APUA
ALLIANCE FOR THE PRUDENT USE OF ANTIBIOTICS

Preserving the Power of Antibiotics®

Report on the APUA Educational Symposium:

"Facing the Next Pandemic of Pan-resistant Gram-negative Bacilli"

Held on Thursday, September 30, 2004
in Boston, MA

Preceding the 42nd Annual Meeting of
The Infectious Diseases Society of America

The Alliance for the Prudent Use of Antibiotics is a non-profit, international organization solely dedicated to preserving the power of antibiotics.

Founded in 1981, APUA conducts educational, research and international networking activities to raise awareness about antimicrobial resistance and to promote more appropriate access to and use of antimicrobials around the world.

Summary

On September 30, 2004, APUA held a luncheon symposium at IDSA to present evidence of a possible pandemic resistance to gram-negative bacteria, and help Infectious Disease specialists prepare to prevent and deal with its emergence.

The symposium was developed and coordinated by APUA staff and clinical advisers with support from Bayer Pharmaceuticals Corporation and Ortho-McNeil Pharmaceutical.

Background and history of resistant gram-negative infections

Occasional clinical bacterial isolates, now mostly *Pseudomonas*, are resistant to all available effective antibiotics and are thus, virtually untreatable. Over at least three time periods in our sixty-year antibiotic era, however, bacteria resistant to all existing antibiotics emerged and spread widely until a new antibiotic restored control.

In the 1950s, strains of *Staphylococcus aureus* resistant to penicillin and eventually to all of the other available antibiotics (tetracycline, chloramphenicol, etc) raged throughout the world's hospitals. It was essentially untreatable, until semi-synthetic penicillins and first-generation cephalosporins became available in the 1960s.

These new beta-lactam antibiotics also restored partial control over pan-resistant gram-negative bacilli, which had become a growing nosocomial problem over the 1950s. That problem then worsened again over the 1960s as resistance to those antibiotics increased. Almost complete control was restored by the introduction of gentamicin and other newer aminoglycosides in the early 1970s, but then lost again in the late 1970s as plasmids encoding aminoglycoside-inactivating enzymes spread widely.

The introduction in the early 1980s of three new classes of agents, third-generation cephalosporins, fluoroquinolones and carbapenems, each initially effective against nearly all gram-negative bacilli, began an unprecedented quarter century in which one or more agents has been available to treat almost any bacterial infection.

APUA symposium message:

New Antimicrobial Resistance Alert to Providers

Genes expressing resistance to third-generation cephalosporins, fluoroquinolones and carbapenems have gradually been emerging and spreading. Their convergence in the same strains has begun once again to produce outbreaks of pan-resistant gram-negative bacilli in some parts of the world, and now in the U.S.

Sponsored by Alliance for the Prudent Use of Antibiotics (APUA)
with support from Bayer Pharmaceuticals Corporation
and Ortho-McNeil Pharmaceutical

Educational Symposium and Luncheon:

"Facing the Next Pandemic of Pan-resistant Gram-negative Bacilli"

Preceding the 42nd Annual Meeting of
The Infectious Diseases Society of America

Program:

Moderated by Stuart B. Levy, MD
APUA President,
Director, Center for Adaptation Genetics and Drug Resistance
Tufts University School of Medicine
Boston, MA

I. Past Pandemics of Pan-resistant Pathogens: Recent Relief and Current Reemergence of Problem
Thomas F. O'Brien, MD
APUA Vice President,
Director, Microbiology Laboratory
Brigham & Women's Hospital
Boston, MA

II. Resistance to Third-Generation Cephalosporins and Carbapenems
Karen Bush, MD
Team Leader, Antimicrobial Drug Discovery,
Johnson & Johnson Pharmaceutical Research and Development Institute
Raritan, NJ

III. The Demise of Beta-Lactam Antibiotics in New York City
John Quale, MD
Associate Professor of Medicine, Infectious Diseases Division,
State University of New York Health Sciences Center
Brooklyn, NY

IV. Roundtable Discussion and Audience Questions

Symposium Publicity

APUA has earned a reputation for successful practitioner education programs at major national and international health provider conferences. APUA's forte is the ability to bring together diverse experts and produce well-balanced educational symposia with unique scientific credibility. APUA conducted this symposium as a part of its public health program to raise practitioner awareness about antimicrobial resistance and to improve prescribing practices.

