Antibiotic Use and Resistance: What Lies Beneath!

Teresa M. Barbosa and Stuart B. Levy, Center for Adaptation Genetics and Drug Resistance, Tufts University School of Medicine, Boston, Massachusetts, 02111 USA

The emergence of resistance
It is irrefutable that antibiotic use promotes resistance development. However some difficulties arise when trying to quantify the specific contribution of antibiotic use to resistance, as it is now evident that social, economic and genetic factors also impact the establishment, maintenance and spread of resistance traits (Fig. 1). An example of this is the spread of multidrug resistant *M. tuberculosis* and penicillin-resistant *Streptococcus pneumoniae* across borders and continents as a result of people traveling. Furthermore, studies that attempt to relate use with resistance frequently apply to large areas as opposed to smaller environments that more closely mirror the antibiotic-bacteria interaction.

It is not only the amount of antibiotics used which selects for resistance, but also the duration and dosage used. For instance, low-doses over long periods of time were more selective for the carriage of penicillin-resistant *Streptococcus pneumoniae* than high doses over short periods.

Two hypotheses have been proposed to explain the selection and development of resistance. Both hypotheses suggest the existence of antibiotic thresholds below which selection for antibiotic-resistant bacteria will not occur and antibiotic resistance will remain at low, if not undetectable, levels. The first of the two hypotheses is based on the specific relationship between drug and microorganism, while the second hypothesis embraces the problem on a larger, ecological scale, namely the relationship between the drug, bacteria and the environment. As more drug is used in a particular environment, there are fewer susceptible bacteria remaining to compete with the resistant organisms. Population genetics methods have been employed in studies of the evolution of the frequency of resistance with the amount of antibiotic used in 1) *M. catarrhalis* resistance to β-lactams in Finland and 2) penicillin-resistant pneumococci in Iceland.

The misuse of antibiotics is reflected in the rise of bacteria resistant to more than one antibiotic; multidrug-resistance is found in virtually all commensal (indigenous) and disease-causing bacteria. Moreover the misuse of antibiotics, especially those with broad-spectrum activity, potentiate the emergence of new pathogens, such as multidrug resistant *Acinetobacter sp.*, which are increasingly involved in outbreaks of hospital-acquired infections.

Antibiotics have also been extensively used for disease prevention and growth promotion in animal, plant and fish farming. While the European Union has banned the use of antibiotics for growth promotion if those antibiotics are employed for human health or promote cross-resistance to these, many are still being used in other countries. The misuse of antibiotics is also reflected in the rise of bacteria resistant to more than one antibiotic; multidrug-resistance is found in virtually all commensal (indigenous) and disease-causing bacteria. Moreover the misuse of antibiotics, especially those with broad-spectrum activity, potentiate the emergence of new pathogens, such as multidrug resistant *Acinetobacter sp.*, which are increasingly involved in outbreaks of hospital-acquired infections.

**Photobactericides — “Lightening” the Antibiotic Load**

Mark Wainwright, Medicinal Chemistry, University of Central Lancashire, Preston, PR1 2HE UK

**Summary**
Widespread drug-resistant bacterial infections in our hospitals lead to a high demand for new drugs and alternative therapies. A combination of photosensitizing drugs and low-power light is one such alternative antimicrobial therapy. Photosensitizers are effective against a range of microbes – bacteria, viruses, yeasts and protozoa. The current emphasis is to use antibacterial and antiviral photosensitizing agents to combat the threat of infection in our hospitals and blood supply respectively. As the mode of action of the photosensitizing drugs is fairly nonspecific with respect to sites of action in microbial cells, photosensitizers may circumvent the evolution of antibiotic resistance mechanisms. Thus, photobactericidal drugs are an option in combating drug-resistant infections and may also save conventional antibiotics for more serious systemic disease.

**Introduction**
The widespread occurrence of antibiotic-resistant bacteria in our hospitals today has resulted from the over- and misuse of drugs in the clinical and agricultural milieu. As we understand that the de-
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used in therapy or prophylaxis (e.g., fluoroquinolones). In the USA, antibiotics that are important for human health, such as tetracyclines and penicillins, are still used as feed additives for animals6. There is cumulative evidence that this practice has a strong impact on the development of resistance, not only in animal and plant bacteria, but also in bacteria associated with people7.

