Bacteria Battle Back: Addressing Antibiotic Resistance

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Introduction

Bacterial resistance to antibiotics continues to curb our ability to treat, cure and control infectious diseases. Antibiotics, often touted as one of the most important discoveries of modern medicine, are losing ground to bacteria that are now resistant to several drugs. The irony, of course, is that antibiotics developed to control bacteria have instead strengthened them, leading to drug-resistant bacteria against which antibiotics are ineffective. Antibiotic resistance was initially found only in hospitals where most antibiotics are still used, but resistance is now a serious problem in the community as well. Infectious diseases that were once easily treated with antibiotics now often thwart treatment. Two organisms in particular that have become major public health threats are methicillin-resistant *Staphylococcus aureus* and penicillin-resistant *Streptococcus pneumoniae*.

The speed at which bacteria can develop antibiotic resistance has made it clear that these drugs are less of a “miracle” than they were once touted to be. While designed to be selective for bacteria and not host cells, antibiotics are not selective enough to distinguish the pathogenic from commensal bacteria. Consequently, antibiotic use alters the microbial ecology by decimating susceptible flora and favoring growth of bacteria that possess resistance traits. These bacteria that possess antibiotic resistance traits can then pass these traits on to future bacterial generations or to pathogens.

It is clear that the fight to control bacterial pathogens is far from won. Scientists are now attempting to develop new classes of antibiotics that uti-
lize different mechanisms for which bacteria have yet to evolve resistance. In addition, research is ongoing to develop methods to revive susceptible commensal flora within human and animal hosts. At the same time, there must be broad, multidisciplinary educational programs dedicated to teaching the public as well as health care professionals about the appropriate use of antibiotics in humans, animals and agriculture.

Increasing awareness of the problem of antibiotic resistance in the community and the threat that resistant bacteria may pose is a key first step in addressing this problem. Training health care practitioners to identify potential pathogens accurately and to treat them with effective agents and appropriate regimens are important additional steps. Patient education is also crucial in ensuring that the public understands and participates in efforts to control the spread of antibiotic resistant bacteria. This continuing education program describes the problem and provides concrete guidelines for improving antibiotic use in the community and within institutional health care settings.

Stuart B. Levy, MD
other major cause of drug-resistant infections in hospitals and, more recently, in the community. Of particular concern are vancomycin-resistant enterococci (VRE). These organisms are generally hospital-based pathogens found on the skin and in the gastrointestinal tract. They can be easily spread from patient to patient and from health care worker to patient. The prevalence of organisms resistant to vancomycin is increasing and is troublesome because vancomycin has been the last line of defense against many gram-positive bacteria resistant to other traditional antibiotics. Penicillin-resistant pneumococcus (PRP) is a respiratory pathogen that generally is associated with community-based respiratory illness. As many as 40 percent of pneumococci strains in some parts of the United States are completely resistant to penicillin and a number of other antibiotics. In addition to penicillin-resistant strains, organisms that are resistant to other antibiotics such as erythromycin, chloramphenicol and cephalosporins also have been reported recently. These organisms are designated drug-resistant pneumococci (DRP).

Tuberculosis, caused by Mycobacterium tuberculosis, is still a leading cause of mortality worldwide. The WHO predicts more than 30 million people will die of tuberculosis in the next 10 years unless global control measures are successfully implemented. The emergence of antibiotic-resistant tuberculosis strains in developing countries has further complicated successful treatment of this disease. This resistance is not just a problem in the developing world. The recent resurgence of tuberculosis in the homeless and HIV-infected populations in developed countries has also become a source of great concern to the health care community. These organisms are particularly prone to becoming antibiotic resistant in populations such as the homeless whose health care is monitored less closely and who are less likely to comply with complex medication regimens. Other bacteria being watched for emerging resistance to antibiotics include Neisseria gonorrhoeae, which is responsible for gonorrhea, H. pylori, which is associated with gastric disease, and nonfermentative gram-negative bacteria such as Pseudomonas aeruginosa.

### Epidemiology of Antibiotic Resistance

The origins of antibiotic resistance in microorganisms are of particular interest to scientists studying the general problem of drug resistance. It is not entirely clear whether antibiotic-resistant bacteria arose with the development and clinical use of antibiotics or if resistant organisms were present in the environment before the widespread use of antimicrobials. Researchers have examined bacteria that predate the discovery of antibiotics taken from populations never exposed to antibiotics. Investigators have reported evidence of some low-level resistance to antibiotics, but overall the bacteria studied were sensitive to most antibiotics prior to exposure. This finding suggests that while some genes for antibiotic resistance likely predate widespread antibiotic use, widespread resistance emerged to a major extent after widespread antibiotic use. It is reasonable to assume that these genes served a protective function in bacteria exposed to the many naturally occurring antibiotics produced by other microorganisms in the environment. The frequency, diversity, and specificity of these antibiotic resistance genes likely all increased as the microorganisms were exposed to increasing amounts of new and synthetic antibiotics being used to treat and prevent disease.

When considering the problem of genetic resistance in bacteria, it is important to understand that bacteria multiply rapidly and continually.

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**Table 1.**

<table>
<thead>
<tr>
<th>Hospital-Acquired</th>
<th>Community-Acquired</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methicillin-resistant</td>
<td>Penicillin-resistant pneumococcus (PRP)</td>
</tr>
<tr>
<td>S. aureus (MRSA)</td>
<td><em>Escherichia coli</em></td>
</tr>
<tr>
<td>Vancomycin-intermediate <em>S. aureus</em> (VISA)</td>
<td>extended-spectrum β-lactamases (ESBL)</td>
</tr>
<tr>
<td>Vancomycin-resistant enterococcus (VRE)</td>
<td><em>Neisseria gonorrhoeae</em></td>
</tr>
<tr>
<td><em>Enterobacter</em></td>
<td><em>Haemophilus influenza</em></td>
</tr>
<tr>
<td><em>Pseudomonas</em></td>
<td><em>Mycobacterium tuberculosis</em></td>
</tr>
<tr>
<td><em>Klebsiella</em></td>
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4 Bacteria Battle Back: Addressing Antibiotic Resistance · November 2000
Bacteria Battle Back: Addressing Antibiotic Resistance

Costs Related to Antibiotic Resistance

At the turn of the 21st century it had been nearly 70 years since antibiotics were first introduced to treat bacterial infections. During this time antibiotics saved countless lives; and for a while it seemed that mankind possessed the means to overcome almost any bacterial infection. Unfortunately, in recent years, concern and fear have replaced this confidence because antibiotic-resistant bacteria have emerged. Antibiotic resistance is now a global problem that requires action by all health care providers, patients, industry and government to decrease the prevalence and costs (both human and financial). This action must include research, education, surveillance and behavioral change.

