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*Streptococcus pneumoniae* is the leading cause of community-acquired pneumonia, otitis media, and meningitis in the United States. Antimicrobial susceptibility results are important for guiding therapy decisions and monitoring emerging resistance patterns. Appropriate methods for pneumococcal susceptibility testing are recommended by the National Committee for Clinical Laboratory Standards (NCCLS).1-3 Recommendations for pneumococcal susceptibility testing are reviewed annually and were the same in 2000 and 2001. To assess laboratory practices for *Streptococcus pneumoniae* susceptibility testing on sterile site isolates, in February 2000, CDC conducted a multistate survey of clinical laboratories. This report summarizes the survey results, which found that most practices of clinical laboratories were consistent with NCCLS recommendations; however, some inconsistencies were noted. As antimicrobial resistance in pneumococci continues to worsen, clinical laboratories should be aware of emerging resistance patterns and follow new recommendations to provide clinicians with precise information about antimicrobial susceptibility.

Laboratories were selected on the basis of their participation in CDC’s Emerging Infections Program/Active Bacterial Core Surveillance,4 through which, since 1995, state and local health departments and universities have conducted active population- and laboratory-based surveillance for invasive pneumococcal disease (defined as isolates from sterile sites such as blood and cerebrospinal fluid [CSF]) in seven to nine geographic areas in the United States. The survey was designed to assess (1) which susceptibility testing practices were being used by clinical laboratories, (2) whether practices followed current NCCLS guidelines, (3) which antimicrobials were being tested routinely, and (4) how microbiology laboratories were reporting susceptibility results to clinicians.

A standardized survey was sent to 659 laboratories, and 547 (83%) laboratories responded. A total of 452 (83%) laboratories reported that they tested susceptibility of pneumococcal isolates either in their own laboratory (in-house) or at a reference laboratory, 353 (78%) of which reported doing some in-house testing. Of these 353 laboratories, 188 (53%) performed in-house oxacillin screening on sterile site isolates; of these, 187 (99%) followed positive screens with confirmatory minimum inhibitory concentrations (MICs) or had disk diffusion (DD) testing for antimicrobials other than oxacillin. Of the 165 laboratories that bypassed initial oxacillin screening as recommended by NCCLS for blood and CSF isolates, 145 (88%) laboratories performed MICs or DD testing in-house, and the remaining 20 laboratories used a combination of testing in-house and at a reference laboratory.

Of the 250 (71%) laboratories that performed MICs or DD testing in-house, 232 (93%) tested sterile site pneumococcal isolates for resistance to penicillin, and 227 (91%) tested a third-generation cephalosporin (cefotaxime or ceftriaxone). In addition, 190 (76%) laboratories tested the three antimicrobials (penicillin, cefotaxime/ceftriaxone, and vancomycin) recommended by NCCLS for blood and CSF isolates, and seven laboratories tested meropenem in addition to these three antimicrobials. Most laboratories also tested sterile site isolates against erythromycin (79%), trimethoprim-sulfamethoxazole (62%), tetracycline (57%), and chloramphenicol (53%); 98 (39%) laboratories tested for resistance to one or more fluoroquinolones. Most laboratories reported using the Etest® (Solna, Sweden) for penicillin (52%) and cefotaxime/ceftriaxone (51%) and disk diffusion for fluoroquinolones (51%); the broth microdilution method was used more frequently (43%-71%) for other antimicrobials.

Of the 250 laboratories that performed MICs or DD testing in-house, 207 (83%) laboratories reported susceptibility results to clinicians as interpretations (i.e., susceptible, intermediate, or resistant [S/I/R]), 175 (70%) laboratories reported an exact MIC value, 12 (5%) laboratories reported by zone diameter, and 142 (57%) laboratories used a combination of these reporting methods. A total of 137 (55%) laboratories reported both interpretations and exact MIC values as recommended by NCCLS; however, 66 (26%) laboratories reported only the interpretations, and 35 (14%) laboratories reported only the exact MIC values.

