

# APA Policy on Clinical and Environmental Factors Contributing to Antibiotic-Resistant Bacteria

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The emergence, growth, and spread of bacteria with increasing resistance to antibiotics represents a significant health risk to children, particularly those children at greatest risk of serious infectious diseases (pre-mature infants, hospitalized children, children who are dependent on immunosuppressive medications, and those with compromised immune systems). Although antibiotics can provide life-saving benefits in the case of bacterial disease, the overuse of antibiotics contributes to the development and spread of resistant organisms as well as the transfer of resistant genes among pathogenic and non-pathogenic organisms. Two examples of such overuse include the use of antibiotics to treat children with nonbacterial infections and treating healthy livestock with antibiotics that are identical to or closely related to antibiotics used in human medicine.

Prestigious medical and public health authorities, such as the Centers for Disease Control and Prevention, the Institute of Medicine, the Food and Drug Administration, the World Health Organization, and the American Public Health Association, have cited bacterial resistance as an increasingly serious and costly medical and public health threat in need of much greater attention and action, including more education, research, and regulation. It is becoming increasingly more evident that the spread of bacterial resistance arises not only from overuse in human medicine but also from overuse in animal agriculture and that resistance developed in animals is spreading to human pathogens. Consistent with these positions, the Ambulatory Pediatric Association (APA; its board, standing committees, and pertinent special interest groups) proposes to raise awareness among pediatricians, families, public health programs, and policy-makers of the environmental factors contributing to antibiotic-resistant bacteria as well as to develop strategies to reduce or eliminate the further growth and serious sequelae of antibiotic-resistant bacteria. These strategies should include the following:

- Health care providers should discourage the overuse of antibiotics in children and adolescents and encourage the prudent, responsible, and sustainable use of antibiotics.

- Families should be informed of the public health risks of the practice of using antibiotics that are identical to or closely related to those used in human medicine in order to treat or promote the growth of healthy livestock so that families may make informed decisions when purchasing meat products.
- Pediatric education of medical students, residents, and fellows, and ongoing continuing medical education of health professionals who care for children should include information on the clinical and public health risks of inappropriate antibiotic use.
- Pediatric health services research should prioritize the evaluation of effective strategies to monitor and improve clinician antibiotic prescribing behavior with regard to appropriate use of antibiotics in infants, children, and adolescents. In addition, this should include the clinical impact and health care costs associated with the agricultural use of antibiotics as growth promoters in livestock production.
- The APA should be active in coalitions advocating for responsible and sustainable clinical and agricultural use of antibiotics in humans and in livestock.

## STATEMENT OF THE PROBLEM

### 1. The Development and Spread of Antibiotic-Resistant Organisms Represents a Significant Health Risk to Children and Adolescents

Antibiotics represent an important scientific advance of the 20th century and a valuable resource in combating serious infectious diseases among infants, children, and adolescents. Factors that limit the effectiveness of antibiotics, such as those that promote bacterial resistance to antibiotics, jeopardize current and future pediatric care. Resistance of *Escherichia coli* to penicillin was first described in 1940, and the transfer of genetic material coding for resistance was described in 1952. It is now known that pathogenic bacteria such as *E coli* can transfer DNA from other bacteria, including genes coding for antibiotic resistance. These transfers can occur in livestock and in the human gastrointestinal tract. Bacteria can also transfer DNA coding for virulent toxins such as *Shiga* toxins.<sup>1</sup>

The rate of penicillin resistance increased by more than 300% and cefotaxime resistance increased by more than 1000% over a recent 5-year period.<sup>2</sup> Erythromycin resistance has increased from 1% in 1992 to 44% of *Strep*

*pneumoniae*; resistance to trimethoprim-sulfamethoxazole has increased to 48% and resistance to penicillin has increased from 6% in 1992 to 42% in 2000 at the Children's Hospital in Columbus, Ohio. Antimicrobial resistance is also a substantial problem in treating *Staphylococcal*, *E. coli*, *Salmonella*, *Campylobacter*, *Pseudomonas*, and other bacterial infections.

The emergence of methicillin-resistant *Staphylococcal aureus* (MRSA) infections in hospitals in the US has been a major public health concern. Soon after methicillin resistance was established, clinicians turned to other antibiotics, such as ciprofloxacin; however, within a few years, 85% of isolates were also resistant to ciprofloxacin.<sup>3</sup> Infections with MRSA have occurred even in children without identifiable predisposing risk factors,<sup>4</sup> and pediatric deaths have been attributed to community-acquired methicillin-resistant bacteria.<sup>5</sup> According to the US Centers for Disease Control and Prevention (CDC), between 1990 and 1997, MRSA rates increased 260% in hospitals participating in international monitoring programs. ([http://www.cdc.gov/ncidod/focus/vol9no3/s\\_aureus.htm](http://www.cdc.gov/ncidod/focus/vol9no3/s_aureus.htm)).

