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## Conference Objectives

At the conclusion of this conference, participants should be able to meet the overall conference objectives and session specific objectives.

### Overall Conference Objectives:

- Discuss the science, prevention and control of antimicrobial resistance.
- Define issues and potential solutions to the problem of antimicrobial resistance.

### Session-Specific Objectives:

#### **Keynote Address**

- Describe factors contributing to the rising levels of antimicrobial resistance

#### **Rapid Diagnostics: Their Role in Detection of Resistance and in Antimicrobial Management**

- Review the technical, economic, and practical hurdles of developing and implementing molecular diagnostics for antimicrobial resistance in clinical and veterinary settings

#### **The Challenge of Community Associated MRSA Infections**

- Discuss the epidemiology, pathogenesis, rapid diagnosis, and treatment options available for a growing epidemic strain of a highly virulent bacterial pathogen

#### **The Re-emergence of *C. difficile***

- Evaluate new outbreaks of *C. difficile*-associated disease (CDAD) in the hospital and community

#### **Pharmacological Predictors of Outcome: Can They Be Used to Treat or Prevent Resistance? What is Their Role in Drug Development?**

- Discuss the strengths and limitations of pharmacodynamic predictors of *in vivo* response;
- Discuss current debates on the relevance of tissue distribution and protein binding; and
- Review current information regarding the impact of therapy duration on the development of microbiological resistance

#### **Controversies in Antimicrobial Resistance**

- Review data regarding several controversies in antimicrobial resistance to include transmission of resistant organisms from pets to humans; resistance related to topical antiseptics, and the role of heteroresistance in clinical infections.

**Innovations and Increasing Efficiency in Clinical Trials for Infectious Disease: What Have We Learned?**

- Examine how the efficiency of clinical trials can be increased allowing effective information about new drugs with a smaller sample size gathered over a shorter period of time; and
- Discuss issues related to adaptive clinical trial design, developing and using patient reported outcomes, and other trial designs

**Innovations and Solutions: Vaccines as a Strategy for Preventing and Controlling Resistance**

- Relate the impact of the conjugate pneumococcal vaccine on disease incidence;
- Describe the pre-clinical and clinical phases of TB vaccines that are under development;
- Discuss issues in malaria vaccine development; and
- Review strategies for pandemic influenza preparedness

## Acknowledgments *(as of June 9, 2006)*

This conference is supported, in part, through unrestricted educational grants from:

Abbott Laboratories

AdvanDx, Inc.

AstraZeneca Pharmaceuticals LP

Astellas Pharma US, Inc.

Cubist Pharmaceuticals, Inc.

Elusys Therapeutics, Inc.

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## Conference Co-Chairs

**Marissa Miller, D.V.M., M.P.H.**

Department of Health and Human Services  
Washington, DC

**Susan J. Rehm, M.D.**

National Foundation for Infectious Diseases  
Bethesda, MD

**J. Todd Weber, M.D.**

Centers for Disease Control and Prevention  
Atlanta, GA

## Former Conference Co-Chair and Founder

**William J. Martone, M.D.**

Cubist Pharmaceuticals  
Lexington, MA

## Organizing and Scientific Program Committee

**John Bradley, M.D.**

Children's Hospital, San Diego  
San Diego, CA

**Mitchell L. Cohen, M.D.**

Centers for Disease Control and Prevention  
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**Stuart H. Cohen, M.D.**

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**Stuart B. Levy, M.D.**

Tufts University School of Medicine  
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**Marissa Miller, D.V.M., M.P.H.**

*Conference Co-Chair*

**N. Kent Peters, M.A., Ph.D.**

National Institute of Allergy and Infectious  
Diseases/NIH  
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**John H. Powers, M.D.**

U. S. Food and Drug Administration  
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**Susan J. Rehm, M.D.**

*Conference- Co-Chair*

**John H. Rex, M.D.**

AstraZeneca  
Macclesfield, Cheshire, United Kingdom

**Jane Robens, D.V.M.**

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**Lyle P. Vogel, D.V.M., M.P.H.**

