Editorial

Antibiotic Resistance in ICUs: A Multifaceted Problem Requiring a Multifaceted Solution

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Antibiotics are a remarkable class of drugs and have had a major impact on public health.[1] Early in this century, infectious diseases were among the most common causes of death. Deaths from these diseases have since decreased dramatically in the US population, largely because of antibiotics. Unfortunately, some of these same diseases are reemerging, largely because the agents that cause them have developed resistance to antibiotics.[2]

Controlling antibiotic resistance is exceedingly important. Newer agents are almost always more costly. If resistance has occurred to the drug of choice, alternative choices often are more toxic, eg, antituberculous agents. However, we are now faced with the loss of efficacy of antibiotics -- something we have not really faced since their introduction as a class of drugs. Multidrug-resistant tuberculosis and vancomycin-resistant enterococci (VRE) have become essentially untreatable in a large percentage of cases.[3]

What is the way out of this pressing problem? We no longer can rely on pharmaceutical companies to bail us out of this predicament. Antibiotic drug discovery waned in the late 1980s. Bringing a new drug to market is an enormous expense -- one that has to be profitable for the company.[4] From a business standpoint, money spent on antibiotic drug discovery might be better spent on other classes of pharmaceuticals. Think about it. What other class of new drugs loses efficacy the moment the drugs are released for widescale use? Signs are developing that the industry has increased their antibiotic discovery efforts, in some cases dramatically, but we are years away from seeing the fruits of these labors. Indeed, drug companies cannot guarantee they will find a new class of antibiotics to heal what ails our patients. Since the introduction of quinolones in the 1980s, no new class of antibiotics has been introduced. Recent reports have shown that resistance to quinolones occurred with alarming swiftness.[5,6] The problem of antibiotic resistance in hospitals cannot be solved solely by the repetitive introduction of new antibiotics. That strategy would be too costly and ultimately would fail.

EPIDEMIOLOGY OF ANTIBIOTIC RESISTANCE

The solution lies with understanding the epidemiology of antibiotic resistance and using that knowledge to control the problem. In this issue of *Infection Control and Hospital Epidemiology*, Bryce and Smith report the use of target surveys of intensive care unit (ICU) resistance patterns that illustrate the differences between the percentage of resistance in ICUs and the general hospital.[7] The finding that resistance among isolates from patients in ICUs is greater than for patients in noncritical units (non-ICUs) is not new.[8,9] For example, data from the National Nosocomial Infections Surveillance (NNIS) system showed that 13.6% of all enterococci associated with nosocomial infections from ICU patients in 1994 were vancomycin resistant, compared with 9.1% from non-ICUs (unpublished NNIS data).[10] For the gram-negative bacilli, the percentage of nosocomial *Escherichia coli* reported as resistant to ampicillin in ICUs was 40.7%, compared with 35% in isolates from non-ICUs in 1994 (unpublished NNIS data). NNIS data also indicate that the percentage of *Enterobacteriaceae* resistant to ceftazidime has increased in isolates from ICUs.[11] An analysis of NNIS data for

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94-ED-042 Gaynes R. Antibiotic resistance in ICUs: a multifaceted problem requiring a multifaceted solution. Infect Control Hosp Epidemiol *1995;16:328-330.*

imipenem resistance among *Pseudomonas aeruginosa* showed that resistance was more common among ICU isolates, in teaching hospitals, and in isolates from the respiratory tract.[12] The report of Bryce and Smith uses a remarkably simple approach -- antibiotic susceptibility tables stratified by place of acquisition. The approach seems so obvious, so widely applicable, that one is astonished that it has not already been adopted widely. Perhaps it is because Bryce and Smith were the first to consider this approach. However, it is more likely that microbiology laboratories are not accustomed to producing the antibiotic susceptibility reports with stratification by ICU versus non-ICU and are unable to produce such reports. Alternatively, the laboratories may be unwilling to commit computer programming time to such an endeavor. Such unwillingness by the hospitals or microbiology laboratories clearly would not be justified. The use of this information allowed the investigators to discover an outbreak of resistant bacteria in the ICU of the hospital. The authors also point out the use of such reports for guiding empiric therapy in the ICU.