The cost of antibiotic resistance in terms of both lives lost and dollars spent has become quite significant. The World Health Organization (WHO) reports that approximately 14,000 individuals die each year in the United States as a result of infections from antibiotic-resistant organisms. Worldwide, the WHO believes drug-resistant bacteria account for up to 60 percent of hospital-acquired infections. A 1995 study reported that antibiotic-resistant S. aureus infections were responsible for nearly 1,500 deaths just in New York city and that treatment costs were $500 million. Also in 1995, it was conservatively estimated that the nationwide cost of antibiotic resistance was at least $1.3 billion.

Some of the resistant pathogens of the most immediate concern to health care professionals are listed in Table 1. One of these organisms, methicillin-resistant S. aureus (MRSA) is one of the most common antibiotic-resistant bacteria found in hospitals and health care facilities. MRSA residing on the skin and in the upper respiratory passages is easily spread from person to person, as is the closely related methicillin-resistant Staphylococcus epidermidis. More than 90 percent of S. aureus strains are resistant to penicillin and related antibiotics. Several cases of infection caused by S. aureus in which the organisms were fully resistant to methicillin and partially resistant to vancomycin have been reported in the United States.

These organisms are classified as vancomycin-intermediate S. aureus and are of particular concern because they may herald the development of vancomycin-resistant strains of this organism.

Enterococcus species are an-
exchange genetic information. In addition, many bacteria frequently transfer between animal, human and plant hosts. While antibiotic resistance may be an intrinsic property of a particular organism (with the genes for antibiotic resistance found within the chromosomal DNA), it is more likely that most bacteria acquire their resistance genes from other resistant organisms.

We now know that many of the genes that confer antibiotic resistance to a particular organism are found on circular, self-replicating strands of DNA called plasmids. Bacteria transfer these plasmids during a process called conjugation. This appears to be a major mechanism for spreading antibiotic resistance among bacteria. Moreover, the actual genes for antibiotic resistance often lie on regions of the plasmid called transposons, or “jumping genes,” which are pieces of DNA that can readily move to and from DNA molecules. This process of gene exchange via transposons is called transposition. The second mechanism by which genes for antibiotic resistance may be spread amongst a bacterial population is bacteriophage transduction. Bacteriophages are viruses that infect bacteria. In the course of their infectious cycle, they can transfer segments of bacterial genomes between the microorganisms they infect. Finally, bacteria may acquire antibiotic resistance genes through the process of transformation. When bacteria die they release into the environment their DNA, which may contain genes for antibiotic resistance. Other viable bacteria can readily take up this DNA and incorporate the genes into their own genome. These resistance genes encode information responsible for a number of resistance mechanisms. The genetic transfer mechanisms of genes for antibiotic resistance are summarized in Table 2.

### Mechanisms of Antibiotic Resistance

With continued exposure to antibiotics, bacteria have developed numerous mechanisms for overcoming the effects of these drugs (see Table 3). These antibiotic-resistance mechanisms are not mutually exclusive and most likely resistant organisms use various mechanisms concurrently. The antibiotic-resistance mechanisms that have been identified thus far include:

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Genetic Transfer Mechanisms of Antibiotic Resistance</th>
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<tbody>
<tr>
<td>1. TRANSPOSITION</td>
<td>The exchange of bacterial DNA containing antibiotic resistance genes during conjugation.</td>
</tr>
<tr>
<td>2. TRANSDUCTION</td>
<td>Bacteriophage transfer of antibiotic resistance genes between the bacteria they infect.</td>
</tr>
<tr>
<td>3. TRANSFORMATION</td>
<td>Live bacteria incorporate antibiotic resistance genes that are released by dead bacteria into the environment.</td>
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<table>
<thead>
<tr>
<th>Table 3</th>
<th>Four Mechanisms of Antibiotic Resistance</th>
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<tbody>
<tr>
<td>ENZYMATIC DESTRUCTION OR MODIFICATION OF ANTIBIOTICS</td>
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<tr>
<td>• β-lactamases (narrow- or extended-spectrum)</td>
<td></td>
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<tr>
<td>• Aminoglycoside-modifying enzymes (acetylase, adenylylase, phosphorylase)</td>
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<tr>
<td>DECREASED UPTAKE OF ANTIBIOTIC INTO BACTERIUM</td>
<td></td>
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<tr>
<td>• Reduced permeability of bacterial membranes and cell wall</td>
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<tr>
<td>• Altered structure or reduced number/affinity of drug (porin) channels</td>
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<tr>
<td>• Reduced electrochemical gradient for transport</td>
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<tr>
<td>INCREASED REMOVAL OF ANTIBIOTIC FROM BACTERIUM</td>
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<tr>
<td>• Active efflux pumps</td>
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<tr>
<td>• “Multi-drug” efflux pumps</td>
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<tr>
<td>ALTERATION OF BACTERIAL TARGETS</td>
<td></td>
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<tr>
<td>• Mutated penicillin-binding proteins no longer bind β-lactam antibiotics</td>
<td></td>
</tr>
<tr>
<td>• Mutated DNA gyrase, topoisomerase, polymerase enzymes are no longer inhibited by fluoroquinolones and rifampicin</td>
<td></td>
</tr>
<tr>
<td>• Altered bacterial ribosomes no longer allow aminoglycoside antibiotics to bind</td>
<td></td>
</tr>
<tr>
<td>• Development of resistant metabolic pathways in which key enzymes are no longer inhibited by antibiotics (e.g., trimethoprim and tetrahydrofolate reductase)</td>
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</tbody>
</table>
1. Enzymatic modification or destruction of the antibiotic. The bacterial genome may code for the production of enzymes that are capable of inactivating or destroying a particular antibiotic. One common bacterial enzyme is β-lactamase, which is capable of splitting the β-lactam ring that comprises the nucleus of carbapenem, cephalosporin, monobactam and penicillin antibiotics. Currently, more than 200 distinct types of β-lactamases have been identified. These β-lactamases may either have a narrow spectrum and act only against a specific β-lactam antibiotic, or they may be extended-spectrum β-lactamases (ESBLs) capable of conferring resistance to multiple antibiotics. A second group of aminoglycoside-modifying enzymes has also been characterized. These enzymes are capable of altering the structure of aminoglycoside antibiotics through acetylation, adenylation or phosphorylation. Covalent modification of the aminoglycoside antibiotics by these enzymes may lead to their inactivation or impair their ability to enter the bacterial cell. More than 20 of these particular enzymes have been identified.

2. Decreased uptake of antibiotic into bacteria. Many gram-negative bacteria are intrinsically somewhat resistant to β-lactam antibiotics because of their outer membrane impermeability. While membrane permeability varies from organism to organism, any genetic mutation that further decreases membrane permeability to antibiotics will confer greater resistance to that organism. As a consequence of their low cell membrane permeability, gram-negative bacteria must use membrane proteins called porins that act as channels by which hydrophilic substances, including antibiotics, can get inside the bacteria cell. Genetic mutations that alter the number or configuration of porin channels in the bacterial membrane can reduce the ability of antibiotics to enter that particular organism. In cephalosporin-resistant enterobacteria, for example, there are reduced numbers of porin F molecules—the main channels by which the cephalosporins enter cells. The specific porin molecules that allow imipenem to enter bacterial cells are essentially absent in imipenem-resistant enterobacteria. In addition to the β-lactam antibiotics, resistance to chloramphenicol, quinolones and trimethoprim may also be partially attributed to changes in bacterial uptake of these agents.