American Veterinary Medical Association  
Schaumburg, IL

**J. Todd Weber, M.D.**

*Conference Co-Chair*

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Children's Hospital  
Birmingham, AL

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Bethesda, MD****Sharon Cooper-Kerr**

Director, Events Planning

**Charlotte Lazrus**

Executive Assistant

**Sheena L. Majette**

Director, Continuing Medical Education

**Len Novick**

Executive Director

**Natasha L. Patterson**

Continuing Medical Education Coordinator

## Invited Presenters\*

### **Allison E. Aiello, Ph.D., M.S.**

*Assistant Professor, Epidemiology*  
University of Michigan School of Public Health  
Ann Arbor, MI

### **David Alland, M.D.**

*Chief, Division of Infectious Diseases*  
*Associate Professor of Medicine*  
University of Medicine and Dentistry of New Jersey  
New Jersey Medical School  
Newark, NJ

### **Michael J. Brennan, Ph.D.**

*Associate Director for Research*  
Center for Biologics Evaluation and Research  
Food and Drug Administration  
Bethesda, MD

### **Laurie B. Burke, R.Ph., M.P.H.**

*Director, Study Endpoints and Label Development*  
Center for Drug Evaluation and Research  
Food and Drug Administration  
Silver Spring, MD

### **Otto Cars, M.D., Ph.D.**

*Professor, Director*  
*Swedish Strategic Programme for Rational Use of*  
*Antimicrobial Agents and Surveillance of Resistance*  
Swedish Institute for Infectious Disease Control  
Solna, Sweden

### **Henry F. Chambers, M.D.**

*Professor of Medicine*  
University of California, San Francisco  
San Francisco General Hospital  
San Francisco, CA

### **Charles K. Cooper, M.D.**

*Medical Officer*  
*Division of Anti-Infective Drug Products*  
Center for Drug Evaluation and Research  
Food and Drug Administration  
Silver Spring, MD

### **Peter J. Dailey, Ph.D., M.P.H.**

*Vice President, Research and Development*  
Cepheid  
Sunnyvale, CA

### **Robert S. Daum, M.D.**

*Professor of Pediatrics*  
*Section Chief, Pediatric Infectious Diseases*  
University of Chicago Hospitals  
Chicago, IL

### **Hartmut Derendorf, Ph.D.**

*Distinguished Professor and Chairman*  
University of Florida  
Gainesville, FL

### **Vance G. Fowler, Jr., M.D.**

*Associate Professor of Medicine*  
Duke University Medical Center  
Department of Medicine  
Durham, NC

### **Daphne TY Lin, Ph.D.**

*Deputy Division Director*  
Center for Drug Evaluation and Research  
Food and Drug Administration  
Office of Biostatistics  
Silver Spring, MD

### **David H. Lloyd, Ph.D., M.R.C.V.S., F.R.C.V.S.**

*Professor in Veterinary Dermatology*  
The Royal Veterinary College  
University of London  
Hertfordshire, United Kingdom

### **Vivian G. Loo, M.D.**

*Chief of Microbiology*  
McGill University Health Center  
Quebec, Canada

### **Franklin D. Lowy, M.D.**

*Professor of Medicine and Pathology*  
Columbia University  
College of Physicians and Surgeons  
New York, NY

### **L. Clifford McDonald, M.D.**

*Medical Epidemiologist*  
Centers for Disease Control and Prevention  
Atlanta, GA

### **Mark Miller, M.D.**

*Chief, Department of Microbiology*  
*Head, Division of Infectious Diseases*  
McGill University  
SMBD-Jewish General Hospital  
Quebec, Canada