The number of bacteria resistant to multiple antibiotics is also increasing, posing a serious threat to hospitalized children. For example, the prevalence of resistance to 5 antibiotics among certain strains of *Salmonella* has increased from 0.6% in 1979 to 34% in 1996.<sup>6</sup> The prevalence of drug-resistant *Streptococcal pneumonia* is also increasing and appears to be directly linked with widespread use of antibiotics.<sup>7-9</sup>

## 2. The Inappropriate Uses of Antibiotics in Both Human Medicine and Livestock Production Contribute to the Development and Spread of Antibiotic Resistance

The US CDC<sup>10</sup> recommends against prescribing antibiotics for children with many common conditions, including otitis media with effusion lasting less than 3 months<sup>11</sup>; nonstrep, nongonococcal pharyngitis<sup>12</sup>; nonspecific upper respiratory tract infection; or the common cold,<sup>13,14</sup> cough, or bronchitis.<sup>15</sup> Inappropriate use of antibiotics remains common, both because of families' expectations and demands for antibiotics and because of physician practices.<sup>16-20</sup> In a survey of 531 pediatric office visits, antibiotics were prescribed for 44% of visits for a cold, 46% of nonspecific upper respiratory infections, and 75% of visits for bronchitis.<sup>21</sup> The available evidence suggests that the more antibiotics are used, the greater the selective pressure to develop antibiotic resistance and the faster resistance emerges. Further, there is evidence that this widespread, clinically unnecessary use of antibiotics has contributed to an increase and spread of resistant organisms. Yet it is evident that reductions in antibiotic use can lower the prevalence of antibiotic-resistant organisms, as has been demonstrated among children in day care centers.<sup>22,23</sup>

Agricultural use of antibiotics is also a factor in the spread of resistant bacteria that causes human disease. Livestock consume a substantial proportion of the antibiotics used in the United States. Many of these antibiotics

are identical to or closely related to antibiotics used to treat human disease. Approximately 40%–70% of all antibiotics used in the United States are given to apparently healthy animals to enhance growth and prevent infections; this accounts for approximately 75%–90% of all animal use of antibiotics.<sup>24</sup> When used to promote growth (rather than to treat specific diseases), antibiotics are given to large numbers of animals at subtherapeutic doses (eg, 10–100 ppm per kg of feed). These are the perfect theoretic conditions to promote antibiotic resistance. Antibiotic use in animals selects for antibiotic-resistant nontyphoid *Salmonella* serotypes, which can be transferred to humans. Up to 80% of antibiotics fed to animals will be discharged into liquid or solid animal waste and may contaminate nearby soil and groundwater.<sup>25</sup> These are the optimal theoretic conditions to promote antibiotic resistance in humans, and there is evidence to indicate that this does occur.

Subtherapeutic use of antibiotics in cattle has been linked to outbreaks of antibiotic-resistant *Salmonella* infections in people who ate hamburger, including resistance to ceftriaxone.<sup>26,27</sup> With the advent of the use of fluoroquinolones, which were given prophylactically to healthy chickens and turkeys starting in 1996, the prevalence of fluoroquinolone resistance appeared in *Campylobacter* in chickens (reaching 18% by 1999). The Food and Drug Administration (FDA) has recently proposed barring the use of quinolone antibiotics in poultry-raising operations because of the rapid emergence of quinolone-resistant bacteria in flocks treated with these antibiotics.<sup>28</sup>

Based on this information, the National Antimicrobial Resistance Monitoring System of the US CDC reports that antimicrobial-resistant *Salmonella* result from the use of antimicrobial agents in food animals, and these antimicrobial-resistant *Salmonella* are subsequently transmitted to humans through the food supply. Further, it urges non-antimicrobial infection control strategies in animals and the establishment of public health safeguards to minimize the development and dissemination of antimicrobial resistance.<sup>29</sup> See the Internet site maintained by the CDC's International Network for the Study and Prevention of Emerging Antimicrobial Resistance: <http://www.cdc.gov/ncidod/hip/SURVEILL/inspear.HTM>.