A novel antibiotic-resistance mechanism was recently described for small-colony variants of staphylococcus in which these bacteria had a reduced rate of electron transport chain activity. Because of this reduced activity, they did not produce sufficient electrochemical gradients necessary to transport aminoglycoside antibiotics into the cell. Furthermore, because these organisms have a slow growth rate, the overall effectiveness of cell-wall active antibiotics such as the β-lactams is significantly reduced.

3. Increased removal of antibiotic from bacteria. Another recently characterized mechanism of antibiotic resistance involves active drug efflux pumps. These energy-driven protein pumps traverse the inner and outer membranes of bacteria and rapidly transport antibiotics out into the environment. It is likely that these membrane pumps operate to varying degrees in almost all bacteria and serve as a protective mechanism against environmental toxins. Many bacteria have numerous drug efflux pumps with varying specificity. Two main types of efflux pumps with a wide affinity for various antibiotics have been identified in gram-negative organisms.

These “multi-drug” efflux pumps are likely key contributors to antibiotic resistance in gram-negative organisms, along with β-lactamases and reduced cell permeability. Antibiotics with hydrophobic domains (β-lactams and fluoroquinolones, for example) appear to be most susceptible to removal by efflux pumps, while hydrophilic compounds such as aminoglycosides and vancomycin appear to be less so. A number of antibiotic-resistant organisms such as Campylobacter jejuni, E. coli, N. gonorrhoea and P. aeruginosa reportedly have elevated expressions of multi-drug transport efflux pumps. This expression markedly reduces the effectiveness of antibiotics against these particular species.

4. Alteration of bacterial targets. Antibiotics act at a number of different sites in the bacterial cell. β-lactams exert their therapeutic effects by binding bacterial proteins called...
penicillin-binding proteins (PBP). When β-lactam antibiotics are bound to intracellular PBPs, bacterial peptidoglycan cell wall synthesis is inhibited and bacterial cell wall integrity is disrupted. In contrast, fluoroquinolone antibiotics target DNA gyrase and topoisomerase enzymes that regulate bacterial DNA coiling. Aminoglycoside antibiotics bind to bacterial ribosomes and interfere with protein synthesis. Rifampicin exerts its effect on bacterial cells by blocking the enzyme RNA polymerase. Sulfonamide antibiotics and trimethoprim inhibit the essential metabolic pathway for tetrahydrofolic acid synthesis in bacteria. For all of these mechanisms, genetic mutations have arisen in which the bacterial target enzyme or protein becomes altered so it no longer binds to, or is inhibited by, an antibiotic. In the case of the β-lactam antibiotics, mutated penicillin-binding proteins will no longer bind to β-lactam drugs. Similar mutations occur with bacterial DNA gyrase, DNA polymerase and ribosomal proteins so they no longer act as substrates for their specific antibiotics. Bacterial mutation also leads to the development of resistant metabolic pathways in which key enzymes are no longer inhibited by antibiotics. For example, a mutation or overproduction of tetrahydrofolate reductase by resistant bacteria overcomes trimethoprim inhibition.

### Factors Contributing to Antibiotic Resistance

Antibiotic use in human medicine is widely accepted as the primary factor driving development of antibiotic resistance in human pathogens. Use of antibiotics in other settings also contributes to the resistant gene pool where antibiotic resistance can emerge and spread. In recent years, the direct relationship between increased antibiotic use and the development of resistance has become increasingly clear. Using antibiotics to treat and prevent bacterial disease in humans, animals and agriculture has grown rapidly in the last few decades. A result of this increased antibiotic use is that more microorganisms are exposed to antibiotics. Exposure to antibiotics appears to be the principal risk factor for emergence and selection of antibiotic-resistant bacteria (see Table 4).

Nearly 50 percent all antibiotics produced are used to treat infected livestock and to encourage growth in livestock and poultry. Drugs such as streptomycin and oxytetracycline are now routinely used to prevent bacterial diseases in fruits and vegetables. Antibiotics are also added to livestock feed or otherwise administered prophylactically to domestic animals used for meat and dairy production as well as to honeybees and farm-raised fish.

Another way exposure is increased is through the use of chemical disinfectants in soaps and detergents—a growing trend. This has been a matter for recent concern since a number of bacterial species have arisen that are less sensitive to commonly used biocide antiseptics, disinfectants and preservatives. Increased use is particularly distressing because there is no evidence of effectiveness. According to the American Medical Association, there are no scientific data proving antimicrobial soaps have any infection-fighting benefit compared to standard soap and water. As a result, the AMA’s Council on Scientific Affairs recently released a statement urging the FDA to more closely regulate use of antimicrobial agents

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**Table 4**

<table>
<thead>
<tr>
<th>Factors Contributing to Antibiotic Resistance</th>
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<tbody>
<tr>
<td>1. Widespread antibiotic use in livestock, agriculture and veterinary medicine</td>
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<tr>
<td>2. Unnecessary antibiotic use</td>
</tr>
<tr>
<td>3. Patient compliance</td>
</tr>
<tr>
<td>• Prescriptions for antibiotics are not filled, not taken correctly, not taken to completion</td>
</tr>
<tr>
<td>4. Exposure to antimicrobial soaps, solutions and lotions</td>
</tr>
<tr>
<td>5. Socioeconomic consideration in developing countries</td>
</tr>
<tr>
<td>• Unskilled health practitioners</td>
</tr>
<tr>
<td>• Misuse of antibiotics</td>
</tr>
<tr>
<td>• Poor-quality drugs</td>
</tr>
<tr>
<td>• Antibiotics widely available through non-professional channels</td>
</tr>
<tr>
<td>• Poor surveillance and compliance</td>
</tr>
<tr>
<td>• Poverty and poor hygiene</td>
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</table>
in products such as soaps, lotions and washes. The Centers for Disease Control (CDC) currently recommends using ordinary soap and water solutions instead of antimicrobial products and the U.S. Food and Drug Administration has recently issued guidelines advising against adding biocides to soap products.

The inappropriate or unnecessary clinical use of antibiotics is a key factor contributing to the increased numbers of antibiotic-resistant bacteria. CDC has estimated that one-third of the total number of prescriptions written yearly for antibiotics may be unnecessary. Antibiotics are often prescribed when the organism causing a particular infection is unknown and, as in the case of the common cold, is of viral origin. Fear of potential malpractice litigation may also motivate physicians to prescribe antibiotics in cases where their use might not be essential. Patients and health care professionals (including physicians, physician assistants, pharmacists, podiatrists, nurse practitioners and physician’s assistants) all share responsibility for such inappropriate use. Any unnecessary use, regardless of where it occurs, contributes to the global emergence of resistance.