**Robert C. Moellering, Jr., M.D.**

*Shields Warren-Mallinckrodt Professor of Medical Research*  
*Chairman, Department of Medicine*  
Harvard Medical School  
Beth Israel Deaconess Medical Center  
Boston, MA

**Matthew R. Moore, M.D.**

*Commander, U.S. Public Health Service*  
*Medical Epidemiologist*  
Centers for Disease Control and Prevention  
Atlanta, GA

**Johan W. Mouton, M.D., Ph.D.**

*Clinical Microbiologist*  
Canisius Wilhelmina Hospital  
Nijmegen, The Netherlands

**Michael S. Niederman, M.D.**

*Professor of Medicine and Vice-Chairman,*  
*Department of Medicine, SUNY at Stony Brook*  
*Chairman, Department of Medicine*  
Winthrop University Hospital  
Mineola, NY

**Richard D. Oberst, Ph.D., D.V.M.**

*Molecular Pathologist*  
Kansas State University  
College of Veterinary Medicine  
Manhattan, KS

**Jacques Pepin, M.D., M.Sc**

*Professor of Infectious Diseases*  
Centre Hospitalier Universitaire de Sherbrooke  
Quebec, Canada

**John H. Powers, M.D.**

*Lead Medical Officer*  
Center for Drug Evaluation and Research  
Food and Drug Administration  
Silver Spring, MD

**Gary W. Procop, M.D.**

*Section Head*  
The Cleveland Clinic Foundation  
Cleveland, OH

**Robin Robinson, Ph.D.**

*Associate Director, Pandemic Preparedness Program*  
Office of Public Health Emergency Preparedness  
U.S. Department of Health & Human Services  
Washington, DC

**Ursula Theuretzbacher, Ph.D.**

*Founder*  
Center for Anti-Infective Agents  
Vienna, Austria

\*Speakers and presentations subject to change

## General Information

### Americans with Disabilities Act

The Hyatt Regency Bethesda is fully accessible to the public in accordance with the Americans with Disabilities Act guidelines. If you have any special meeting needs or requirements, please contact either Sharon Cooper-Kerr or a member of the hotel staff.

### Conference Information Desk

The Conference Information Desk is located in the Waterford Lobby area outside the **Crystal Ballroom**. Conference staff will be available at the desk throughout the conference.

### Conference Language

The official language for the conference is English.

### Conference Location

All sessions of the conference will be held at:

#### Hyatt Regency Bethesda

One Bethesda Metro Center  
Wisconsin Avenue at Old Georgetown Road  
Bethesda, Maryland 20814  
(301) 657-1234

Meeting rooms for specific sessions are listed in the **Final Program** (see Table of Contents).

## Continuing Education

### *Continuing Medical Education*

The National Foundation for Infectious Diseases (NFID) is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide Continuing Medical Education (CME) for physicians. NFID takes responsibility for the content, quality, and scientific integrity of this CME activity.

NFID designates this CME activity for a maximum of 17 *AMA PRA Category 1 credits*<sup>™</sup>. Physicians should claim credit commensurate with the extent of their participation in the educational activity.

### *Continuing Nursing Education*

This offering has been approved for 17.4 contact hours by the Maryland Nurses Association which is accredited as an approver of continuing education in nursing by the American Nurses' Credentialing Center's Commission on Accreditation.

## Designated Continuing Education Activities

Sessions designated with a **CE** symbol have been approved for both CME and Nursing credit. Sessions designated with a **CME** symbol have been approved for CME credit only. No other sessions are eligible for credit hours.

## CME and Nursing Certificates

In order to ensure that you receive the credits to which you are entitled, please note the following:

1. Complete the application for credits located at the Conference Information Desk.
2. Return your completed application and conference evaluation to conference staff at the Conference Information Desk.
3. **FOR NURSES ONLY:** you must also sign in before each session in order to receive credit for attendance.