Corporate support was acknowledged on APUA's invitations, programs and other materials, including APUA's website and newsletter (circulation 7,000).

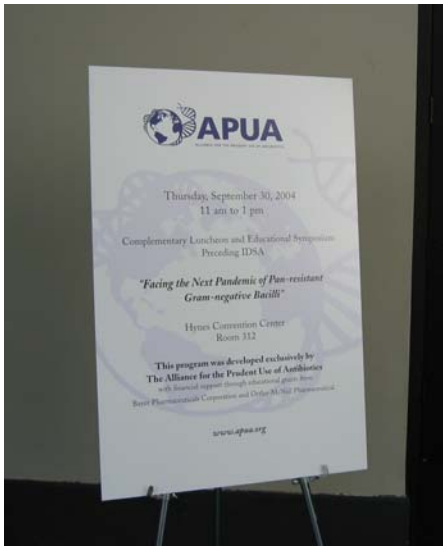
Informational registration materials were sent to nearly 3,000 IDSA pre-registrants. APUA publicized the symposium through brochures (see appendix), on the IDSA meeting website, in IDSA emails, and in IDSA's Affiliated Event Guide.

Participants were encouraged to register early since the session was expected to fill up early (and it did).

Educational materials were distributed prior to and after the program.

Symposium participants and passersby were reminded of the sponsors and program with this a large poster just outside of the meeting room.

Additionally, the symposium was promoted at APUA's exhibit booth at IDSA, reaching a large audience of interested and active healthcare practitioners and raising awareness about antibiotic resistance problems. APUA distributed symposium brochures, fact sheets, newsletters, and other information about appropriate antibiotic use initiatives.



Attendance at the Symposium

The symposium was planned as an affiliated event on the day before the IDSA conference opened. Over 175 professionals attended from major medical centers in the **USA, Belgium, Canada, France, Greece, Israel, Mexico, Nicaragua, Pakistan, Taiwan and Thailand.**

IDSA attendees are physicians, pharmacists, scientists and other health care professionals involved in the research, patient care, public health, disease prevention and education in the field of infectious diseases.

Attendees included several influential Infectious Disease experts, including Dr. Michael Scheld, IDSA President; and Dr. Sherwood Gorbach, Editor of Clinical Infectious Diseases. Dr. Gorbach personally invited hundreds of IDSA members via email. The invitation noted corporate sponsors and key symposium messages. Additionally, each of the 3000 pre-registrants received the brochure noting sponsors and messages.

IDSA Annual Meeting Attendance	2003	**2004**
Members	1849	**1919**
Nonmembers	917	**1152**
Member Trainees	326	**469**
Nonmember Trainees	144	**206**
Other		**4**
Total Scientific Attendees	3236	**3780**

Over 175 professionals from 11 countries attended the symposium.

Learning objectives met at the IDSA Symposium:

1. An historical review and analysis of how resistance has developed in antimicrobial therapeutics and the relationships in time between the arrival of new classes of antimicrobials and the subsequent appearance of new resistance problems.

2. An overview, including trends and consequences, of the newer alarming resistance problems confronting infectious disease physicians in the current decade, particularly as manifested in intensive care units (ICUs) of large city hospitals.

3. Knowledge of specific trends towards pan-resistance that are emerging in problematic pathogens such as *Klebsiella pneumoniae*; *Enterobacter* ; *Pseudomonas aeruginosa*; and the "newer" pathogens, *Acintobacter* and *Stenotrophomonas maltophilia*.

4. An awareness of the link between fluoroquinolone and cehpalosporin usage and the increase in carbapenem resistance and problems encountered in the identification of carbapenem-resistant isolates.

5. An introduction to the great variety of resistance mechanisms manifested by the gram-negative pathogens, which render them highly resistant to all, or nearly all, available antibiotics.

6. Familiarity with the pros and cons of the remaining few treatment choices for multi-resistant and pan-resistant gram-negatives.

7. An introduction to the available methods used to prevent and control the emergence and spread of pan-resistant gram-negatives, including antimicrobial surveillance, aggressive infection control coupled with environmental decontamination, and rational antibiotic use policies.