Many studies report the transfer of resistant bacteria, for example, Salmonella and Campylobacter, from animals to humans and the important role played by the food chain on the spread of resistance determinants and resistant bacteria. Importantly, the use of large quantities of antibiotics at sub-therapeutic doses as feed additives creates special conditions for the development of a large pool of resistant bacteria. These include the obligate anaerobes, which predominate the gut microflora and therefore can play an important role as reservoirs of resistance. Evidence has been found for recent horizontal transfer of resistance genes among these bacteria from animal and human hosts8,9, but little is known about the extent of the impact of antibiotic use in the commensal microflora.

Bacterial evolutionary perspective

The complexity and number of different mechanisms of bacterial resistance reflect the genetic and ecological flexibility with which bacteria deal with antibiotics. Bacteria not only develop resistance mechanisms to individual antibiotics, for example by acquiring exogenous DNA or chromosomal mutations, but they evolve means of associating, accumulating and rearranging resistance determinants and mechanisms in the same genetic unit and/or bacterial cell. Additionally they develop ingenious ways of sharing those defenses with their phylogenetic relatives and “unrelated family” via different transfer mechanisms10. Bacteria use these genetic tools to avoid the inhibitory effects of antibiotics.

Fate of antibiotic residues

An important aspect of antibiotic use, which is largely disregarded, relates to the fate of antibiotic residues leftover or excreted into the environment following treatment. Bacterial defensive mechanisms towards many classes of antibiotics do not involve structural inactivation of the drugs, e.g. tetracyclines and macrolides. What happens to the tons of tetracycline, which are yearly fed to animals as growth promoters, sprayed over trees or prescribed to patients? A study has shown that tetracyclines in human or rodent feces are quite stable at room temperature11. Therefore one can speculate that antibiotics such as tetracyclines will accumulate in nature and continue their selective effect even after treatment6. More importantly, once in the environment, they will be diluted in soil or water to sub-therapeutic concentrations that are known to encourage the selection and transfer of resistance. Regrettably, little or no data exist on the impact of antibiotic residues on the microflora in different ecosystems.

Reversal and stability of resistance

Can we reverse the resistance phenomenon? It is now clear that removal of an antibiotic from general consumption will not necessarily result in a decline of resistant strains and the return of susceptible strains. Epidemiological data show a high-level of resistance among the commensal bacteria in healthy individuals and in the environment8,12. These observations could be explained by the accumulation of antibiotics in the environment or by contamination of food products.

Bacteria evolved different ways of stabilizing the resistance traits. Bacteria accumulate and link resistance genes within the same genetic units so that resistance to a specific antibiotic can be...
maintained by a variety of different compounds, in a co-selection process. Related antibiotics can cause cross-resistance, such as virginiamycin for quinupristin/dalfopristin. Via these mechanisms, resistance to a given antibiotic develops or persists even in the absence of that antibiotic. Many pumps, such as AcrAB in E. coli\textsuperscript{13}, can export structurally unrelated substrates, which means that their stabil-

Despite this dark scenario, several successful attempts to control antibiotic resistance have been described in hospitals, communities and in animal farming upon introduction of antibiotic control measures\textsuperscript{4}. For example, after the European ban of the growth promoter avoparcin, which selects for cross-resistance to vancomycin, a significant decrease in vancomycin-resistant enterococci in animals, food products and people was observed\textsuperscript{20}. In Finland, increased erythromycin resistance among group A streptococci was successfully reversed by considerably reducing erythromycin consumption.\textsuperscript{21} However, from these same studies it is evident that the replacement of resistant bacteria by susceptible strains takes much longer than for the establishment of resistance. The susceptible levels do not routinely revert to original values.\textsuperscript{2}

A main lesson from the last six decades of antibiotic use is that bacterial resistance is evolutionary. Better understanding of the problem can be achieved by well designed surveillance programs and epidemiological studies which define the molecular and genetic mechanisms behind antibiotic resistance. This knowledge can be used to develop new drugs and effective alternative clinical approaches to treat bacterial disease. More importantly, we need to institute strategies to encourage and maintain a return of susceptible strains to our environment.