### *CME Disclosures*

As a sponsor accredited by the ACCME, NFID must ensure balance, independence, objectivity, and scientific rigor in its educational activities. All faculty and planning committee members are required to disclose, both written and verbally, any relevant financial interest or other relationship with the manufacturer(s) of any product or service discussed in an educational presentation and/or with the commercial supporters of this activity. Disclosure information is reviewed in advance to manage and resolve any conflict of interest that may affect the balance and scientific integrity of an educational presentation. A summary of these conflicts of interest is printed separately in this book under the heading **Disclosure Index** (see Table of Contents).

## Messages

All sleeping rooms in the **Hyatt Regency Bethesda** are equipped with a voice mail system. This system is accessible via the hotel operator using the house phone. In case of emergencies requiring immediate attention, your party should call the general hotel number listed below and instruct the switchboard to deliver a message to Sharon Cooper-Kerr or Sheena Majette at the Conference Information Desk outside of the Crystal Ballroom. The general hotel number is **1-301-657-1234**.

## No Smoking Policy

The Hyatt Regency Bethesda is a non-smoking facility except for specially designated guest rooms. No smoking is allowed in any of the session rooms, coffee break area or in the foyer area adjoining the session rooms.

## Poster Session

The Poster Session/Reception will be held on Monday, June 26, 5:30 p.m. in the Waterford/Lalique Room. Presenters will be at their boards to answer questions and discuss their research. The Posters will continue to be on display throughout the conference.

## Press Room

NFID will have a Press Room located in the Tiffany Salon. Press should sign in at the Conference Information Desk during registration hours.

## Program and Abstracts

Each registered participant will receive one complimentary copy of the Final Program and Abstract Book as part of his/her registration fee. Additional copies, if available, can be purchased for \$25. Orders for additional copies can be taken at the Conference Information Desk and after the conference, by e-mail to [resistance@nfid.org](mailto:resistance@nfid.org), or by calling (301) 656-0003 x19.

## Registration Fees and Hours

The onsite registration fee: **US \$450.00**

The registration fee includes a program/abstract book, continental breakfast on each day of the conference, all scheduled coffee breaks, and the reception on Monday. Accommodations and additional meals are not included.

Individuals interested in registering onsite may do so at the Conference Information Desk between the following times:

Sunday, June 25	7:00 p.m. – 9:00 p.m.
Monday, June 26	8:00 a.m. – 5:00 p.m.
Tuesday, June 27	7:00 a.m. – 5:00 p.m.
Wednesday, June 28	7:30 a.m. – 10:30 a.m.

## Speaker Ready Room and Audiovisual Equipment

A room has been set aside for speakers to preview their slides. All speakers should check in at the Conference Information Desk to be directed to the ready room. The room will be open during the registration hours (see **General Information-Registration Fees and Hours**) and will be equipped with a laptop for preview of your PowerPoint presentation.

Standard session room setup includes a PC, 250 zip drive, laser pointer, podium microphone, and aisle microphones.

## Verification of Attendance

Attendees may obtain a letter of attendance verification from the staff at the Conference Information Desk during registration hours.

