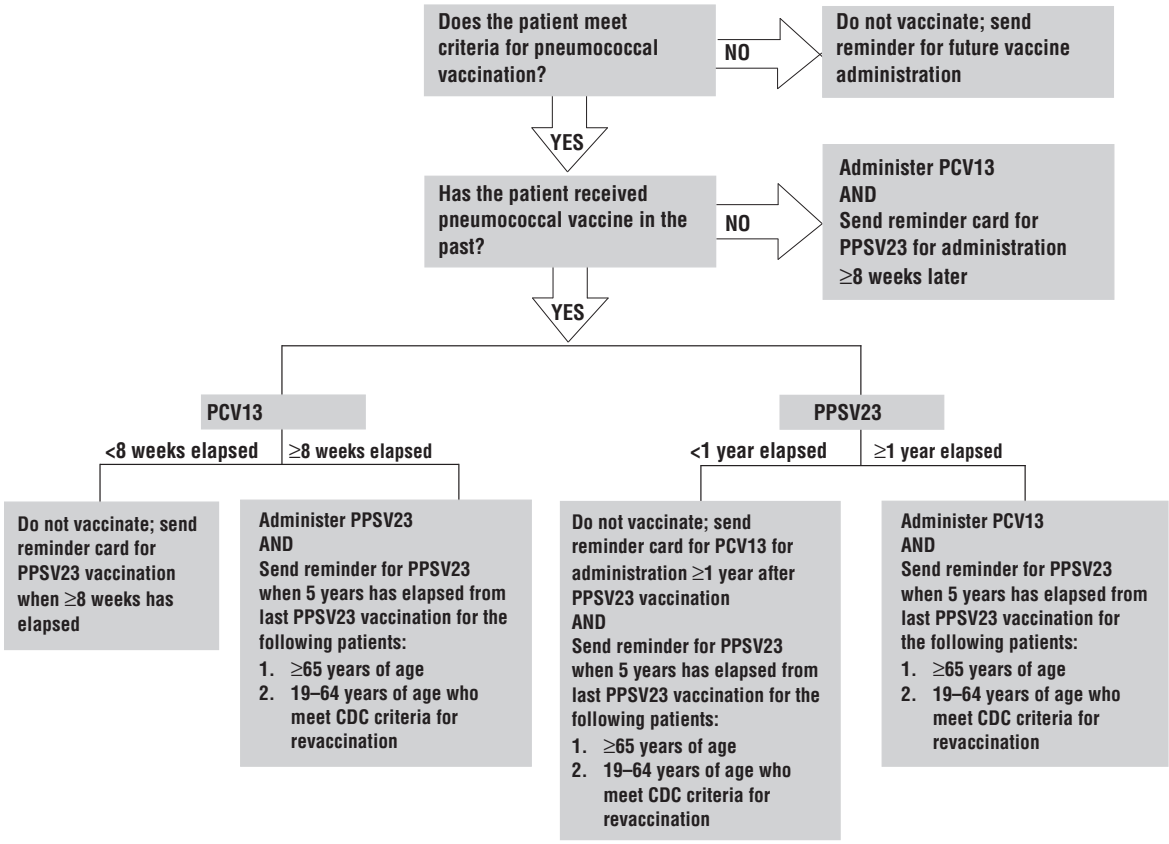
Summary

The incidence of MDRSP continues to increase, causing significant morbidity and mortality. Health care providers should seize the opportunity to promote the judicious use of antimicrobials and vaccinate patients with the pneumococcal vaccines as a means to lessen this significant health problem. Pharmacists are poised to play a key role in patient care by assessing for the need and administering vaccines in compliance with the current guidelines. A pharmacist should have a key role on the antimicrobial stewardship team.

References

1. Pallares R, Fenoll A, Liňares J, for the Spanish Pneumococcal Infection Study Network. The epidemiology of antibiotic resistance in *Streptococcus pneumoniae* and the clinical relevance of resistance to cephalosporins, macrolides and fluoroquinolones. *Int J Antimicrob Agents.* 2003; 22(suppl 1):S15–24.
2. Performance standards for antimicrobial susceptibility testing; 23rd informational supplement. Wayne, PA: Clinical and Laboratory Standards Institute; 2013.
3. Centers for Disease Control and Prevention. ABCs report: *Streptococcus pneumoniae,* 2001. www.cdc.gov/abcs/reports-findings/survreports/spneu01.html (accessed 2013 Nov 20).
4. Jacobs MR, Felmingham D, Appelbaum PC, et al. The Alexander Project 1998–2000: susceptibility of pathogens isolated from community-acquired respiratory tract infection to commonly used antimicrobial agents. *J Antimicrob Chemother.* 2003; 52:229–46.
5. Doern G, Rybak MJ. Activity of telithromycin against *Streptococcus pneumoniae* resistant to penicillin, macrolides and fluoroquinolones isolated from respiratory tract infections: PROTEK US year 2 (2001–2002). Presented at 43rd Annual Interscience Conference on Antimicrobial Agents and Chemotherapy. Chicago, IL; 2003 Sep.
6. Doern GV, Heilmann KP, Huynh HK, et al. Antimicrobial resistance among clinical isolates of *Streptococcus pneumoniae* in the United Stated during 1999–2000, including a comparison of resistance rates since 1994–1995. *Antimicrob Agents Chemother.* 2001; 45:1721–9.
7. Karlowsky JA, Thornsberry C, Jones ME, et al. Factors associated with relative rates of antimicrobial resistance among *Streptococcus pneumoniae* in the United States: results from the TRUST surveillance program (1998–2002). *Clin Infect Dis.* 2003; 36:963–70.
8. Centers for Disease Control and Prevention. ABCs report: *Streptococcus pneumoniae,* 2010. www.cdc.gov/abcs/reports-findings/survreports/spneu10.html (accessed 2013 Nov 20).