### CURRENT POLICY AND ADVOCACY ACTIVITIES TO REDUCE DISEASE DUE TO RESISTANT BACTERIA

Many groups have begun to develop information, policies, and advocacy campaigns to address the overuse of antibiotics both in human medicine and among livestock. The California Medical Association has recognized that "the spread of bacterial resistance arises not only from overuse in human medicine, but also from massive use in animal agriculture, with increasing evidence that resistance developed in animals is spreading to human pathogens." The World Health Organization has recommended banning use of medically important antibiotics as growth promoters for livestock.<sup>30</sup> The European Union has banned the use of antibiotics

for growth promotion in livestock.<sup>31</sup> In 1999, the Center for Science in the Public Interest, Environmental Defense Fund, and Union of Concerned Scientists petitioned the US FDA to rescind approvals for subtherapeutic uses in livestock of any antibiotic identical to or closely related to those used in human medicine—including penicillin, tetracyclines, and erythromycin. The National Academy of Sciences National Research Council reports that agricultural uses of antibiotics pose a risk to human health.<sup>32</sup> An American interagency Task Force on Antimicrobial Resistance was created in 1999. The task force is co-chaired by the CDC, the FDA, and the National Institutes of Health. Participants also include the Agency for Healthcare Research and Quality, the Health Care Financing Administration, the Health Resources and Services Administration, the Department of Agriculture, the Department of Defense, the Department of Veterans Affairs, and the Environmental Protection Agency. These groups are consistent in their recommendations to evaluate, communicate, and advocate with regard to the need to reduce the increasing prevalence of resistance through the clinically and agriculturally appropriate use of antibiotics (eg, <http://www.cdc.gov/drugresistance/index.htm>. See also <http://www.cdc.gov/ncidod/dbmd/antibioticresistance/default.htm>).

### CONCLUSION

The inappropriate use of antibiotics in clinical medicine and in raising livestock contributes to the development and spread of antibiotic-resistant organisms. These organisms represent a serious threat to children and adolescents. The APA proposes to raise awareness among pediatricians, families, public health programs, and policy-makers regarding the problem of environmental factors contributing to antibiotic resistance and to develop strategies to reduce or eliminate the further growth and serious sequelae of antibiotic-resistant bacteria. It proposes to do this via the work of its board, standing committees, and pertinent special interest groups.

### RECOMMENDATIONS

The APA will support and encourage quality health services programs that

- Discourage the overuse of antibiotics in children and adolescents and encourage the prudent, responsible, and sustainable use of antibiotics.
- Inform families about the public health risks of the practice of using antibiotics that are identical to or closely related to those used in human medicine to treat animals.
- Inform families regarding the public health risks of using any kind of antibiotics to promote the growth of healthy livestock.
- Provide information to families regarding the selection of meat products from livestock raised without the use of antibiotics.

The APA will encourage and support the development

of curricular materials to be used by medical students, residents, and fellows, as well as the ongoing continuing medical education of health professionals who care for children so that such professionals are aware of the practices, costs, risks, and reduction methods associated with

- the overuse of antibiotics for infants, children, and adolescents;
- the use of antibiotics that are identical to or closely related to those used in human medicine to treat illnesses in livestock; and
- the use of antibiotics as growth promoters in otherwise healthy livestock.

The APA will support and encourage pediatric research focused on the following:

- effective strategies to monitor and improve clinician behavior with regard to appropriate use of antibiotics in children;
- assessing and monitoring the clinical impact and health care associated with using antibiotics in livestock;
- the public health and environmental effects of antibiotic use in livestock production; and
- the impact of changing clinical and animal husbandry practices on antibiotic resistance.

The APA will participate and collaborate with other health and environmentally focused groups advocating for responsible and sustainable use of antibiotics in humans and in livestock. These groups will include (but are not limited to) the following:

- the American College of Preventive Medicine,
- the American Medical Association,
- the American Public Health Association,
- the American Society for Microbiology,
- the Canadian Association of Physicians for the Environment,
- the Center for Science in the Public Interest,
- the Environmental Defense Fund,
- the Institute for Agricultural and Trade Policy,
- the Tufts University–affiliated Alliance for the Prudent Use of Antibiotics,
- the Union of Concerned Scientists, and
- the World Health Organization.

The APA will publish articles and news about this issue in APA publications.

### IMPLEMENTATION

The Ambulatory Pediatric Association will undertake these efforts through the utilization of the Board and its relevant standing committees and special interest groups over the next 3 years, at which time this policy statement shall be reviewed and amended as necessary.

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