## Affiliated Events and Other Meetings

Tuesday, June 27, 2006

**Conference on Antimicrobial Resistance Organizing and Scientific Program Committee Meeting**  
(Closed meeting)

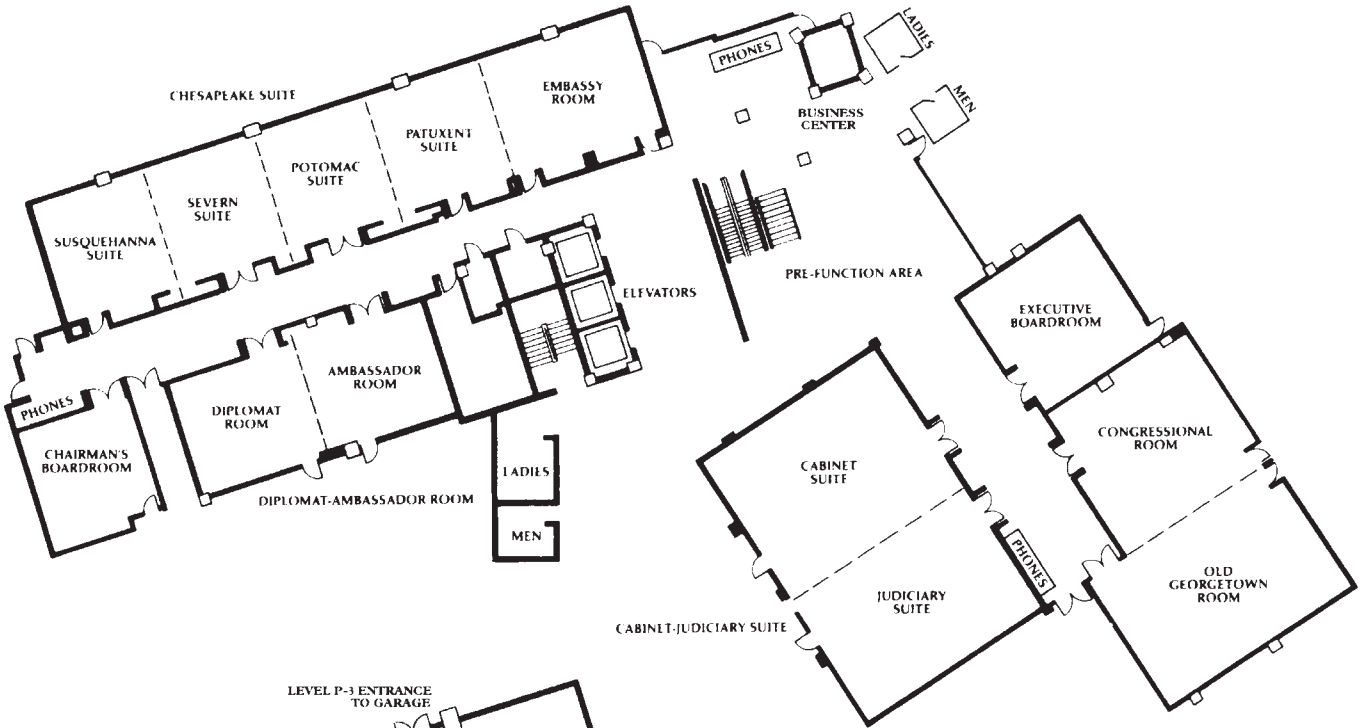
5:00 p.m. – 8:00 p.m., *Susquehanna/Severn Room*