References

Continuing Education
To support healthcare providers in appropriate antibiotic use, APUA produced three continuing education programs for healthcare providers:
• A CME-accredited journal article, “Antimicrobial Resistance: A Plan of Action” by Drs. Thomas M. Hooton and Stuart B. Levy, aims to make community physicians aware of the role they play in reducing antibiotic resistance. The CME article, published in the March 15, 2001 American Family Physician, summarizes the proceedings of an APUA-coordinated meeting that discussed the scope of the problem, reviewed current protocols for treating respiratory tract infections, acute otitis media, and uncomplicated urinary tract infections, recommended improved prescribing practices, and discussed key steps for clinicians to preserve the power of antibiotics.
• A CEU program “Bacteria Battle Back: Addressing Antibiotic Resistance” reviews the organisms that have become significant management problems, treatment guidelines, diagnostic uncertainty, and pharmacists’ involvement in the medical team. To obtain the CEU home-study program, see http://ce@mcp.edu/ac/ce/antibiot.pdf.
PHOTOBACTERICIDES continued from page 1

degree of exposure of bacteria to antibiotics correlates with the amount of resistance encountered, we should also understand the need for conservative use of effective, conventional chemotherapeutics. However, the question “Where do we go from here?” remains. An embattled pharmaceutical industry will undoubtedly continue — heroically — to supply new variations on old drugs. However, only agents with novel modes of action can make significant inroads against the “superbugs.”

Microorganisms manifest a much shorter evolutionary timescale than our own, as shown by their ability to develop resistance rapidly to drugs that attack a specific site. Thus any new class of antibacterial agents with only one site of action has a limited useful lifetime. However, suppose agents could be developed having multiple or even random sites of action? Such agents would be active where conventional drugs are not, and would also make the development of resistance much more difficult.

Photosensitizing drugs—photo-bactericides and photovirucides—are indeed such agents.

How do photosensitizers work?
As the term suggests, photosensitizers are chemicals that absorb light energy (“photo”) and transmit it to their environment either by direct energy transfer or chemical reaction (“sensitizers”). The illumination of photosensitizers in an oxygen-containing environment causes the production of reactive oxygen species (ROS).

ROS are lethal antimicrobials, meaning that they kill their targets rather than just inhibit them. The high reactivity of an ROS, such as singlet oxygen, ensures rapid oxidation of, and damage to, nearby molecules. Once bound to a cell, illumination of the photosensitizer causes the production of ROS within the cell, which can damage the cell wall, nucleic acids, and enzymes, leading to cell death (Table 1).

Although some photosensitizers attach at specific parts of pathogenic organisms, the damage caused on illumination is more widespread, reflecting the generation of ROS. For example, the photosensitizer methylene blue damages many vital areas of the AIDS virus, such as its nucleic acids, viral envelope, and enzymes, including reverse transcriptase.

Several photosensitizers are selective for bacteria and therefore can be used to destroy bacterial cells.

History of photosensitizers
It is not widely appreciated that the demonstration of photoantimicrobial action predates the discovery of antibiotics by decades. Oskar Raab showed that the coal tar dye acridine was phototoxic to paramecia as early as 1900, while the photoviralcidal activity of methylene blue was reported in 1928 and its photobacterialid action in 1935. However, the promise of effective antibiotics, pioneered by Fleming and then Domagk in the late 1920s and 1930s, probably reduced interest in pursuing photosensitizing antimicrobials. Since bacteria resistant to both β-lactams and sulfonamides are now widespread, it is perhaps fitting that such organisms are susceptible to the photodynamic effect.

ROS have been employed over many years in commercial oxidation reactors by the chemical industry. Photosensitizers are available in a variety of structures including the phenothiazine dyes (e.g. methylene blue, dimethyl methylene blue, Figure 1), phthalocyanines and porphyrins (e.g. ZnTSPc and Ce₆ respectively, Figure 1).