Patients who do not take their medications as directed or who do not finish the course of their treatment risk exposing bacteria to sublethal concentrations of antibiotics, thus breeding more dangerous bacteria. The high cost of certain antibiotics may contribute to decisions by low-income or uninsured patients to discontinue or not renew prescriptions for some drugs. Patients may choose not to complete the current course of therapy and save some of their prescription medications should another illness arise. Inadequate doses or duration of therapy contributes to resistance whether a result of poor patient compliance, inadequately dispensed drug product or a poorly designed dosing regimen.

An epidemic of antibiotic resistance exists in many developing countries where various socioeconomic and behavioral factors create a prime environment for such bacterial strains. These behavioral factors include misuse of antibiotics by unskilled health professionals, poor drug quality and the widespread over-the-counter availability of antibiotics through untrained or unlicensed practitioners. In many third-world countries, antibiotics can be purchased without a prescription from pharmacies, at outdoor markets or from parapharmacies with unqualified staff. Often these drugs are of dubious origin and quality. Poor compliance and a lack of economic resources may mean that even when antibiotics are correctly prescribed, the appropriate doses and time course are not followed. Inadequate surveillance and unhygienic conditions that foster the spread of resistant bacteria further compound the problem.

The evolution of antibiotic resistance is a growing problem in the United States and around the world. Increased exposure to antibiotics through unnecessary and inappropriate use in human medicine, agriculture and food production contribute to the problem and help breed more dangerous bacteria. As a matter of survival, bacteria continue to develop novel ways of resisting antibiotics. To address this global problem, two predominant health organizations, WHO and CDC, have established practical guidelines and goals for scientists and practitioners to research and develop new drugs, monitor the development of resistant bacteria, prescribe accurately, prevent infection and educate the public on antibiotic resistance and their role in preventing it.

Guidelines for Controlling Antibiotic Resistance

Certain organizations including the CDC, the Alliance for the Prudent Use of Antibiotics (APUA), and WHO have long served as leaders in developing programs to curb antibiotic resistance and improve antibiotic use. The CDC has identified surveillance, research and development, and prevention and control as the major programs needed to combat antibiotic resistance. Surveillance of antibiotic resistance patterns and associated antibiotic-use patterns, both nationally and internationally, are of primary importance in demonstrating and understanding antibiotic resistance. Reliable drug-susceptibility and antibiotic use information must be made available to health care providers and governments. By identifying known resistance and inappropriate
antibiotic use patterns these groups can optimize treatment strategies to contain antibiotic resistance and move toward eradicating important infections. Further, by monitoring antibiotic resistance in agricultural settings, plant and animal health can be ensured, leading to a safer food supply and a healthier population.

Applied microbial and product development can begin once drug-susceptibility information is available, linking laboratory science and bacterial resistance patterns. By knowing the risk factors for infectious and chronic diseases, scientists and the health care community can develop research-derived prevention, control and treatment strategies. CDC encourages research and development of new antibiotics and vaccines to combat drug resistant illnesses. In their June 2000 draft article “Public Health Action Plan to Combat Antimicrobial Resistance – Domestic Issues,” the following action plan is recommended for applied microbiological and product development research. In the area of microbiological research it is important to:

- increase understanding of microbial physiology, ecology, genetics and resistance mechanisms;
- augment existing research infrastructure to support a critical mass of resistance mechanisms;
- translate research findings into clinically useful products, such as novel approaches to detecting, preventing and treating antimicrobial resistant infections.

With regard to product development research, the CDC emphasizes:

- ensuring that researchers and drug manufacturers are informed of current and projected gaps in the arsenal of antimicrobial drugs, vaccines and diagnostics, and of potential markets for these antibiotic-resistant products;
- stimulating the development of priority antimicrobial resistant products for which market incentives are inadequate, while fostering their appropriate use; and
- optimizing the development and use of veterinary drugs and related agricultural products that reduce the transfer of resistance to pathogens that can infect humans.

The third prong of the CDC plan involves prevention and control. By improving local, state and federal public health infrastructure, planning, delivery and evaluation of important public health practices can be supported. While the CDC can serve as a reference center for diagnosing infectious diseases and testing for drug-resistance, public domains must play an active role in training, educating, developing policy and properly implementing available control measures. Global communication and cooperation is imperative to ensure that society can respond to emerging infectious disease threats. A summary of the CDC plan, extracted from the June 2000 draft of the CDC “Public Health Action Plan to Combat Antimicrobial Resistance – Domestic Issues” includes the following steps to be taken by health care and health care professionals:

- Extend the useful life of antimicrobial drugs through prudent use policies that discourage overuse and misuse.
- Improve diagnostic testing practices.
- Prevent infection transmission through improved infection-control methods and vaccine use.
- Prevent and control emerging antibiotic resistance problems in agriculture.
- Ensure that comprehensive programs to prevent and control antibiotic resistance involve a wide variety of non-governmental partners, and that the public becomes part of prevention practice.

The blueprint proposal by CDC for combating antibiotic resistance includes increasing worldwide preparations to fight diseases once believed to be under control such as tuberculosis and *Streptococcus pneumoniae*, and maintaining a vigilant watch for new diseases. Food-, water- and blood-borne contaminants must be addressed through various public measures, and experts in various disciplines must be watchful of pathogens passed from animals. Public health standards should strive to protect the most vulnerable in society, such as children, pregnant women, the sick, elderly and people without access to health care.

Complementing the efforts of the CDC, WHO suggests interventions and global action with eight recommendations (listed below) to national governments to curb the glo-
Bacterial problem of antibiotic resistance: Adopt WHO strategies and policies for disease prevention, treatment and control, the most important relate to immunization.

1. Educate health care workers and the public on appropriate use of antimicrobials.
2. Contain resistance in hospitals.
3. Reduce antimicrobial use in livestock.
4. Increase research on new drugs and vaccines.
5. Build alliances and partnerships to increase access to antimicrobials in countries where availability is a problem.
6. Increase the availability of medications on WHO’s list of essential drugs.
7. Make effective antimicrobials available to poor people.

An important aspect of the WHO plan is that it encompasses antibiotic resistance, disease prevention, treatment and control issues on a global level because infectious illness is an international concern. For the full report and specific policies, see www.who.int. While national and global communication and cooperation is imperative to ensure that society can respond to emerging infectious disease threats in the future, it is local healthcare providers and facilities that can make the most difference in controlling antibiotic resistance. Every health care provider can play a role in building awareness about antibiotic resistance and improving antibiotic use.

Health Care Practitioner Interventions

Responsibility for many of the antibiotic-resistance-curbing strategies outlined here rests with health care practitioners. By practicing prudent prescription strategy, staff and public education, and hygienic office procedures, the health care provider plays a vital role. Consider that antibiotics comprise between 10 and 40 percent of hospital drug expenditures. Almost one-half of the antibiotics used in institutions results in treatment failures and adverse events, which lead to longer hospital stays. Approximately 25 percent of all adverse drug events in hospitalized patients are antibiotic related. In the community setting, patients feel the financial burden of resistance. Treating infections caused by resistant organisms often requires newer or parenteral therapies, which are more expensive. These problems are a direct result of the generalized use of broad-spectrum agents without appropriate antibiotic management strategies. There are opportunities to reduce or optimize antibiotic exposure, which will, in turn, slow the microbial march toward resistance.