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CDC Editorial Note: This survey assessed consistency between reported practices in surveyed laboratories and NCCLS recommendations about oxacillin screening. Although oxacillin screening is endorsed, the NCCLS guidelines indicate that laboratories may use one or more alternative methods (e.g., MIC, zone diameter). Most laboratories in the survey used a combination of oxacillin screening and other methods.
cillin disk screening, acceptable MIC testing methods and reporting, and antimicrobial agents tested. Most clinical laboratories surveyed were using appropriate methods for pneumococcal susceptibility testing; however, some inconsistencies with NCCLS guidelines were found.

In the United States, Streptococcus pneumoniae causes an estimated 63,000 invasive infections and 6,100 deaths per year. Since the emergence of penicillin-resistant isolates in the United States in the early 1990s, a high proportion of pneumococci has become resistant to multiple antimicrobial agents. In 1998, approximately 25% of pneumococcal isolates had decreased susceptibility to penicillin, and 14% were resistant to three or more classes of antimicrobial agents. The increase in resistance to antimicrobials used to treat pneumococcal infections has resulted in changes in recommended empiric treatment regimens for otitis media, meningitis, and pneumococcal pneumonia.5-8

Initial oxacillin disk screening for pneumococcal isolates is not recommended when isolates come from patients with a potentially life-threatening infection (e.g., meningitis or sepsis). This survey found that 53% of laboratories conducted oxacillin screening on isolates from sterile sites. In the absence of information about the clinical severity of a patient’s illness, laboratories should test all isolates from CSF and blood by bypassing oxacillin disk screening and using a more reliable MIC method. Otherwise, definitive MIC results will be delayed by >24 hours, which might prolong use of broad-spectrum antimicrobials chosen for initial empiric treatment. For isolates from other sites (e.g., respiratory), initial oxacillin disk screening is acceptable; however, if the oxacillin zone size is <20 mm, MICs for penicillin and other agents should be determined.

Acceptable MIC methods differ for different classes of antimicrobial agents. For β-lactam agents other than oxacillin, reliable MIC methods include broth microdilution or Etest®. Disk diffusion testing is unreliable for β-lactam agents including penicillins, cephalosporins, and carbapenems. Either MIC (broth microdilution, Etest®) or disk diffusion should be used for other antimicrobials (e.g., vancomycin, macrolides, trimethoprim-sulfamethoxazole, clindamycin, tetracycline, and fluoroquinolones). If an MIC is determined for an isolate, the exact MIC results should be reported in combination with interpretations (i.e., S/I/R) to assist clinicians with therapeutic decisions, which might vary based on clinical syndrome and severity of illness.3

Antimicrobial choices used for susceptibility testing should include the agents that clinicians use to treat common pneumococcal syndromes. Laboratories should conduct susceptibility testing of all isolates from blood or CSF directly against penicillin, cefotaxime or ceftriaxone, and vancomycin. Meropenem testing also might be performed depending on local clinician preferences and institutional formularies. Because many clinicians use fluoroquinolones as first-line treatment for community-acquired pneumonia or bacteremia, laboratories should perform susceptibility testing against fluoroquinolones. For isolates from patients whose diseases are not life-threatening, such as from middle ear fluid or joint fluid, NCCLS recommends that laboratories perform susceptibility testing for macrolides, trimethoprim-sulfamethoxazole, clindamycin, tetracycline, and fluoroquinolones. Other authorities have recommended that laboratories test against a more extensive primary antimicrobial panel comprising penicillin, cefotaxime or ceftriaxone, and erythromycin, doxycycline or tetracycline, clindamycin, and fluoroquinolones, with trimethoprim-sulfamethoxazole and vancomycin as optional.7

The findings in this report are subject to at least four limitations. First, the survey did not address testing methods used for nonsterile site isolates. Second, the survey assessed laboratory practices in 2000, which might not reflect current practices. Third, the survey assessed reported rather than actual practices. Finally, these laboratories were part of an ongoing surveillance system and might be more likely than other laboratories to be aware of and follow current recommendations.