Disinfecting with photosensitizers
Topical, or surface, disinfection of the body is an important area that is amenable to photosensitizing drugs. While this may not seem to offer a

Table 1. Cytotoxicity (cell death) in microbial cells due to photosensitization

<table>
<thead>
<tr>
<th>Site of Action</th>
<th>Action</th>
<th>Result</th>
<th>Consequence</th>
<th>Cytotoxic Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nucleic acid residues</td>
<td>Oxidation of base or sugar</td>
<td>8-Hydroxyguanosine</td>
<td>Nucleotide degradation</td>
<td>Base substitution, Strand cleavage, Mutation, Inhibition of replication</td>
</tr>
<tr>
<td>Cytoplasmic enzymes</td>
<td>Oxidation, Hydrogen abstraction</td>
<td>Oxidation or cross-linking</td>
<td>Sugar degradation / cleavage</td>
<td>Inhibition of ribosome assembly, Inhibition of replication / infectivity</td>
</tr>
<tr>
<td>Respiratory chain</td>
<td>Redox reactions</td>
<td>Electron transfer affected</td>
<td></td>
<td>Inhibition of respiration</td>
</tr>
<tr>
<td>Viral protein coat</td>
<td>Oxidation of Try/His/His residues</td>
<td>Protein degradation</td>
<td></td>
<td>Loss of viral infectivity</td>
</tr>
<tr>
<td>Cell wall</td>
<td>Peroxidation of unsaturated lipids / steroids</td>
<td>Peroxidation</td>
<td>Hydroperoxide formation / oxidative damage</td>
<td>Increased ion permeability (Na⁺ / K⁺ leakage)</td>
</tr>
<tr>
<td>Peptide</td>
<td>Hydrogen abstraction</td>
<td>Peptide cross-linking</td>
<td>Enzyme inactivation</td>
<td>Loss of repair facility, lysis</td>
</tr>
<tr>
<td>Cytosol</td>
<td>Hydrogen abstraction from water</td>
<td>Hydroxyl radical (HO⁻)</td>
<td>Hydrogen peroxide, superoxide (O₂⁻)</td>
<td>Oxidation of environment</td>
</tr>
</tbody>
</table>

Figure 1. Chemical structures of photosensitizers

- Methylene Blue (MB)
- Dimethyl Methylene Blue (DMMB)
- Zinc Phthalocyaninetrutetrasulfonic acid (ZnTSPc)
- Chlorin ε₆ (Ce₆)
great advantage in the fight against hospital superbugs, if the transmission of infection between patients via hospital staff were halted, infection rates would logically fall dramatically also. Topical disinfection could be used both to clean infected wounds and to inhibit the spread of infection by otherwise healthy staff and visitors. This is particularly important as current topical disinfectants are showing decreased efficacies against a range of common pathogens.\(^4\) In addition, patient compliance can be a problem with current disinfection techniques, for example, the use of mupirocin to disinfect the nostrils is an unattractive proposition for the patient. Therefore, the rapid, one treatment disinfection offered by photobactericides is a desirable goal.

Although the logical limit of photodynamic action lies in light delivery, this leaves considerable clinical scope. As well as the topical disinfection mentioned above, light can be delivered to many interior regions of the body via endoscopes. This means that infections of the digestive and respiratory tracts are potentially treatable with photosensitizers. Colonization of the stomach by *Helicobacter pylori* is associated with gastric ulcers and even stomach cancer. The normal management of these diseases, using a combination of antimicrobials and an anti-ulcer drug, is costly and long-term. However, *H. pylori* can be eradicated from gastric mucosa using a single treatment with the photosensitizer toluidine blue O.\(^5\) Thus, the photodynamic approach can not only kill drug-resistant microorganisms, it also allows effective systemic drugs to be kept for serious diseases such as septicaemia.

**Current Situation**

At present, several groups have demonstrated the efficacy of photosensitizers against microbial species, but the main developments of the technique are aimed at the treatment of bacterial disease and viral contamination of blood products.

Both methylene blue derivatives and phthalocyanines have been shown to be effective against currently important drug-resistant bacteria, such as epidemic methicillin-resistant *Staphylococcus aureus* (EMRSA, Figure 2) and vancomycin-resistant strains.\(^6,7\) Photosensitizing drugs are currently under development based on the phenothiazine and phthalocyanine structures (Figure 1). In addition, encouraging results are being obtained from targeting bioconjugates (photosensitizers attached to biomolecules such as antibodies that bind specifically to bacteria).\(^8\)

Light sources for use with photosensitizers vary from simple white light lamps to expensive lasers, although only low-power light is required—milliwatts rather than the megawatts used in ablative surgery. Clinically, the delivery of requisite light may demand an endoscope, but the important factor is the ability to excite the chosen photosensitizer at its site of action with the correct wavelength.