Prescribing an antibiotic is difficult at best. It takes a great deal of knowledge to make optimal decisions regarding a patient’s antibiotic therapy. According to David Greenwood of the Division of Microbiology and Infectious Diseases at Queen’s Medical Center in Nottingham, U.K., “teaching about antimicrobial chemotherapy in medical schools is generally spasmodic and uncoordinated.” This statement is true of the education of all health care providers as well. Once out of school, practitioners often rely on practice guidelines, industry input and institutional mandates to firm up their knowledge about rational antimicrobial prescribing. Now more than ever it is imperative that health care providers have a good working knowledge of resistance patterns, diagnostic techniques and updated information sources. Given enough exposure to an antibiotic, microbes will undoubtedly become resistant. To date, there are no antibiotics to which resistance has not been demonstrated.

The risks of either undertreating or overprescribing antibiotics for bacterial infections or misprescribing an antibiotic for a viral infection cannot be overemphasized. Each situation can lead to bacterial resistance, which further complicates individual treatment decisions and contributes to the resistant gene pool in an institution or community. Once the decision to treat is made, the correct antibiotic in the appropriate dose for the proper duration should be selected. Many factors contribute to this decision-making process.

In the community, an accurate diagnosis is required to determine the need for and type of antibiotic therapy required. The appropriate targeted antibiotic must be selected based on knowledge of the specific pathogen and knowledge of local bacterial patterns. An important part of any therapy decision is
Table 5

Basic Principles for Controlling the Spread of MRSA

<table>
<thead>
<tr>
<th>SURVEILLANCE</th>
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<tbody>
<tr>
<td>• Review culture and susceptibility test results regularly</td>
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<tr>
<td>• Maintain a list of patients known to be colonized or infected with MRSA</td>
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<tr>
<td>• Conduct culture surveys to assess the prevalence of MRSA as necessary</td>
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<tr>
<td>• Obtain surveillance cultures on admission from patients transferred from institutions known to have a high prevalence of MRSA</td>
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<tr>
<td>• Develop a method for evaluating patients with histories of MRSA colonization or infection when they are readmitted</td>
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<tr>
<th>CONTACT PRECAUTIONS</th>
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<tr>
<td>• Place patients in private rooms or cohort with other patients who have MRSA</td>
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<tr>
<td>• Wear gloves for contact with patient and environment</td>
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<tr>
<td>• Wear gowns if likely to soil clothes</td>
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<tr>
<td>• Use antimicrobial soap to wash hands</td>
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<tr>
<td>• Use standard housekeeping techniques</td>
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<tr>
<th>MICROBIOLOGY SUPPORT</th>
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<tr>
<td>• Use appropriate susceptibility test methods</td>
<td></td>
</tr>
<tr>
<td>• Notify clinicians and infection-control staff when an MRSA isolate is identified</td>
<td></td>
</tr>
<tr>
<td>• Save isolates when appropriate</td>
<td></td>
</tr>
<tr>
<td>• Conduct or obtain molecular typing when appropriate</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>ADDITIONAL MEASURES</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Consider decolonizing colonized or infected patients during epidemics or periods of hyperendemic transmission</td>
<td></td>
</tr>
<tr>
<td>• Consider decolonizing colonized health care workers during epidemics or periods of hyperendemic transmission</td>
<td></td>
</tr>
<tr>
<td>• Decrease use of antimicrobial agents</td>
<td></td>
</tr>
<tr>
<td>• Consider instituting an isolation ward if routine measures do not control spread of MRSA</td>
<td></td>
</tr>
</tbody>
</table>


whether local flora includes or does not include resistant organisms. In the community, it is important to differentiate between viral and bacterial infections—only patients presenting with bacterial infections should be treated with antibiotics. Reliance on, and knowledge of, new rapid bacterial identification methods (rapid strep test, for example) may be useful when obtaining culture and susceptibility tests is not prudent. Practitioners should use available diagnostic methods and tools to identify causative pathogens and target the treatment to that microbe.27 Community practitioners should resist patient pressure for antibiotics; avoid prescribing antibiotics for the common cold and recognize the importance of relieving symptoms when appropriate through decongestants, cough medicine or antipuretics when an antibiotic is not required.28 Empiric antibiotic therapy for various infectious disease conditions can be found in medical society guidelines for treating specific infections (for example, Infectious Disease Society of America, ISDA, and CDC). Naturally, these guidelines may need to be adapted for specific practice settings.

In a hospital setting, practitioners must be aware of their environment, which includes bacterial factors as well as available tools for treatment. In these settings, patients are more likely to contract resistant nosocomial pathogens such as extended-spectrum β-lactamase (ESBL)-producing E. coli or Klebsiella pneumoniae, MRSA, VRE and drug-resistant S. pneumoniae (DRSP).29 (Guidelines for controlling the spread of MRSA and VRE are listed in Tables 5 and 6, respectively.)

Practitioners should also keep in mind the capabilities of the hospital’s microbiology lab. For example, is the lab able to adequately test for ESBLs? If not, how should that fact alter treatment selection? What is the prevalence of resistant nosocomial pathogens within a particular institution and on which units? A small outlying community hospital, for ex-
**Elements of a Successful Vancomycin-Resistant Enterococcus (VRE) Prevention and Control Program**