## PROGRAM-AT-A-GLANCE

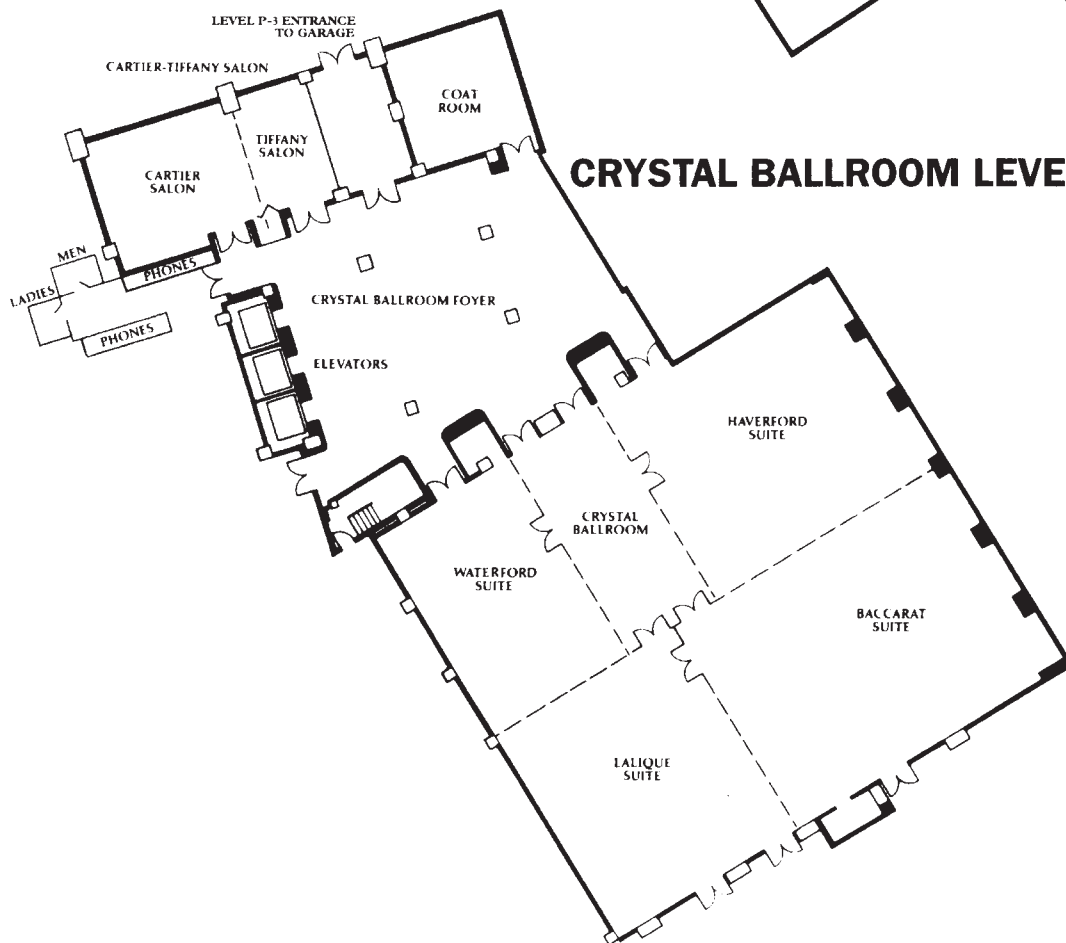
	SUNDAY, JUNE 25	MONDAY, JUNE 26	TUESDAY, JUNE 27	WEDNESDAY, JUNE 28
7:00			Registration Meet the Experts Breakfast Session	Meet the Experts Breakfast Session
7:30			Continental Breakfast	Registration Continental Breakfast
8:00		Registration	<b>Symposium 3:</b> The Re-Emergence of <i>C. difficile</i>	<b>Symposium 6:</b> Innovations and Increasing Efficiency in Clinical Trials for Infectious Disease: What Have We Learned?
8:45		Continental Breakfast/ Poster Set-up		
9:20		Welcome and Introductions		
9:30		Keynote Address		
10:00			Coffee Break	Coffee Break
10:30		Coffee Break	<b>Symposium 4:</b> Pharmacological Predictors of Outcome: Can They be Used to Treat or Prevent Resistance? What is Their Role in Drug Development?	<b>Symposium 7:</b> Innovations and Solutions: Vaccines as a Strategy for Preventing and Controlling Resistance
11:00		<b>Symposium 1:</b> Rapid Diagnostics: Their Role in Detection of Resistance and in Antimicrobial Management		
12:30			<b>Lunch (on your own)</b>	Adjournment/Participant Evaluation
1:00		<b>Lunch (on your own)</b>		
1:30			<b>Submitted Presentations</b>	
2:00		<b>Symposium 2:</b> The Challenge of Community Associated MRSA Infections		
2:30			Coffee Break	
3:00			<b>Symposium 5:</b> Controversies in Antimicrobial Resistance	
4:00		Coffee Break		
4:30		<b>Submitted Presentations</b>	Adjournment	
5:30		<b>Poster Session and Reception</b>		
7:00-9:00	Registration			

## HOTEL FLOOR PLAN

### CONFERENCE LEVEL



### CRYSTAL BALLROOM LEVEL



## FINAL PROGRAM

Sunday, June 25, 2006

7:00 p.m.–  
9:00 p.m.