Although photosensitizers have been shown to kill microorganisms without killing human tissue,\(^9\) more work remains to make photosensitizers a standard treatment of bacterial disease. Clinical trials and studies addressing industrial interests have been scarce thus far. Research into the disinfection of the blood supply has been supported by millions of dollars due to the commercial value of blood products. Hopefully, the problem of drug-resistant bacterial disease does not become much more serious before significant investment is made here also.

**References**

3. T'ung T. 1935. ibid. 33: 328-330

**Letter to the Editor**

To the editor:

The FRAT formula\(^1\) compared activity for various antimicrobial agents against community acquired pneumonia by comparing etiology and antimicrobial susceptibility data. Recent changes of the NCCLS breakpoints for amoxicillin against *S. pneumoniae* result in a higher percentage of isolates being deemed susceptible to this compound. Recalculation with the FRAT formula would, therefore, result in a higher level of activity of amoxicillin in CAP than initially reported. Similarly, any changes to breakpoints for other compounds may also affect FRAT calculations. It is important to re-emphasize that the appropriate utilization of the FRAT formula involves use of the most up-to-date data on etiology and local antimicrobial susceptibility data.


Joseph Blondeau
University of Saskatchewan
Canada
Editorial: *Antibiotics, Animals, and People—Again!*

Stanley Falkow, Microbiology & Immunology, Stanford, former president of ASM and Donald Kennedy, Editor-in-Chief of Science, former Commissioner of FDA

In 1996, the FDA approved the use of fluoroquinolones in chickens and turkeys, primarily to prevent mortality associated with *Escherichia coli* infection. This inexplicable decision was reached despite strong opposition from the Centers for Disease Control (CDC), which cited the extraordinary value of these compounds in treating community- or hospital-acquired enteric infections in humans. Subsequent events showed that the CDC’s concerns were prescient: Fluoroquinolone resistance quickly appeared in *Campylobacter* isolated from chickens, and by 1999 17.6% of *C. jejuni* and 30% of *C. coli* isolated from human patients showed fluoroquinolone resistance. *Campylobacter* infections are the leading cause of food-borne illness in the United States. Adding to the human and economic costs are chronic sequelae associated with *C. jejuni* infection: Guillain-Barré syndrome and reactive arthritis. Armed with such evidence, the FDA’s Center for Veterinary Medicine proposed on 31 October 2000 to withdraw the approval of fluoroquinolones for animal use. Of the two manufacturers, Abbott Laboratories agreed voluntarily to cease manufacture of its product; Bayer Corporation did not, and is submitting its case for continued marketing along with its request for a hearing. We think the FDA should pursue its case aggressively to stop Bayer from marketing.

In the end, the FDA has taken the right stand, and we may dodge this bullet. But we will be wise to reflect on the problems that remain. It is hardly surprising that compounds useful in human health also help animals. Nearly half of the total volume of antibiotics used in the United States is fed to animals, and this practice continues despite a strong scientific consensus that it is a bad idea. The resulting struggle between good science and strong politics has simmered fruitlessly for a quarter of a century; it’s time to end it, and some entrepreneurial energy might do the trick. We now know enough to begin developing novel antimicrobials that work specifically against animal pathogens yet do not create resistance in human ones. It looks to us like an economic opportunity as well as a scientific challenge. Anyone out there care to try?


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**APUA News**

**APUA Survey of Physicians**

In July 1998, all primary care physicians in Massachusetts, USA were asked about fifteen factors influencing their antibiotic prescribing. Of the 499 usable questionnaires returned (out of about 6,000, a response rate of 8%), 93% answered yes to the general question: Do you think physicians overprescribe antibiotics? Factors influencing physicians to increase antibiotic prescribing are shown in Figure 1. For more findings, see www.apua.org and click on the Research & Surveillance tab.