Figure 1. Example pneumococcal vaccine administration pathway with notification for adult patients. PCV13 = 13-valent pneumococcal conjugate vaccine, PPSV23 = 23-valent pneumococcal polysaccharide vaccine, CDC = Centers for Disease Control and Prevention.



9. Chen DK, McGeer A, de Azavedo JC, et al. Decreased susceptibility of *Streptococcus pneumoniae* to fluoroquinolones in Canada. *N Engl J Med.* 1999; 341:233–9.
10. Centers for Disease Control and Prevention. Resistance of *Streptococcus pneumoniae* to fluoroquinolones—United States, 1995–1999. *MMWR.* 2001; 50:800–4.
11. Nuorti JP, Butler JC, Farley MM, et al. Cigarette smoking and invasive pneumococcal disease. *N Engl J Med.* 2000; 342:681–9.
12. Appelbaum PC. Resistance among *Streptococcus pneumoniae*: implications for drug selection. *Clin Infect Dis.* 2002; 34:1613–20.
13. Lynch JP, Martinez FJ. Clinical relevance of macrolide-resistant *Streptococcus pneumoniae* for community-acquired pneumonia. *Clin Infect Dis.* 2002; 34(suppl 1):S27–46.
14. Hooper DC. Fluoroquinolone resistance among gram-positive cocci. *Lancet Infect Dis.* 2002; 2:530–8.
15. Shales DM, Gerding DN, John JF. et al. Society for Healthcare Epidemiology of America and Infectious Diseases Society of America Joint Committee on Prevention of Antimicrobial Resistance: guidelines for the prevention of antimicrobial resistance in hospitals. *Clin Infect Dis.* 1997; 25:584–99.
16. Analysis and presentation of cumulative antimicrobial susceptibility test data; approved guideline, third edition. CLSI document M39-A3. Wayne, PA: Clinical and Laboratory Standards Institute; 2009.
17. World Health Organization. Surveillance standards for antimicrobial resistance. http://whqlibdoc.who.int/hq/2002/WHO_CDS_CSR_DRS_2001.5.pdf (accessed 2013 Nov 20).
18. Davies J, Davies D. Origins and evolution of antibiotic resistance. *Microbiol Mol Biol Rev.* 2010; 74:417–33.
19. Freire-Moran L, Aronsson B, Manz C, et al. Critical shortage of new antibiotics in development against multidrug-resistant bacteria-Time to react is now. *Drug Resist Updat.* 2011; 14:118–24.
20. Peleg AY, Hooper DC. Hospital-acquired infections due to gram-negative bacteria. *N Engl J Med.* 2010; 362:1804–13.
21. Meyer E, Schwab F, Schroeren-Boersch B, et al. Dramatic increase of third-generation cephalosporin-resistant E. coli in German intensive care units: secular trends in antibiotic drug use and bacterial resistance, 2001 to 2008. *Crit Care.* 2010; 14:R113.
22. Diekema DJ, Brueggemann AB, Doern GV. Antimicrobial-drug use and changes in resistance in *Streptococcus pneumoniae. Emerg Infect Dis.* 2000; 6:552–6.
23. Hicks LA, Chien YW, Taylor TH Jr, et al. Outpatient antibiotic prescribing and nonsusceptible *Streptococcus*