**Registration**

*Waterford Lobby*

Monday, June 26, 2006

8:00 a.m.–  
5:00 p.m.

**Registration**

*Waterford Lobby*

8:45 a.m.

**Continental Breakfast**

*Waterford Lobby*

8:45 a.m.

**Poster Set-Up**

*Waterford/Lalique Ballroom*

9:20 a.m.

**Opening Remarks**

*Haverford/Baccarat Ballroom*

Susan J. Rehm, M.D.

*National Foundation for Infectious Diseases  
Bethesda, MD*

**Keynote Address** **CE**

*Haverford/Baccarat Ballroom*

Moderator: Susan J. Rehm, M.D.

*National Foundation for Infectious Diseases  
Bethesda, MD*

9:30 a.m.

**1. Antimicrobial Resistance: The Next Pandemic**

Robert C. Moellering, Jr., M.D.

*Beth Israel Deaconess Medical Center  
Boston, MA*

10:20 a.m.

**Questions and Answers**

10:30 a.m.

**Coffee Break**

*Waterford Lobby*

## FINAL PROGRAM

Monday, June 26, 2006 *(continued)***Symposium 1. Rapid Diagnostics:  Their Role in Detection of Resistance and in Antimicrobial Management***Haverford/Baccarat Ballroom*

Moderator: N. Kent Peters, M.A, Ph.D.  
*National Institute of Allergy and Infectious Diseases  
Bethesda, MD*

- 11:00 a.m.      **2. Using Diagnostic Testing to Reduce the Overuse of Antibiotics in Nosocomial Pneumonia**  
Michael S. Niederman, M.D.  
*Winthrop University Hospital  
Mineola, NY*
- 11:25 a.m.      **Questions and Answers**
- 11:30 a.m.      **3. Rapid Assays for Drug Resistant Tuberculosis and Their Application to Developing and Developed Countries**  
David Alland, M.D.  
*New Jersey Medical School  
Newark, NJ*
- 11:55 a.m.      **Questions and Answers**
- 12:00 p.m.      **4. Preventing Antimicrobial Resistance with Nuclear Acid Diagnostics: A Strategy for Success**  
Peter Dailey, Ph.D., M.P.H.  
*Roche Molecular Systems, Inc.  
Alameda, CA*
- 12:25 p.m.      **Questions and Answers**
- 12:30 p.m.      **5. Diagnostics in Agriculture**  
Richard D. Oberst, Ph.D., D.V.M.  
*Kansas State University  
Manhattan, KS*
- 12:55 p.m.      **Questions and Answers**
- 1:00 p.m.      **Lunch (on your own)**

## FINAL PROGRAM

**Symposium 2. The Challenge of CE Community Associated MRSA Infections***Haverford/Baccarat Ballroom*

Moderator: Barry I. Eisenstein, M.D.  
*Cubist Pharmaceuticals, Inc.*  
*Lexington, MA*

2:00 p.m.

**6. Treatment Options and Trends**

Vance G. Fowler, M.D.  
*Duke University Medical Center*  
*Durham, NC*

2:25 p.m.

**Questions and Answers**

2:30 p.m.

**7. Rapid Diagnostics of Bacterial Pathogens and Mechanisms of Resistance**

Gary W. Procop, M.D.  
*The Cleveland Clinic Foundation*  
*Cleveland, OH*

2:55 p.m.

**Questions and Answers**

3:00 p.m.

**8. Community MRSA: Epidemiology**

Henry F. Chambers, M.D.  
*San Francisco General Hospital*  
*San Francisco, CA*

3:25 p.m.

**Questions and Answers**

3:30 p.m.

