Antibiotic Resistance: The Impact on Care of Hospitalized Patients

Donna J. Plonczynski
Katrina J. Plonczynski

Incidence of antibiotic-resistant infections is increasing at an alarming rate. The concern about antibiotic resistance has been propelled by increasing questions over the effectiveness of current therapies in the treatment and prevention of severe infections in hospitalized patients. Nurses influence antibiotic resistance in the hospital through infection control procedures, knowledge of evidence-based antibiotic administration protocols, and surveillance of infection incidence and treatments.

The evolving failure of antibiotics to cure some bacterial infections is an unforeseen result of their reputation for curing. Their effectiveness at eradicating previously fatal illnesses and preventing acquired infections fueled their demand by patients and families. This overuse of antibiotics resulted in resistant strains of bacteria, and there is widespread concern over the future ability to control infections due to antibiotic resistance (Movahed, Kasravi, & Bryan, 2004). Questions also have arisen about the effectiveness of current therapies in the prevention and treatment of severe infections in hospitalized patients.

Antibiotic resistant infections have become a frequent cause of mortality and morbidity in hospitalized patients (Kopp, Nix, & Armstrong, 2004). Although bacterial infections were nearly eradicated with antibiotics, septicemia alone is now the 10th leading cause of death in the United States. The occurrence of sepsis in nearly 750,000 individuals per year results in 32,000 fatalities (National Center for Health Statistics, 2001). In addition to the significance of the morbidity and mortality, hospital infections cause increased lengths of stay for the patient (Pirson, Dramaix, Struelens, Riley, & Leclercq, 2005). Antibiotic resistant infections are significant, particularly for hospital-based nurses with their delivery of care to high-risk, high-acuity patients (Wenzel & Edmond, 2001). Hospitalized patients are susceptible to bacterial infections because of invasive procedures, diseases, or immune compromise.

The causative organisms of concern include the virulent methicillin-resistant Staphylococcus aureus (MRSA), vancomycin-resistant Staphylococcus aureus, and 3rd generation cephalosporin-resistant Pseudomonas aeruginosa and Klebsiella pneumoniae (Abramowitz, 2004). To address this growing problem of antibiotic resistance in health care facilities, the Centers for Disease Control and Prevention developed a multifaceted campaign that includes guidelines for the appropriate use of antibiotics (CDC, 2001).

Understanding antibiotic resistance is necessary in order to
change antibiotic overuse patterns. Nurses can protect their hospitalized patients by understanding how overuse of these drugs contributes to antibiotic resistance. The purposes of this article are to discuss (a) antibiotic effectiveness, (b) antibiotic resistance, and (c) the implications of antibiotic resistance while caring for patients in the hospital.

**Antibiotic Effectiveness**

For individuals alive before 1928, the year penicillin was found to inhibit microbial growth, infectious diseases were the major causes of death (Armstrong, Conn, & Pinner, 1999). Antibiotics dramatically changed the illness patterns within a generation in the mid-20th century. In the 14 years immediately following 1928, deaths from infectious disease declined at the rapid rate of 8.2% per year (Armstrong et al., 1999) due to the use of penicillin for pneumonia and streptomycin for tuberculosis (Das, 2000). However, new warnings indicate that a failure to respond to the growing problem of antibiotic resistance could mean a return to life without antibiotics for infectious disease (Dancer, 2004).

Starting in the late 1940s, antibiotic concentrations were thought to be related to their effect against bacteria (Eagle, 1948). It is now understood that concentration alone does not eliminate bacterial infections. An antibiotic’s effectiveness is related to its ability to prevent replication of the bacteria, a phenomenon based on the relationship between antibiotic concentrations over time and bacterial resistance to the antibiotic (Andes, Anon, Jacobs, & Craig, 2004). The ratio of the concentration-time curve/minimum inhibitory concentration is seen as a useful measure of antibiotic effectiveness (Barger, Fuhst, & Wiedemann, 2003). The amount of medication concentration over time is referred to as the concentration-time curve (AUC). The AUC considers the antibiotic dose and serum concentration over time. This measure is also dependent on the half-life of the antibiotic, or the amount of time that is required for half of the drug to be eliminated from the patient’s serum. The concentration at which the bacterium is susceptible to the antibiotic is referred to as the minimum inhibitory concentration level (MIC). This level is specific to each antibiotic and bacterium. For example, with S. aureus, an MIC of ≤2 g/ml indicates sensitivity to methicillin, while an MIC of ≥4 g/ml indicates resistance (National Committee for Clinical Laboratory Standards, 2003). The MIC was developed as a measure of the lowest level of antibiotic that caused inhibition of bacterial replication in vitro and can be viewed by hospital nurses on laboratory sensitivity reports.