<table>
<thead>
<tr>
<th>ISOLATION FOR HOSPITALIZED PATIENTS</th>
<th>EDUCATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>- The isolation strategy should be identical and uniform regardless of whether the patient is infected or colonized</td>
<td><strong>All personnel</strong></td>
</tr>
<tr>
<td>- Barrier precautions should include private room, gown and gloves</td>
<td>- Families and volunteers, physicians, medical and pharmacy students, nurses, nursing students and nurses aids, other health care workers, ancillary personnel (e.g. housekeepers, contractors) patients and families</td>
</tr>
<tr>
<td>- Used dedicated equipment (stethoscopes, thermometers, glucose meters)</td>
<td><strong>Organism’s epidemiology</strong></td>
</tr>
<tr>
<td>- Use chlorhexidine gluconate or an alcohol-based product to wash hands</td>
<td>- Significance and magnitude of the problem (US/state/hospital)</td>
</tr>
<tr>
<td>- Disinfect items removed from a patient’s room</td>
<td>- Transmission</td>
</tr>
<tr>
<td>- Terminally clean the room when a patient is discharged</td>
<td>- Control measures including hand washing, isolating patients, cleaning the environment, culturing patients</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ISOLATION FOR PATIENTS IN AN OUTPATIENT DEPARTMENT</th>
<th><strong>Methods</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>- Identify patient by flag or master list</td>
<td>- Didactic lectures</td>
</tr>
<tr>
<td>- Attempt to schedule infected/colonized patients on the same day</td>
<td>- Training sessions</td>
</tr>
<tr>
<td>- Dedicate a room or pod</td>
<td>- Cultures of hands, the environment</td>
</tr>
<tr>
<td>- Dedicate equipment (blood pressure cuff, stethoscope) and change it at the end of the day</td>
<td>- Data feedback</td>
</tr>
<tr>
<td>- Use disposable equipment if possible</td>
<td></td>
</tr>
<tr>
<td>- Disinfect all equipment at the end of the day or when a patient leaves the room</td>
<td></td>
</tr>
<tr>
<td>- Isolate patient when placed in room</td>
<td></td>
</tr>
<tr>
<td>- Use hospital isolation precautions (see above)</td>
<td></td>
</tr>
<tr>
<td>- Designate separate bathroom for patients with VRE</td>
<td></td>
</tr>
<tr>
<td>- Clean room or pod at end of session</td>
<td></td>
</tr>
<tr>
<td>- Communicate isolation status to other areas/services of the hospital</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>DISCONTINUING ISOLATION FOR VRE</th>
<th><strong>MICROBIOLOGY LABORATORY</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>- The patient must have three stool cultures or rectal swabs, each separated by a week, without VRE growth</td>
<td>- Speciate strains</td>
</tr>
<tr>
<td>- The Infection-control department should reset the isolation flag on that patient</td>
<td>- Test all clinical isolates for resistance</td>
</tr>
<tr>
<td>- On high-risk services, consider obtaining surveillance cultures when a previously colonized patient is readmitted or placed on antibiotics or immunosuppressants</td>
<td>- Use a susceptibility technique that detects vancomycin resistance</td>
</tr>
<tr>
<td>- Confirm vancomycin resistance</td>
<td>- Determine percentage of isolates resistant to vancomycin</td>
</tr>
<tr>
<td>- Save isolates</td>
<td>- Examine phenotype and genotype (fingerprints) of VRE isolates</td>
</tr>
<tr>
<td>- Examine phenotype and genotype (fingerprints) of VRE isolates</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>USE AND CONTROL OF ANTIBIOTICS</th>
<th><strong>OUTBREAK MANAGEMENT</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>- Limit vancomycin use to institutional-specific guidelines</td>
<td>- Verify the diagnosis and define the problem (who, what, when, where)</td>
</tr>
<tr>
<td>- Reduce cephalosporin use/alter hospital formulary</td>
<td>- Isolate all patients whether VRE colonized/infected or not</td>
</tr>
<tr>
<td>- Limit perioperative antibiotic use to efficacious drugs, appropriate time periods, agents recommended in prophylaxis guidelines</td>
<td>- Group all patients geographically (this may require a VRE ward)</td>
</tr>
<tr>
<td>- Group nursing staff</td>
<td>- Perform routine surveillance weekly</td>
</tr>
<tr>
<td>- See non-infected before infected patients</td>
<td>- Save/type all isolates</td>
</tr>
<tr>
<td>- Perform routine surveillance weekly</td>
<td>- Perform molecular epidemiology and use epidemiologic studies to determine whether there is a point source outbreak</td>
</tr>
<tr>
<td>- Obtain environmental and hand cultures when appropriate</td>
<td>- Obtain environmental and hand cultures when appropriate</td>
</tr>
</tbody>
</table>

Bacteria Battle Back: Addressing Antibiotic Resistance  13

Table 7
Suggested Drug Therapy for Resistant Organisms

<table>
<thead>
<tr>
<th>INTERVENTION</th>
<th>COMMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Extended Spectrum β-lactamase-Producing Organisms</strong></td>
<td></td>
</tr>
<tr>
<td>(E. coli, K. pneumoniae)</td>
<td></td>
</tr>
<tr>
<td>β-lactam/β-lactamase inhibitor combo</td>
<td></td>
</tr>
<tr>
<td>Aminoglycosides, Fluoroquinolones, Trimethoprim/Sulfamethoxazole</td>
<td>Drug of choice</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Methicillin-Resistant Staphylococcus aureus</strong></td>
<td></td>
</tr>
<tr>
<td>Vancomycin</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Vancomycin-Resistant Enterococcus</strong></td>
<td></td>
</tr>
<tr>
<td>Quinupristin/Dalfopristin</td>
<td>I.V. requires a central venous access</td>
</tr>
<tr>
<td>Linezolid</td>
<td>Can be given as both P.O. and I.V.</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Drug-Resistant Streptococcus pneumoniae</strong></td>
<td></td>
</tr>
<tr>
<td>Extended-spectrum macrolides</td>
<td>Use as outpatient or inpatient agents</td>
</tr>
<tr>
<td>Non-antipseudomonal, third generation Cephalosporin</td>
<td>Ceftriaxone is most commonly used</td>
</tr>
<tr>
<td>Fluoroquinolones targeted for respiratory use</td>
<td>Levofoxacin, gatifloxacin, sparfloxacin, moxifloxacin, trovafloxacin</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>No demonstrated resistance at this point</td>
</tr>
</tbody>
</table>


ample, may not be confronted with the types of resistance present in a large teaching facility.30

Another important consideration is whether the patient is only colonized or has an infection. Is the patient demonstrating signs of an overt infection presenting with fever and increased white blood cells, or is the patient simply colonized without objective signs of infection?31 When considering antibiotic therapy for an infection caused by a known resistant pathogen, the principles for controlling institutional antimicrobial resistance must be kept in mind.32-35 Empiric and/or specific antibiotic therapies for suspected or documented pathogens are illustrated in Table 7.

Factors such as patient disability level and carry-over infection from a prior hospital stay also factor into treatment decisions. Infections contracted nosocomially may need to be treated with different agents than community-acquired infections. In cases where culture and susceptibility reports are not readily available, such as in outlying facilities, practitioners must decide both when to treat and what organisms are the most likely pathogens.

Prescribing antibiotics in long-term care facilities presents unique challenges in part because patients are typically admitted from other institutional settings and could have been exposed to resistant bacteria. The following are suggested guidelines for antibiotic use in long-term care facilities.36

- Maintain an antibiotic review program to monitor use of all systemic and topical antibiotics.
- Develop and enforce antibiotic restriction policies, especially for oral and intravenous vancomycin, third-generation cephalosporins and fluoroquinolones antibiotics.
- Avoid treating asymptomatic bacteriuria; patients must demonstrate clinical or pre-determined laboratory evidence of infection.
- Treatment of patients residing in long-term care facilities should be cared out by health care practitioners who are familiar with the nature of the patient population.
- Use narrow-spectrum antibiotics whenever possible for empiric coverage; when culture susceptibilities have been verified, the antibiotic spectrum should be narrowed if possible. Because institutional settings
can be a breeding ground for resistant bacteria, guidelines for controlling antimicrobial resistance are much more stringent than in the community. In addition to emphasizing effective prescriptions, ways of controlling institutional antimicrobial resistance include:

- introducing limited antibiotic choices to the hospital formulary along with guidelines for rational antibiotic use,
- changing empiric therapy to selected, narrow-spectrum therapy in response to culture and susceptibility results as they become available,
- using antibiotics for the shortest effective duration,
- dosing antibiotics optimally,
- using local susceptibility patterns to aid in appropriate empiric antibiotic selection,
- treating infections in outpatients with oral or home intravenous antibiotics as soon as possible,
- not prescribing antibiotics for viral syndromes,
- correctly interpreting culture and sensitivity results, and
- limiting antimicrobial prophylaxis to accepted indications. Institutions also commonly overuse broad-spectrum, third-generation cephalosporins, vancomycin and clindamycin, which select for VRE. Overusing ceftazidime may select for an ESBL strain of *K. pneumoniae*. Guidelines for using vancomycin suggest that patients needing this therapy should meet one of six treatment criteria (see Table 8). Vancomycin use outside these guidelines can promote drug-resistant enterococcus.