pneumoniae in the United States, 1996–2003. *Clin Infect Dis.* 2011; 53:631–9.
24. Dellit TH, Owens RC, McGowan JE Jr, et al. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. *Clin Infect Dis.* 2007; 44:159–77.
25. Centers for Disease Control and Prevention. Public health action plan to combat antimicrobial resistance. www.cdc.gov/drugresistance/actionplan/introduction_overview.html (accessed 2014 Jan 23).
26. Leung E, Weil DE, Raviglione M, et al. The WHO policy package to combat antimicrobial resistance. *Bull World Health Organ.* 2011; 89:390–2.
27. ASHP statement on the pharmacist's role in antimicrobial stewardship and infection prevention and control. *Am J Health-Syst Pharm.* 2010; 67:575–7.
28. Centers for Disease Control and Prevention. About the Get Smart campaign. www.cdc.gov/getsmart/campaign-materials/about-campaign.html (accessed 2013 Nov 20).
29. Specifications manual for national hospital inpatient quality measures discharges 07-01-12 (3Q12) through 12-31-12 (4Q12). Oakbrook Terrace, IL: Joint Commission; 2011.
30. Centers for Disease Control and Prevention. Recommended adult immunization schedule—United States, 2013. www.cdc.gov/vaccines/schedules/downloads/adult/adult-schedule.pdf (accessed 2013 Nov 20).
31. Centers for Disease Control and Prevention. Preventing pneumococcal disease among infants and young children: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR.* 2000; 49(RR-9):1–35.
32. Centers for Disease Control and Prevention. Birth—18 years and "catch-up" immunization schedules; Uniteed States, 2013. www.cdc.gov/vaccines/schedules/hcp/child-adolescent.html (accessed 2013 Nov 21).
33. Artz AS, Ershler WB, Longo DL. Pneumococcal vaccination and revaccination of older adults. *Clin Microbiol Rev.* 2003; 16:308–18.
34. Centers for Disease Control and Prevention. Epidemiology and prevention of vaccine-preventable diseases. The pink book: course textbook. www.cdc.gov/vaccines/pubs/pinkbook/pneumo.html#vaccines (accessed 2013 Nov 20).
35. Department of Health and Human Services. Healthy People 2020. www.healthypeople.gov (accessed 2012 Sep 27).
36. Dagan R, Fraser D. Conjugate pneumococcal vaccine and antibiotic-resistant *Streptococcus pneumoniae*: herd immunity and reduction of otitis morbidity. *Pediatr Infect Dis J.* 2000; 19(suppl):S79–88.
37. Whitney CG, Farley MM, Hadler J, et al. Decline in invasive pneumococcal disease after the introduction of protein-polysaccharide conjugate vaccine. *N Engl J Med.* 2003; 348:1737–46.
38. Williams WW, Hickson MA, Kane MA, et al. Immunization policies and vaccine coverage among adults. The risk for missed opportunites. *Ann Intern Med.* 1988; 108:616–25.
39. Fedson DS, Hickson MA, Kane MA, et al. Hospital-based pneumococcal immunization. Epidemiologic rationale from the Shenandoah study. *JAMA.* 1990; 264:1117–22.
40. Fedson DS. Influenza and pneumococcal immunization strategies for physicians. *Chest.* 1987; 91:436–43.
41. Magnussen CR, Valenti WM, Mushlin AI. Pneumococcal vaccine strategy. Feasibility of a vaccination program directed at hospitalized and ambulatory patients. *Arch Intern Med.* 1984; 144:1755–7.
42. Vondracek TG, Pham TP, Huycke MM. A hospital-based pharmacy interventions program for pneumococcal vaccination. *Arch Intern Med.* 1998; 158:1543–7.
43. American Society of Health-System Pharmacists. ASHP guidelines on the pharmacist's role in immunization. *Am J Health-Syst Pharm.* 2003; 60:1371–7.
44. Grabenstein JD, Bonasso J. Health-system pharmacists' role in immunizing adults against pneumococcal disease and influenza. *Am J Health-Syst Pharm.* 1999; 56(suppl 2):S2–24.
45. Immunization Action Coalition. States authorizing pharmacists to vaccinate. www.immunize.org/laws/pharm.asp (accessed 2012 Dec 27).
46. American Pharmacists Association. Pharmacist administered vaccines. www.pharmacist.com/sites/default/files/files/PharmacistIMZAuthority_June18_2012%20%5BRead-Only%5D.pdf (accessed 2012 Dec 27).
47. Noped JC, Schomberg R. Implementing an inpatient pharmacy-based pneumococcal vaccination program. *Am J Health-Syst Pharm.* 2001; 58:1852–5.

Kimberly A. Couch, Pharm.D., M.A., FIDSA, FASHP, is President, Infectious Diseases Pharmacy Associates, Stevensville, MD, and Clinical Pharmacist, Complete Rx, Seaford, DE. Teresa Geide, Pharm.D., BCPS, CGP, is Clinical Pharmacy Specialist, Infectious Diseases, Orlando Veterans Affairs Medical Center, Orlando, FL.

Developed through the ASHP Council on Therapeutics and approved by the ASHP Board of Directors on August 2, 2013.

The following individuals are acknowledged for reviewing draft versions of this statement: Arthur Chaput; Steven Dzierba, Pharm.D., M.S., FASHP; Kathleen M. Gura, Pharm.D., BCNSP, FASHP, FPPAG; Mojdeh Heavner, Pharm.D., BCPS; Jody Jacobson Wedret, B.S.Pharm., FASHP, FCSHP; Kristi Kuper, Pharm.D., BCPS; Fred Meister, Pharm.D., FASHP; Robert J. Moura, B.S.Pharm., M.S.; Michael Postelnick, B.S.Pharm, BCPS-AQ Infectious Diseases; and Michael Powell, B.S.P., M.S.P., FASHP.

The authors have declared no potential conflicts of interest.

This document supersedes the ASHP therapeutic position statement for identifying and preventing pneumococcal resistance approved by the ASHP Board of Directors on April 15, 2004.

The bibliographic citation for this document is as follows: American Society of Health-System Pharmacists. ASHP therapeutic position statement on strategies for identifying and preventing pneumococcal resistance. *Am J Health-Syst Pharm.* 2014; 71:417–24.