Antibiotics work either by inhibiting or stopping the one-celled bacterial organisms from mutating and replicating. Antibiotics disrupt the bacteria’s cellular activity through several mechanisms (Page, Curtis, Sutter, Walker, & Hoffman, 2002). Some may inhibit or destroy cell wall synthesis or functioning. Other antibiotics work by impairing the synthesis of bacterial proteins, deoxyribonucleic acid (DNA), ribonucleic acid (RNA), or their components. When administering medications, safe practice requires knowledge of side effects and contraindications, as well as the application of effectiveness principles. An antibiotic such as methicillin is effective on bacterial cell walls. If it is used to treat a bacterial infection caused by Chlamydia trachomatis, which does not have a cell wall, then ineffective and potentially unsafe treatment has been given.

**Antibiotic Resistance**

Bacteria change or mutate randomly according to the evolutionary theory of natural selection. Mutation produces genetically different characteristics that are inheritable by future generations from that bacterium (Donangelo & Fort, 2002). Bacteria developed within an environmental exposure to antibiotics may be eradicated or mutate to resist the antibiotic. Bacteria exposed to antibiotics may evolve into more virulent organisms and thus increase the percentage of resistant bacteria. Most bacteria replicate by cell division multiple times per day. Therefore, mutations that occur randomly can be passed rapidly on to generations of bacteria. Bacteria that develop resistance to antibiotics survive to reproduce, allowing this genetic mutation to dominate the population (National Institute of Allergy and Infectious Diseases, 2004). Resistant bacteria mutate and spread as a result of many factors. The escalating resistance occurs due to an antibiotic treatment failure (incorrect antibiotic, dose, schedule, etc.), an increase in the population of resistant bacteria available to spread, a variety of host susceptibility factors, or a decrease in the normal protective colonized flora (Lipsitch & Samore, 2002). Mutations are fostered if a patient is given unnecessary or inappropriate antibiotics, or if antibiotics are discontinued prior to complete eradication of the bacteria.

The resistance to antibiotics is due to the changes in the bacteria’s genes (Levy, 2002). Mutations may change the virulence of the infecting bacteria markedly. Should a mutation fos-
ter survival of bacteria in an environment with an antibiotic, then only the non-mutated, non-resistant bacteria will be eradicated. This elimination of susceptible bacteria leaves the resistant ones to replicate without inhibition. The resistant gene can then be transferred to other bacteria, both within a specie, as well as between species.

Antibiotics are believed to become resistant in four ways (Levy, 2002). The bacteria may code for mutations which make it difficult or impossible for the antibiotic to enter the bacteria. This can occur through the obstruction of entry by blocking the antibiotic’s binding site on the bacterial cell wall. Additionally, the mutation may change the membrane transport protein of the bacteria, ensuring that the antibiotic cannot proceed further into the cell. Another method of genetic mutation for antibiotic resistance is the development of a pump in the bacteria that exports the antibiotic when it enters the cell. The antibiotic may have so little exposure to the bacteria that it is unable to have an impact. Finally, the bacteria may be able to encode enzymes to degrade the antibiotic. If the antibiotic is inactive in this way, its presence in the body does not eradicate the infection. An example of enzyme producers is β-lactamase bacteria. A mutation in bacteria led to the survival and multiplication of resistant organisms despite previously accepted therapeutic antibiotic serum levels (Bagge et al., 2004). The bacteria that have mutated to produce the enzyme β-lactamase are able to inactivate the core structure, the β-lactam ring of some antibiotics, notably penicillin (Page et al., 2002).