**Figure 1. Influences Increasing Antibiotic Prescribing Practices**

- Purulent Discharge: 64
- Diagnostic Uncertainty: 62
- Patient Request/Expectation: 62
- Patient Satisfaction: 48
- Fever: 42
- Treatment Uncertainty: 42
- Payer Policies: Formularies: 42
- Time Pressure: 40
- Potential Return Visit Cost: 35
- Litigation Concern: 20
- Payer Policies: Patient Surveys: 17
- Drug Promotion: 13
- Antibiotic Resistance Concerns: 5
- Payer Policies: QA/Pee Review: 3
- Medication Cost: 2

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**Reaction to FDA’s proposed ban on fluoroquinolones in poultry**

Response to the FDA’s October 2000 proposal to withdraw approval for fluoroquinolone use in poultry has been mixed:
- Abbott Laboratories voluntarily withdrew their fluoroquinolone products from the poultry market.
- Bayer Pharmaceuticals appealed the FDA decision, stating that the scientific evidence showing a health risk to humans is not compelling and does not justify the resulting health risk to poultry.
- APUA supports the FDA’s ban on fluoroquinolone use (see www.apua.org and click News tab).

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**APUA Symposium in Mexico**

Join fellow APUA members and friends on May 1, 2001 for a symposium on “Improving Knowledge and Practice Regarding Antibiotic Use in the Americas” at the 10th Pan American Congress on Infectious Diseases in Guadalajara, Jalisco, Mexico. The full-day program, sponsored by the APUA, Pan American Health Organization (PAHO), Pan American Society for Infectious Diseases (API) and American Society for Microbiology (ASM), to be held in the Hilton Hotel auditorium in the Expo Center complex, addresses current issues and model interventions in Latin America and the US, surveillance capabilities, management of resistant nosocomial infections and tuberculosis, and the role of vaccines in managing resistance. Registration is requested but not required; contact Dr. Sosa at anibal.sosa@tufts.edu.
Stakeholders’ Meeting on Animal and Plant Antibiotic Use

On January 23, 2001, APUA sponsored a meeting for stakeholders concerned with the ecological impact of antibiotic use in food animals. This meeting was the third in a series of Stakeholders’ Meetings that are part of the Facts about Antibiotics in Animals and their Impact on Resistance (FAAIR) Project of APUA.

Forty leaders from academia, advocacy and industry groups, government agencies, and professional organizations convened in a neutral forum to share their opinions on critical issues being discussed at the FDA/CVM meeting, such as the use of subtherapeutic dosages of antibiotics as growth promotants in food animals, the contribution of animal sources to resistance in human infections, and the disparity of available estimates of antibiotic use data in food-producing animals.

Dr. Scott McEwen gave a presentation on non-foodborne animal issues, e.g. farm animals, wildlife, and domestic animals, and whether these animals serve as vehicles or reservoirs of resistant organisms. Dr. Patricia McManus spoke on plant use of antibiotics and bacteria associated with plants as a part of a larger ecosystem. For more information, contact Dr. Stephen DeVincent at stephen.devincent@tufts.edu.

APUA Chapters Spur Collaboration

Two studies initiated through APUA’s 2000 Small Grants Program are: 1) Dr. Jaime Robledo, APUA-Colombia Chapter Leader and head of the Bacteriology Unit, Corporacion para Investigaciones Biologicas, aims to set up a network for the collection, analysis and dissemination of antibiotic resistance data from 10 third-level hospitals in five cities in Colombia. Matching funds for this study are being provided by the Fundacion Pedro Nel Cardona with additional support from the Colombian Society for Infectious Disease and the Colombian Society of Clinical Pathology. 2) A second study, “Risk Factors for Antibiotic Resistance of S. pneumoniae among Guatemalan children from different socioeconomic strata and health care delivery systems,” is a collaboration between APUA-Guatemala, the Center for Disease Studies and Control (CECEN) and Johns Hopkins School of Public Health-INCAP. Olga Torres, Chapter Leader and Director of INCAP Laboratories, will coordinate the sample processing and susceptibility testing. Dr. Edwin Asturias, CECEN, will coordinate the study which will enroll subjects from both private and government clinics.