Patients in long-term care facilities with conditions such as persistent cough following a viral illness or asymptomatic bacteriuria are often unnecessarily treated with broad-spectrum antibiotics such as fluoroquinolones. The decision to treat may be based on patient and nursing convenience or an attempt to avoid a hospitalization. Unnecessary therapy gives rise to bacterial selection and subsequent antibiotic resistance that could lead to an institutional epidemic. The following guidelines can help reduce fluoroquinolone resistance when use of this antibiotic class is indicated.

- When using fluoroquinolones, optimize the drug’s natural pharmacokinetic properties to achieve adequate concentration-dependent organism killing.
- Administer adequate dosage/duration for infection type and location.
- Avoid co-administration of chelating medications such as sucralfate or antacids that may bind to and chemically inactivate the fluoroquinolone.
- When treating difficult infections such as *P. aeruginosa*, combine fluoroquinolones with another anti-pseudomonal drug that has an alternate mechanism of action to maximize killing.
- Avoid excessively long (greater than 14 to 28 days) fluoroquinolone treatment in hospitalized patients.
- Avoid using fluoroquinolones for non-serious infections (cystitis in young women and simple upper respiratory tract infections, for example).
- Consider fluoroquinolones in situations where therapeutic failure is imminent (colonizing bacteria in severely ill patients, patients with MRSA infections, ischemic skin ulcer infections, non-correctable structural abnormalities and patients with non-removable foreign bodies). Once practitioners have the appropriate information to effectively prescribe antimicrobials, they must
ensure that all members of their health care team practice not only infection-control procedures but proper and appropriate antibiotic prescribing. To accomplish this, all staff must be kept up to date on local infection-control guidelines that avoid or minimize the spread of resistant organisms. Prescribers should be specifically aware of microbiological susceptibility patterns and available methods for identifying pathogens. It is vital that the correct antibiotic be used in the proper amounts to effectively eradicate bacterial infections such as strep throat. They are useless against viral infections such as the common cold or flu. In fact, if an antibiotic is taken for a viral infection, the risk of developing an infection from an antibiotic-resistant bacteria increases, and if the antibiotic is taken for too long or too short a time, the greater the chance a resistant organism will prevail. Health care providers including physicians, nurses and pharmacists have a key role in educating patients about the importance of antibiotic resistance and careful antibiotic use. All health care providers should discuss with their patients the following ways to catch an antibiotic-resistant infection.43,44

- Simply taking an antibiotic increases the risk because bacteria develop ways to resist the antibiotic’s effects in order to survive. If enough bacteria are present, they can multiply and become problematic. These bacteria can be transmitted to others.
- Infections can be contracted from people or objects around that are infected with or contain resistant bacteria.
- Resistant bacteria are commonly found among people in hospitals, nursing homes and day care centers.
- Improper hand washing increases the risk of catching all types of infections. Bacteria enter the body through the nose, mouth and open wounds; however, the bacteria are often transmitted to those areas from the hands. Hand washing is the most effective way to prevent the spread of any type of infection. Most Americans are untruthful about how often they wash their hands. Typically, hands should be washed prior to food preparation or inserting or removing contact lenses and after treating a cut or wound on someone who is sick. Hands should also be washed after using the bathroom, handling uncooked foods such as raw meat, poultry or fish, changing diapers, nose blowing, sneezing or coughing, playing with or touching a pet (especially reptiles and exotic animals), handling garbage or tending to someone who is sick or injured. Patients should be reminded that antibiotic resistance not only affects the sick, but other family members and people the patient comes in contact with.45
- Prescribers and consumers can help limit the emergence and spread of antibiotic resistant organisms by following hygiene guidelines that have become commonplace in the medical work environment as well as in many homes.
- An integral part of controlling antibiotic resistance is combating the spread of resistant contagions. Several organizations, including the CDC, have published specific resistance prevention tips that can be applied in both health care settings and at home.24,44,45
To help prevent infection and limit antibiotic resistance all health care providers should remind patients to:

• Handle, prepare and store food correctly, wash fruits and vegetables thoroughly; avoid raw eggs and undercooked meat (especially ground beef).
• Avoid using antibacterial soaps except when caring for someone who is ill.
• Wash hands thoroughly using soap and water for 10 to 30 seconds.
• Take all medication as directed for the full course of treatment.
• Discard unused antibiotics. Do not save for later use or to share with others. Do not take antimicrobial drugs for viral infections such as colds, coughs or the flu.
• Ask health care providers about ways to help relieve symptoms for infections not caused by bacteria.
• Not share medications that require a delivery device (nasal inhalers, oral inhalers and eye drops, for example) because they can transmit infection between patients.
• Get immunized and ask their health care provider which immunizations they or their children should receive.

**Conclusion**

Addressing the growing problem of antibiotic resistance requires a global approach. This issue crosses the boundaries between many disciplines. In order to retain the effectiveness of the current antibiotic drug arsenal and stay a step ahead of bacterial adaptation, practitioners must be vigilant about educating themselves, their colleagues and their patients. Practitioners must also be vigilant about their own hygiene practices, whether at home or in clinics or institutions. To reduce transmission of antibiotic resistance it is imperative that practitioners follow strict infection control and hygiene guidelines, such as hand washing between patient visits and isolation of hospitalized patients with multi-drug resistant infections. They must take time to recommend or prescribe the most appropriate antibiotic agent for each situation and do everything in their power to make sure patients understand the implications of not following dosing instructions—for themselves and society at large.
Bacteria Battle Back: Addressing Antibiotic Resistance
1. The mechanism by which genes for antibiotic resistance are spread by bacteriophage is called:
   a) transformation
   b) conjugation
   c) transposition
   d) transduction

2. Porin proteins:
   a) are pumps that remove antibiotics from bacterial cells
   b) are penicillin-binding proteins
   c) allow hydrophobic molecules to enter bacteria
   d) are channels by which water-soluble antibiotics can enter bacteria

3. Resistance to fluoroquinolone antibiotics may be caused by:
   a) mutation of bacterial penicillin-binding proteins
   b) mutation of bacterial ribosomes
   c) mutation of bacterial DNA gyrase
   d) mutation of bacterial DNA polymerase