The progression of MRSA. With the advent of penicillin use in 1944, S. aureus was managed effectively until resistance developed due to β-lactamase (CDC, 2002). In 1962, methicillin was used commonly to combat the infections caused by S. aureus. Methicillin resistance was identified in 1996 with a subsequent change to vancomycin, the drug traditionally considered one of last resort to control infection. Warnings were published soon thereafter that overuse of vancomycin could lead to further resistance (CDC, 1997; Shlaes et al., 1997). The time between widespread use and emerging vancomycin resistance shortened dramatically, according to a national laboratory report (Lundstrom & Sobel, 2000). The report detailed a burgeoning intermediate resistance rate to vancomycin in 39% to 100% of cultures. In 2002, vancomycin-resistant Staphylococcus aureus was identified.

Bacteria are considered virulent in various ways, such as adherence to patient access sites (for example, intravenous or urinary catheters) or invasiveness into a cell. The virulence of MRSA is related to toxin production, which is promoted by inappropriate antibiotic administration (Dancer, 2004). In the presence of β-lactam antibiotics, α-toxin production increases dramatically. This toxin increases the lethal activity of MRSA. Because the wrong choice of antibiotic can increase production of α-toxin, the patient may be subjected to more harm than is possible with an informed antibiotic choice by prolonging the infection or by increasing the bacteria’s virulence by way of higher bacterial toxin output.

Individuals have colonies of bacteria that provide assistance (for example, in gastrointestinal tract) or are not usually harmful (for example, on skin). A colonized site is so named when there is bacterial growth; while an infection occurs when that bacterial growth causes disease or releases a toxin. Approximately 25% to 30% of people are colonized, but not infected, with S. aureus; however, it is not known how much of this is MRSA (Kluytmans, Van Belkum, & Verbrugh, 1997). This resistant strain occurs most frequently in hospitalized patients who are aging, very ill, or immune compromised (Herwaldt, 1999). Risk of infection is particularly high if the patient has a wound, surgical or otherwise, or in the presence of intravenous or urinary catheters (Herwaldt, 1999). Patients are at high risk for MRSA infections if they have long hospital stays, received broad-spectrum antibiotics, or require surgical care or admission to the burn or intensive care unit (ICU) (Herwaldt, 1999).

The rising rate of MRSA infection is a major concern. MRSA is a common organism of nosocomial infections and has been recognized by the World Health Organization (WHO, 1996) as a major cause of morbidity and mortality in hospitals for over a decade. Questions have arisen as to whether hospitals can control this infection adequately (Boyce, Havill, Kohan, Dumigan, & Ligi, 2004). In ICUs, over 50% of S. aureus is MRSA, while other hospital units report 40% rates (CDC, 1999). The focused concern over MRSA is due to the rapid progression of its resistance. It is predicted that MRSA will become even more difficult to treat in the future due to independent mutations of lines of S. aureus (Howe, Monk, Wootton, Walsh, & Enright, 2004). National guidelines for preventing its transmission have been published by the Society for Healthcare Epidemiology of America (Muto et al., 2003).
Implications of Antibiotic Resistance on Patient Care

The problem of antibiotic resistance was identified over 20 years ago; higher rates of antibiotic resistance have been believed to be related to high rates of antibiotic use (McGowan, 1983). Recent studies support this belief. Although surgery and ICU admission are higher risks for antibiotic resistant infections, the highest rate of resistance to antibiotics is found in patients who had received those drugs, such as third generation cephalosporins (Schwaber, DeMedina, & Carmeli, 2004). A 4-year study found that MRSA rates rose with increased use of the broad-spectrum antibiotics (Monnet, Molstad, & Cars, 2004). This same correlation has been identified worldwide as high rates of antibiotic use in Spain, France, the United States, and Greece correspond with high rates of antibiotic resistance, while low use rates in the Netherlands, Norway, Denmark, and Sweden correspond to low resistance rates (Álbrich, Monnet, & Harbath, 2004).