APUA-India held a symposium on antibiotic use in conjunction with the XXXIII Annual Conference of the Indian Pharmacological Society, Gandhinagar Gujarat State, India. The symposium was chaired by Professor KB Sharma, Indian Society of Antimicrobial Chemotherapy, who gave an overview of prudent use, and Dr. Emma Keuleyan, APUA-Bulgaria chapter leader, who spoke on antimicrobial surveillance issues. Dr. JS Bapna, APUA-India chapter member from the Institute of Human Behavior and Allied Sciences, New Delhi, spoke on antibiotic use and economic considerations. The Organizing Secretary for the conference was Professor NS Parmar, K.B. Institute of Pharmaceutical Education and Research, Gujarat. Dr. Keuleyan’s presentation at the symposium resulted in an invitation to present at the 8th Scientific Meeting of the European Society of Chemotherapy.

APUA-Bulgaria, represented by Drs. Keuleyan, Markovska and Strateva, will present posters at the 2001 European Congress of Clinical Microbiology and Infectious Diseases (ECCMID) highlighting research findings supported by a 1999 APUA Small Grants Program. The abstracts are: “ESBL producing Enterobacteriaceae from APUA-Bulgaria Chapter Survey”, “Methicillin-resistant Staphylococcus aureus and coagulase-negative staphylococcus from APUA-Bulgaria Chapter Survey”, and “Antimicrobial susceptibility in gram-negative non-fermentative bacteria from APUA-Bulgaria Chapter Survey.”

Dr. Giuseppe Cornaglia, APUA-Italy chapter leader, was recently elected to serve on the Executive Committee of the European Society of Clinical Microbiology and Infectious Diseases (ESCMID).

APUA Board Changes

APUA welcomes Dr. Stephen C. Schoenbaum to its Board of Directors. Dr. Schoenbaum is the Senior Vice President of the Commonwealth Fund, a New York City based non-profit group supporting independent research on health and social issues and making grants to improve health care practice and policy.

APUA thanks the following retiring members of its Scientific Advisory Board for their years of dedicated service: Drs. Janusz Jeljaszewicz, Leonardo Mata, Theodore Sacks, Ewe Hui Sng, Tze-ying Tai, and Frantisek Vymola.

Join APUA’s 20th Anniversary Celebration at ICAAC

APUA has reached the 20-year milestone in our mission to preserve the power of antibiotics. As part of our 20-year celebration, APUA will host a special reception at the 2001 ICAAC in Chicago. Three past presidents of ASM will join APUA and share their perspectives on the past and future effectiveness of antibiotic therapy. APUA will present APUA Leadership Awards to a science writer who has increased public awareness of the problem and for an international public health leader who has crystallized solutions and engaged appropriate collaborators to have a major impact. APUA members and friends are invited to join us Sunday evening, September 23rd, 6:30 pm to 8 pm at the Hyatt Regency in Chicago. For more information, please contact sarann.bielavitz@tufts.edu.
If you are concerned about the public health threat of antibiotic resistance, become part of the solution. Make a tax-deductible contribution and join our global network of citizens, clinicians, researchers and policy makers.

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<thead>
<tr>
<th>Individual Member*</th>
<th>Supporting Member*</th>
<th>Corporate Member*</th>
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Note: APUA is a 501(c)3 nonprofit; donations are tax-deductible in the US. Supporting members help sponsor memberships in developing countries. Two-year memberships are charged the full rate the first year and will be granted a complimentary membership for the second year.

The Alliance for the Prudent Use of Antibiotics is a non-profit organization dedicated exclusively to curbing antibiotic resistance and improving the use of antibiotics throughout the world. Founded in 1981 as a global grassroots organization, APUA's mission is to improve public health through education and research concerning antibiotic use and resistance. With members in over 100 countries and numerous foreign affiliated chapters, APUA provides a unique network to support country-based activities and facilitate international communication and planning. APUA's resources include an international scientific advisory board with members of national academies of medicine and science, and a professional staff with specialized expertise. APUA's global network of affiliated chapters serves to tailor interventions to local customs and practices.

APUA, 75 Kneeland Street, Boston, MA 02111-1901, USA  •  Telephone: 617-636-0966  •  Fax: 617-636-3999  •  www.APUA.org