As the problem of antimicrobial resistance for pneumococci worsens, recommendations for susceptibility testing will change, and having precise information on antimicrobial susceptibility will be even more important to clinicians. Clinical laboratories should be aware of new recommendations and emerging resistance patterns. Conducting comprehensive susceptibility testing will enhance the work of public health agencies in tracking emerging resistance patterns in their communities.

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REFERENCES


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Respiratory Illness in Workers Exposed to Metalworking Fluid Contaminated With Nontuberculous Mycobacteria—Ohio, 2001

In January 2001, three machinists at an automobile brake manufacturing facility in Ohio (plant A) were hospitalized with respiratory illness characterized by dyspnea, cough, fatigue, weight loss, hypoxia, and pulmonary infiltrates. Hypersensitivity pneumonitis (HP) was diagnosed in all three workers. In March 2001, additional employees began seeking medical attention for respiratory and systemic symptoms. In May 2001, union and management representatives requested assistance from CDC’s National Institute for Occupational Safety and Health (NIOSH) in determining the cause of the illnesses and preventing further illness in employees. This report describes two case reports and the preliminary results of the ongoing investigation, which found that exposure to aerosolized nontuberculous mycobacteria (NTM) might be contributing to the observed respiratory illnesses in this manufacturing facility. Clinicians and public health professionals should be alert to the variable presentation of occupational respiratory disease that might occur in workers in the machining industry.

Plant A is an automobile brake manufacturing facility machining primarily cast-iron parts. Approximately 400 persons work at plant A, including approximately 150 workers in machining areas and 250 workers in nonmachining areas. The nonmachining areas of plant A are separated from the machining areas by a wall and are serviced by a separate ventilation system. Plant A machines receive metalworking fluid (MWF) from either dedicated sumps or one of four central MWF systems, with volumes of 4,500-20,000 gallons. The semisynthetic MWF in use at the plant included a formaldehyde-releasing biocide; a second biocide (isothiazolinone-based) was added as indicated to control microbial growth.

Case Reports

Case 1. In mid-January 2001, a male machinist aged 45 years who had been employed at plant A for 26 years was hospitalized for worsening respiratory symptoms, hypoxia, and pulmonary infiltrates.

He had been treated by his family physician 1 month earlier with a course of antibiotics for a nonspecific respiratory illness that improved during a holiday layoff from work. On his return to work in early January 2001, the patient’s symptoms of dyspnea, chest tightness, and non-productive cough recurred. On admission, a high-resolution computed tomography (HRCT) scan revealed diffuse interstitial infiltrates with a nodular pattern superimposed on the infiltrates. Oxygen tension on room air at rest was 49 millimeters of mercury (mm Hg) (normal: 80-100 mm Hg) with 87% saturation (normal: 96%-100%); a white blood cell count was 8,000 (normal: 4,800-10,800) with a normal differential; and a Legionella titer was <1:256 (normal: <1:256). HP was diagnosed, and the patient was removed from work and treated with oral and inhaled corticosteroids and with bronchodilators. Repeat HRCT scan 1 month after hospitalization, while the patient was still away from work, revealed clear lung fields. Pulmonary function tests (PFTs) revealed improvement in initial restrictive findings and diffusing capacity. Two months after hospitalization, oxygen saturation on room air at rest was 96%.

Serum precipitin analysis was strongly positive for precipitating antibodies to Mycobacterium sp. cultured in February 2001 from MWF at plant A. The same tests performed on two co-workers from plant A who also had been hospitalized in January 2001 with HP also were strongly positive.