Remarkably, changing the pattern of antibiotic overuse can result in a reversal of the antibiotic resistant trend. One prospective 4-year trial found that a change in antibiotic use to a research-based level led to a decrease in antibiotic resistance rates in addition to improved outcomes in high-risk patients (Fridkin et al., 2002). Several studies have identified differences in infection rates by locale, suggesting that health care practices affect infection rates (Stein, Weber, & Kelly, 2003; Tiermersma et al., 2004).

Solutions to antibiotic resistance. Detailed surveillance plans for hospitals have been developed by the CDC (2001). Plans include monitoring trends in antibiotic use and resistance, providing education on their relationship, and identifying solutions to current and emerging resistance. In addition to surveillance, primary prevention to reduce the risk of infection is indicated (CDC, 2001). Primary prevention, the actual prevention of the disease, can be accomplished by immunizations to such bacteria as *Streptococcus pneumoniae* and *Neisseria meningitidis*. Other vaccine trials are underway, including for *Mycobacterium tuberculosis*. Risk reduction also can be accomplished by removing indwelling intravenous and urinary catheters as soon as clinically indicated rather than by routines, such as with next day’s medical rounds (CDC, 2001).

Nurses play a pivotal role in the care of patients with infections. Part of that care is preventing infection. Basic infection prevention policies should be followed with personal rigor. Control measures have reduced the transmission of nosocomial infection. These include standardized precautions that are used for all patients and include handwashing between patients and procedures, as well as transmission-based precautions such as respiratory isolation for patients with MRSA pneumonia (Garner & The Hospital Infection Control Practices Advisory Committee, 1996). The clinical significance of careful handwashing is reinforced with research that has demonstrated the same bacterial genotype present on a nurse’s hand, the unit computer keyboard, and worst of all, a patient’s bloodstream (Dancer, 2004).

The presence of antibiotic guidelines that delineate current research-based bacterial antibiotic effectiveness and resistance on each hospital unit may ensure availability of current antibiotic information. For example, reliable guides updated annually can be found in various formats such as book, hand-held computer, or the Internet (Sanford Guide, 2004). It is important to note that the excess prolongation of antibiotic administration may also lead to the development of antibiotic-resistant organisms but does not correspond to a decreased infection rates (Harbath, Samore, Lichtenberg, & Carmeli, 2000).

Choosing the correct antibiotic is important in the prevention and treatment of infection (Soriano & Ponte, 2004). Culture-based antibiotic use can prevent the inappropriate use or overuse of antibiotics (Soriano & Ponte, 2004). Most hospital laboratories develop antibiograms that detail the rates of infectious organisms and antibiotic resistance in the facility (CDC, 2001; Scheckler et al., 1998). These data are essential to focus antibiotic use. The use of the hospital’s antibiogram will allow for the inclusion of local resistance rates when choosing the appropriate antibiotic. This knowledge also can be used to develop and implement strategies to address patterns of antibiotic overuse.

While changing perspectives are important, the mere presence of a surveillance has been demonstrated to reduce both infection and antibiotic prescribing rates. Surveillance is effective at both the local (Fridkin et al., 2002) and national levels (Gaynes et al., 2001).

While the development of treatments such as newer antibiotics (Dandliker et al., 2003) and non-pathogenic phages that can consume the infecting organism (Matsuzaki et al., 2003; Novick,
2003) hold promise for managing resistant infections, these treatments may fail eventually as well if the trend of antibiotic overuse continues. Evidence suggests that newer treatments will develop the same patterns for resistance that have developed already (Levy, 2002). Success requires a multidisciplinary approach that includes informed personnel across departments such as infectious disease and pharmacy, as well as prescribers and nurses. This multidisciplinary team approach includes the research, development, implementation, and reevaluation of antibiotic use and resistance patterns in a hospital.

**Conclusion**

Antibiotic resistant infections merit attention from hospital nurses across units due to their association with antibiotic overuse. Stopping the patterns of antibiotic overuse can reduce microbial resistance rates over time. Nurses influence antibiotic resistance in the hospital through infection control procedures, knowledge of evidence-based antibiotic protocols, and surveillance of infection incidence and treatment. The significance of antibiotic resistant infections cannot be overstated. Without measures to reduce the overuse of antibiotics in hospitals, the future effectiveness of antibiotics is in doubt.

**References**


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