4. Resistance to this antibiotic may occur when bacteria develop alternate metabolic pathways.
   a) vancomycin
   b) trimethoprim
   c) imipenem
   d) chloramphenicol

5. Antibiotics are currently used in which of the following?
   a) livestock feed
   b) farm animals
   c) farm-raised fish
   d) all of the above

6. According to the American Medical Association there is no scientific data proving that antimicrobial soaps have any infection-fighting benefit over standard soap and water.
   a) true
   b) false

7. Which of the following factors may contribute to the development of antibiotic resistance in developing countries?
   a) unregulated antibiotic use
   b) poor drug quality
   c) unskilled health practitioners
   d) all of the above

8. Transposons are:
   a) small viruses that infect bacteria
   b) self-replicating, circular strands of bacterial RNA
   c) also called “jumping genes”
   d) not associated with antibiotic resistance

9. According to the Centers for Disease Control, ______ percent of all yearly prescriptions for antibiotics may be unnecessary.
   a) 10
   b) 15
   c) 25
   d) 33

10. The Centers for Disease Control recommendations for preventing the spread of antibiotic resistance include all of the following except:
    a) proper immunizations
    b) counseling patients to take antibiotics exactly as prescribed
    c) not using antibiotics for viral infections
    d) counseling patients to take antibiotics until they feel better

11. Which of the following global objectives does the Centers for Disease Control plan to develop in the future?
    a) implement a national plan for resistance surveillance; ensure reliability of susceptibility data for surveillance; monitor patterns of antibiotic use
    b) survey antibiotic resistance and encourage applied microbiological and product development research as well as resistance prevention and control
    c) increase understanding of microbial physiology, ecology and mechanisms of resistance; augment existing research infrastructure; translate research findings into clinically useful products
    d) extend useful life of antimicrobial drugs; improve diagnostic testing practices; improve infection control methods and vaccine use

12. All of the following are considered antibiotic resistance control tips except:
    a) take medicine exactly as prescribed by health care provider
    b) take the antibiotic until it is finished, even if you feel better
    c) use antibacterial soaps when washing hands
    d) do not pressure your health care provider into prescribing antibiotics
13. Which of the following statements best characterizes the economics of antibiotic use?
   a) developing resistance patterns in the community allow for cheaper, more common antibiotic use
   b) antibiotics comprise between 50 and 70 percent of a hospital pharmacy’s drug budget
   c) antibiotic failures in the hospital lead to rapid discharges back to the community in an effort to evade resistance
   d) antibiotic cost escalations prevail when newer, more expensive agents or intravenous therapy is warranted to treat infections

14. Education is the key to overcoming antibiotic resistance. All of the following principles are important to overcome resistance except:
   a) antibiotics should routinely be prescribed post viral illness to ward off bacterial infection
   b) antibiotics should be used appropriately with the correct indication, dose, and identification and adherence to definitive monitoring parameters
   c) antibiotics can be cycled to avoid resistance
   d) practitioners should adhere to infection control guidelines

15. Under which circumstances should vancomycin be used?
   a) when there is a low prevalence of methicillin-resistant Staphylococcus aureus (MRSA)
   b) this drug is always a good first choice
   c) when there is no b-lactam allergy
   d) when infections are caused by gram-positive cocci resistant to b-lactam antibiotics

16. A three-year-old child in the community has received a course of amoxicillin for an otitis media infection. The child attends a child-care program full time. The course of amoxicillin fails. The child returns to the practitioner’s office four days after starting the amoxicillin continuing to be febrile and tugging at the ears. Which of the following would be the most reasonable antibiotic selection for home therapy for this child from the selections provided?
   a) tetracycline
   b) extended-spectrum macrolide
   c) fluoroquinolone
   d) vancomycin

17. Fluoroquinolones are powerful antibiotics that retain a broad spectrum of activity and are useful agents in treating a wide array of both inpatient and outpatient infections. Fluoroquinolone resistance is problematic in that the organism that is resistant to one fluoroquinolone will be resistant to all agents in the fluoroquinolone class. All of the steps listed below are aimed at reducing fluoroquinolone resistance except:
   a) fluoroquinolones should be used as first line therapy in treating many infections
   b) the natural pharmacokinetic properties of the fluoroquinolones should be maximized for adequate concentration-dependant killing
   c) avoid therapy that lasts longer than 14 to 28 days
   d) avoid prescribing for simple upper respiratory tract infections and uncomplicated cystitis in young women

18. Which of the following are antibiotic control measures that should be followed in long-term care facilities?
   a) develop and enforce antibiotic restriction policies especially with oral and intravenous vancomycin, third-generation cephalosporins and fluoroquinolone antibiotics
   b) avoid treating asymptomatic bacteriuria, require patients to demonstrate clinical or predetermined laboratory evidence of infection
   c) narrow-spectrum antibiotics should be used whenever possible for empiric coverage
   d) all of the above control measures should be followed

19. In the era of antibiotic resistance and the publicity of the problem, “catching” a resistant organism is concerning. All of the following are ways to contract a resistant organism except:
   a) simply taking an antibiotic because this allows some bacteria to fight off the effect of the antibiotic in order to survive
   b) having contact with people who are in hospitals, nursing homes or day care centers
   c) improper hand washing
   d) catching a cold

20. The basic principles for controlling the spread of MRSA include:
   a) notify clinicians and infection-control staff when an MRSA isolate is identified
   b) increase use of antimicrobial agents
   c) maintain a list of patients known to be colonized or infected with MRSA
   d) a and c only
CE Registration, Answer Sheet and Program Evaluation

This lesson affords 2 (two) contact hours (0.2CEU) of continuing education credit in all states that recognize the American Council on Pharmaceutical Education (ACPE) approved providers.

The Massachusetts College of Pharmacy and Health Sciences and/or the American Academy of Nurse Practitioners will grant 2 contact hours to pharmacists and/or nurse practitioners who obtain a grade of 70% or higher on the post test. Those not successfully completing the post test on the first try will receive notice and be offered another chance to answer the post-test at an additional charge of $6.

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Initial release date November, 2000. ACPE# 026-999-00-206-H01

Answer each question by circling the correct answer in the space provided

Bacteria Battle Back: Addressing Antibiotic Resistance – ACPE # 026-999-00-206-H01

Name_________________________________________________________________________________________
Address____________________________________________________________________________________
City____________________________________________ State_____________ Zip Code_________________
State and Pharmacy/Nursing License Number__________________________________________________

Please indicate your exam response by circling only ONE answer for each.


Program Evaluation:

1. The topic was relevant to my practice. Agree Disagree 1  2  3  4  5
2. The learning objectives were met. 1  2  3  4  5
3. The test questions corresponded well to the lesson. 1  2  3  4  5
4. The faculty is knowledgeable in the area. 1  2  3  4  5
5. The program was educational and not promotional. 1  2  3  4  5
6. How long did it take you to complete this program? _____________ hours

20  Bacteria Battle Back: Addressing Antibiotic Resistance · November 2000