The symposium session was audio taped. A transcript and summary could be produced if funding were available.

"This is a very good discussion. I really appreciate all the different factors."
-- A symposium participant

I. Past Pandemics of Pan-resistant Pathogens: Recent Relief and Current Reemergence of Problem

Thomas F. O'Brien, MD
APUA Vice President,
Director, Microbiology Laboratory
Brigham & Women's Hospital
Boston, MA

The presentation commenced with an historical perspective on the development and introduction of new antimicrobials, spanning from the introduction of sulfa in the 1930's to the third-generation cephalosporins, fluoroquinolones, and finally the carbapenems in the 1980's.

With a detailed timeline, Dr. O'Brien traced the subsequent development of antimicrobial resistance, first to single agents, then to multiple agents, which has culminated in pan-resistance among certain gram-negative species.

Patterns showing periods of reprieve from resistance problems, followed by re-emergence of old pathogens with new resistances were described. Dr. O'Brien presented the example of the convergence and dramatic rise of quinolone and ceftazidime co-resistance in *Klebiella* in a single hospital over a ten-year period.

II. Resistance to Third Generation Cephalosporins and Carbapenems

Karen Bush, MD
Team Leader, Antimicrobial Drug Discovery, Johnson & Johnson Pharmaceutical Research and Development Institute
Raritan, NJ

Dr. Bush provided a description of the growing problems associated with gram-negative pathogens, which are the current major causative agents of urinary tract infections (UTIs) and ICU infections.

Of particular focus were the highly problematic pathogens, P*. aeruginosa*, *Acinetobacter* and *Stenotrophomonas maltophilia*, all of which exhibit marked decreases in antibiotic susceptibility. The mechanisms for this resistance are multiple and include a great variety (~500) of chromosomal- or plasmid-encoded beta lactamase-inactivating enzymes, coupled with decreased porins or increased export by efflux pumps.

The ESBL and metallo-beta lactamase varieties are of particular concern due to their pan resistance. The unusual features and epidemiology of the latter were outlined.

III. The Demise of Beta-Lactam Antibiotics in New York City

John Quale, MD
Division of Infectious Diseases, University Hospital of Brooklyn and Kings County Hospital, Brooklyn, NY

Beginning with an historical overview of resistance problems in the Northeast, Dr. Quale traced the development of the current problematic pathogens in New York City (*P. aeruginosa, A. baumanii,* and *K. pneumoniae*). The epidemiology of current susceptibilities and ribotypes, and the mechanisms of resistance were described.

Antibiotic usage patterns were traced, showing a correlation between increasing fluoroquinolone and cephalosporin exposure and the development of carbapenem resistance in these strains. KPCs (*K. pneumoniae* carbapenemases) were described in detail, including recent outbreaks, consequences of imipenem-resistant *K. pneumoniae* and *Enterobacter* in NYC hospitals and the problems inherent in identification.

Measures outlined for controlling antibiotic resistance included surveillance, aggressive infection control, reducing environmental contamination, and effective antibiotic control policies.

The symposium was promoted and APUA's materials were distributed at APUA's exhibit at IDSA. Sponsors were acknowledged in the promotional brochure. The following month at ICAAC, APUA's exhibit included the symposium brochures as a way to share the symposium messages.

Evaluation

- Over 175 professionals attended the symposium and discussion, including the President of IDSA.

- 3780 people attended IDSA in 2004. Attendance was up from 3236 in 2003, a 17% increase. Each registrant received a list of affiliated events, including the APUA symposium listing, which promoted and detailed the symposium.

- 3000 brochures sent to pre-registrants (see brochure in appendix). The brochures informed recipients of key messages and acknowledged corporate sponsors.

- Participants came from major medical centers in 11 countries including the USA, Belgium, Canada, France, Greece, Israel, Mexico, Nicaragua, Pakistan, Taiwan, and Thailand.

- Approximately 175 slide sets were distributed to participants.

- The symposium generated lively discussion with 14 questions from participants discussed during the roundtable portion of the program.

- A summary of the symposium was posted on APUA's website to further extend the reach of the key messages.

Appendix

I. Sample of Symposium Attendees' Affiliations

II. Symposium Promotional Brochure

III. Symposium Listing in IDSA Program

IV. Symposium Slide Sets