Bryce and Smith also found that the epidemiology of antibiotic resistance depends on the pathogen and the antibiotic that one examines. For example, the place of acquisition (ICU versus non-critical care areas) was not always important in the epidemiology of resistance for certain pathogen-antibiotic combinations, such as those for *Enterobacteriaceae*. For this pathogen, the percentage resistant in the ICU was similar to that from the non-critical care areas. Conversely, for *P aeruginosa*, the percentage was higher in the ICU. Weinstein et al reported a similar finding for aminoglycoside resistance in these two groups of gram-negative bacilli in the 1980s.[13]

ANTIBIOTIC RESISTANCE AND ICUs

There are a variety of reasons that antibiotic resistance in ICUs may be different than for non-ICUs, but they seem to fall into two categories: infection control and antibiotic use issues. Infection control concerns for ICUs may include ICU patients with carriage of resistant pathogens from other hospitals, other parts of the hospital, or the community; lapses of asepsis during crisis care; and increasing severity of illness in ICUs and resultant use of invasive devices. The invasive devices, in turn, may allow resistant organisms access to the vascular space, respiratory tract, or urinary tract.

Amplification of resistance by antibiotic use is a major, perhaps the major factor, however. Bryce and Smith mention that the antibiotic susceptibility tables were used to guide empiric therapy, Unfortunately, Bryce and Smith do not cite the antibiotic use patterns in their units. This information may become essential if interpretations of percentages of resistance are followed to their natural conclusion-control of resistance.

CONTROL OF ANTIBIOTIC RESISTANCE

Because the number of new antimicrobials is decreasing, the only available means of controlling resistance in ICUs are curbing cross-transmission of pathogens and optimizing antibiotic use. However, the interpretation of the percentage resistant to an antibiotic-pathogen combination is limited. Either infection control or antibiotic use issues (or both) may be responsible for a high percentage of resistance. Moreover, the relative importance of either of these issues probably differs, depending on the pathogen-antibiotic combination examined.

To interpret the percentage of resistance, it seems most prudent and practical to control for variations in a major risk factor selecting for resistance-antibiotic use. A parallel situation arose when risk adjustment was advocated for interhospital comparison of nosocomial infection rates.[14] In a similar vein, to control problems of antimicrobial resistance among hospital-acquired pathogens in the ICU, two questions must be posed: 1) Is the ICU using antibiotics optimally? 2) Once antibiotic use has been controlled for, are other factors such as possible cross-transmission evident? A strategy to answer these questions in an efficient and cost-effective manner is needed urgently. The report by Bryce and Smith is an extraordinarily simple, practical first step that all hospitals can pursue. However, examining antibiotic use will require further efforts. Approaches have been advocated,[15-21] but acquiring pharmacy data seems to be more difficult than acquiring microbiologic data. Finally, no strategy will be satisfactory unless the entire healthcare delivery system views the problem of antibiotic resistance as a vital one. Too often, the infection control practitioners are handed the problem to solve. Clearly, they have an important role, along with infection control committees and hospital epidemiologists; but these people do not own the problem, nor do they own the solution. The entire healthcare delivery system, including administrators, nurses, surgeons, and pharmacists, must view antibiotic resistance as a meaningful problem. Only in this way will we be able to address a multifaceted problem with a multifaceted solution.

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Community Exposure Predicts Healthcare Worker TB Skin-Test Conversion

by Gina Pugliese, RN, MS
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Dr. Thomas Bailey and colleagues from Barnes Hospital in St. Louis, Missouri, a large urban teaching hospital, recently completed a study that assessed the risk for positive tuberculin skin tests among employees. The annual incidence of tuberculosis is approximately five cases per 100,000 persons in Missouri and approximately 11 cases per 100,000 persons in St. Louis. During the period January 1989 to July 1991, three patients with pulmonary tuberculosis were admitted to Barnes hospital.

Of the 6,070 active employees for whom TB screening data was available, 684 (11.3%) had a positive tuberculin skin test (TST) during the study period. Risk factors associated with a positive skin test were age >35 years, minority group status (black, Asian, Hispanic), and percentage of low-income persons within the employee's residential postal zone. Of 3,106 employees who had at least two skin tests, 29 had TST conversion; 15 (52%) occurred among employees who had no direct patient contact. Skin-test conversion was independently associated only with the percentage of low-income persons in the employee's residential postal zone. Stratifying the employees according to the degree of contact with patients or according to departmental group was not useful in determining risk for a positive TST or for TST conversion.

For certain groups of employees, an exposure to tuberculosis in the community poses a greater risk than exposure in a hospital setting. The authors concluded that their findings support the Centers for Disease Control and Prevention recommendation to include healthcare workers from "risk groups with increased prevalence of tuberculosis ... even if they do not have potential occupational exposure ... " in a periodic TST program.

FROM: Bailey TC, Fraser VJ, Spitznagel EL, and Dunagan WC. Risk factors for a positive tuberculin skin test among employees of an urban, midwestern teaching hospital. *Ann Intern Med* 1995;122(8):580-*585.*