Case 2. In July 2001, a woman aged 47 years presented to a private physician with a 1-day history of dyspnea, cough, chest tightness, wheezing, epistaxis, nausea, emesis, and fatigue that began <2 hours after she began steam-cleaning machining equipment in plant A.

She had not performed this type of job previously and wore no respiratory protection. Physical examination revealed diminished breath sounds in all lung fields. Oxygen tension was 65 mm Hg with 92% saturation. PFTs revealed an obstructive deficit that improved after the administration of bronchodilators. HRCT was normal. Occupational asthma and hypoxemia were diagnosed; the patient was removed from work and treated with oral and inhaled corticosteroids and with bronchodilators. The patient returned to work in August 2001; follow-up PFTs and oxygen saturation were within normal ranges.

Medical Record Review

In November 2001, CDC investigators reviewed plant A records and found that 107 (27%) of 400 workers had been placed on work restriction by their treating physicians during the preceding 11 months because of respiratory conditions; 37 (35%) of these 107 workers remained on medical leave and 70 (65%) had returned to work. Medical records through October 2001 were reviewed for 32 (86%) of the 37 workers remaining on medical leave. All 32 workers had either full- or part-time work duties in the machining side of the plant; the median length of time working at plant A was 18 years (range: 3-32 years). Initial symptom onset for these workers occurred during October 2000–April 2001, with onset for 13 of these 32 workers occurring in Decem-
ber 2000. Of the 32 workers, 14 (44%) met a definition for occupational asthma (OA)† and 12 (38%) met a definition for HP.† Of the six workers with respiratory or upper respiratory symptoms not meeting definitions for OA or HP, three had illnesses consistent with work-related bronchitis, two had illnesses consistent with work-related rhinosinusitis, and one was symptomatic primarily with dyspnea.

Environmental Sampling
Multiple samples of bulk MWF from all central MWF systems at plant A analyzed for microbial contaminants during February–July 2001 revealed predominant growth of M. immunogenen, a newly proposed species of the Mycobacterium abscessus/Mycobacterium chelonae group,‡ at levels up to 10⁶ colony-forming units per milliliter. Subsequent sampling conducted weekly since July 2001 has revealed noncultivable mycobacteria at decreasing concentrations‡ but virtually no viable bacteria. Area and personal air sampling performed during April 2001 in the machining areas revealed concentrations of MWF aerosol of <0.1–0.9 milligrams of total particulate per cubic meter (mg/m³) of air (median: 0.6 mg/m³). Two of five personal samples were above the NIOSH-recommended exposure limit (REL).§

To minimize potential exposures to MWF and MWF contaminants, plant A conducted steam-cleaning of the MWF systems and machines, improved local ventilation of selected machines, and installed a conditioned air system for the machining areas and fresh MWF combined with a new biocide effective against mycobacteria. No workers at plant A with symptom onset after April 2001 have been identified. Local health-care providers continue to monitor workers who have been ill and assess their ability to return to work. Plant A and CDC representatives are assessing control measures already in place and the need for additional measures.

References

†Defined as one or more work-related respiratory symptoms (cough, dyspnea, wheezing, or chest tightness) and the absence of systemic signs or symptoms; no infiltrate seen on CXR or HRCT scan; and spirometry consistent with reversible airway obstruction (an obstructive pattern with ≥12% improvement in FEV₁, after administration of inhaled bronchodilators).

‡Defined as the presence of one or more work-related respiratory symptoms (cough, dyspnea, wheezing, or chest tightness), one or more systemic signs or symptoms (fever, chills, extreme fatigue, myalgia, or night sweats), an infiltrate seen on chest radiograph or HRCT scan, and abnormal spirometry (either an obstructive or restrictive pattern).

§Assessed semi-quantitatively by comparison of microscopic evaluation (acid-fast stain) of a pellet obtained by centrifugation of an MWF sample (which evaluates both viable and nonviable organisms) with culture techniques (which evaluate viable organisms).

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