Bacterial Resistance Due to Antimicrobial Drug Addiction Among Physicians

Time for a Cure!

The last few decades saw the development of many new antibiotics (including extended-spectrum penicillins and cephalosporins) that had impressive in vitro activity against the bacteria causing disease in most patients. Given the wide armamentarium of antibiotics, many began to think that only unusual bacteria, especially in immunocompromised hosts, would be resistant to these and other readily available antibiotics. Later, when enterococci resistant to all available antibiotics were becoming a problem, it was still limited to a small segment of the population. Now, however, resistance of bacteria to antibiotics, including extended-spectrum agents, is a major problem for all hosts of all ages.

In the United States, Streptococcus pneumoniae is the most common cause of acute otitis media (AOM) (7 million cases annually), bacterial pneumonia (500,000 cases) and meningitis (3000 cases), and bacteremia in young children (50,000 cases in children and adults combined).1 Until 1974,2 all pneumococci reported in the United States were susceptible to penicillins and cephalosporins. Resistance levels increased slowly thereafter until the 1990s, when the rates increased substantially. The US Pediatric Multicenter Pneumococcal Surveillance Study Group prospectively studied almost 1300 systemic infections caused by pneumococci at 8 children’s hospitals.3 They found that from 1993 to 1996, the overall percentage of pneumococci that were penicillin nonsusceptible increased from 14% to 21%. The resistance rate for ceftriaxone tripled, from 3.1% to 9.3%. Rates of resistance varied among the different communities. Multidrug resistance is often noted among these strains, thus limiting the usefulness of many commonly used antimicrobials, such as sulfamethoxazole-trimethoprim and the macrolides.4 Compared with normally sterile sites, higher rates of resistance are likely in the respiratory tract (including AOM isolates).3 Clinicians now must deal with the repercussions of such antibiotic resistance every day.

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This problem is having a great impact on the treatment of AOM. Although many clinicians use other drugs, amoxicillin remains the drug of choice as a first-line agent for AOM. Amoxicillin achieves high levels in middle ear fluid, is effective against most pathogens causing AOM, and is inexpensive and well tolerated. In this issue of the ARCHIVES,6 Block reviews much of the data currently available with regard to treatment of so-called amoxicillin failures, outlining recommendations for therapy. It is clear that much information is still needed. Further, the levels of resistance to commonly used antibiotics are likely to continue to rise, thus affecting treatment alternatives. It is important to review current antimicrobial options as outlined by Block and others.6,7 However, given the difficulty of predicting the offending organism and its antibiotic susceptibility pattern, we would consider tympanocentesis after failure of a second, or certainly the third, course of antibiotics rather than waiting until later as recommended by Block.6

The treatment of other diseases commonly caused by the pneumococcus also has been affected by the increase in antibiotic resistance. For pneumococcal meningitis, failure of therapy with extended-spectrum cephalosporins has been reported.8 Thus, empiric treatment of bacterial meningitis now should include vancomycin as well as ceftriaxone9 because of the increasing resistance of pneumococcus to this latter drug. Treatment is then tailored according to the results of culture and susceptibility testing. While no vancomycin-resistant pneumococci have yet been reported, the recent reports of Staphylococcus aureus with intermediate resistance to vancomycin in the United States10 are worrisome with respect to future therapies for infections caused by both of these organisms. The potential for infections with bacteria that are virulent, occur commonly, and are resistant to all available antibiotics is chilling.

What factors increase a patient’s risk for colonization and/or infection with a resistant bacterial organism? Risk factors identified include age (infant or young child), white race, attendance in day care, and recent use of antimicrobial agents, especially β-lactam antibiotics.11-13 The association between the development of bacterial resistance and recent use of antibiotics is particularly strong and has been documented in both the inpatient14 and outpatient15 setting. Furthermore, the use of antimicrobial agents in children is pervasive. For example, Bergus et al16 recently reported that by 3 and 6 months of age, 37% and 70% of children, respectively, had received 1 or more antimicrobial agents.

Given that previous antibiotic use is an important determinant of drug resistance, the question then is whether such antibiotic use (prescription) is always appropriate, and if not, how extensive the problem of inappropriate use of these drugs is. The answer is depressingly clear. An estimated 18 million courses of antibiotics are prescribed each year, in the United States, for the common cold, a disease for which there is clear evidence that these agents are ineffective.17 In 1 study, antibiotics were prescribed to 60% of outpatients (most of these being children) with an up-
Seven million fewer antibiotic prescriptions would be written yearly if antimicrobial agents were given only to those patients who truly had AOM and not those with questionable signs and symptoms of AOM or those with otitis media with effusion. Furthermore, if antibiotics were also used judiciously for the other 3 most common infections for which these agents are prescribed (ie, sinusitis, bronchitis, and pharyngitis), it is estimated that 26 million fewer prescriptions would be written each year.21-23

Would the judicious use of antimicrobial agents protect children and adults from carriage and infection with resistant bacteria? The answer is a resounding yes. Studies have demonstrated that decreasing or more appropriate use of antibiotics can reduce the proportion of patients with resistant organisms. In Finland and Japan, with increased use of macrolide antibiotics (erythromycin, azithromycin, and clarithromycin) for treatment of pharyngitis, resistance of group A Streptococcus to macrolides reached greater than 50%. After educational campaigns urging the use of penicillin rather than macrolides for bacterial pharyngitis, resistance of group A streptococci to macrolides decreased to less than 10%.24,25 Studies in the United States and Iceland have shown that decreasing use of antibiotics results in a lower prevalence of resistant S pneumoniae.26,27

Why do physicians prescribe unnecessary antibiotics? Reasons include inadequate understanding of the lack of effectiveness of these drugs for certain diseases, fear of a poor outcome or lawsuits, and the answer most often cited by practitioners: pressure from patients or parents. However, a recent study showed that patient satisfaction was correlated with the quality of the physician-patient interaction, not with the prescription of an antibiotic.28

What is being done to correct this problem? Recently, the Centers for Disease Control and Prevention, the American Academy of Pediatrics, and the American Academy of Family Physicians have joined forces to promote the judicious use of antibiotics. Evidence-based practice guidelines have been developed for treatment of otitis media, sinusitis, pharyngitis, bronchitis, and the common cold.17-20 In addition, a national campaign has been undertaken to improve public awareness about the negative impact of unnecessary antibiotic use. While decreasing the overuse of antibiotics is good for the community as a whole, this campaign emphasizes the risk to the individual patient of infection caused by drug-resistant organisms as well as potential side effects from these drugs. A pamphlet entitled Your Child and Antibiotics: Unnecessary Antibiotics CAN Be Harmful is available from the Centers for Disease Control and Prevention free of charge (fax: [404] 639-0817) and can be given to patients and parents.

We must cure our addiction to antimicrobial agents if we are to decrease the rate of bacterial resistance.29 Either physicians will use antibiotics more judiciously, or we will enter into a postantimicrobial era where many of the common bacterial infections are no longer effectively treated with antibiotics.30 The responsibility for preventing this from happening lies with each and every physician who prescribes antimicrobial drugs.

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