**9. The Community Angle: Biology and Epidemiology**

Franklin D. Lowy, M.D.  
*Columbia University*  
*New York, NY*

3:55 p.m.

**Questions and Answers**

4:00 p.m.

**Coffee Break***Waterford Lobby*

## FINAL PROGRAM

Monday, June 26, 2006 (continued)

**Submitted Presentations 1: CME**  
**Epidemiology and Prevention  
of Community-Associated MRSA**

Haverford/Baccarat Ballroom

Moderator: George Eliopoulos, M.D.  
Beth Israel Deaconess Medical Center  
Boston, MA

4:30 p.m.

**S1 Prevalence, Profile, and Predictors of Community-Associated Methicillin-Resistant *Staphylococcus aureus* (CA-MRSA) Colonization among Pregnant Women**

**K. T. Chen**<sup>1</sup>, R. C. Huard<sup>2</sup>, P. Della-Latta<sup>2</sup>, H. Campbell<sup>3</sup>, L. Borrell<sup>4</sup>, P. M. Schlievert<sup>5</sup>, L. Saiman<sup>6</sup>;

<sup>1</sup>Ob/Gyn and Epidemiology, Columbia University, New York, NY, <sup>2</sup>Pathology, Columbia University, New York, NY, <sup>3</sup>Ob/Gyn, Columbia University, New York, NY, <sup>4</sup>Epidemiology, Columbia University, New York, NY, <sup>5</sup>Microbiology, University of Minnesota, Minneapolis, MN, <sup>6</sup>Pediatrics, Columbia University, New York, NY.

4:45 p.m.

**S2 Cluster of Neonatal Methicillin-Resistant *Staphylococcus aureus* (MRSA) Infections due to Unrecognized MRSA Colonization at Birth**

**J. L. Murillo**<sup>1</sup>, P. Harmon<sup>1</sup>, W. Cruz<sup>1</sup>, T. Chan<sup>2</sup>, M. Cohen<sup>3</sup>, M. Koraboina<sup>4</sup>, B. Kreiswirth<sup>4</sup>;

<sup>1</sup>Epidemiology, Newark Beth Israel Medical Center, Newark, NJ, <sup>2</sup>Microbiology, Newark Beth Israel Medical Center, Newark, NJ, <sup>3</sup>Neonatology, Newark Beth Israel Medical Center, Newark, NJ, <sup>4</sup>Public Health Research Institute, Newark, NJ.

5:00 p.m.

**S3 Dominant Clones of Methicillin Resistant *Staphylococcus aureus* (MRSA) in Asuncion, Paraguay**

**M. van Westreenen**;

Med Microbiology and Infectious Diseases, Erasmus Medical Center, Rotterdam, The Netherlands.

5:15 p.m.

**S4 Identifying Target Groups for Prevention of Community-Associated Methicillin Resistant *Staphylococcus aureus* Infection, New York City**

**M. A. Marx**<sup>1</sup>, A. Yeung<sup>1</sup>, D. Kapell<sup>1</sup>, D. Kreiger<sup>1</sup>, T. Denton<sup>2</sup>, L. Amoroso<sup>1</sup>, M. Higdon<sup>1</sup>, J. Kattan<sup>1</sup>, S. McKelvey<sup>1</sup>, S. Vassell<sup>1</sup>, A. Colon-Serrant<sup>1</sup>, Y. Lue<sup>3</sup>, R. Aquino<sup>3</sup>, J. Kornblum<sup>4</sup>, B. Kreiswirth<sup>2</sup>, D. Weiss<sup>1</sup>;

<sup>1</sup>Communicable Diseases, NYC Department of Health and Mental Hygiene, New York, NY, <sup>2</sup>Public Health Research Institute, Newark, NJ, <sup>3</sup>Quest Diagnostics Incorporated, Teterboro, NJ, <sup>4</sup>Public Health Laboratory, NYC Department of Health and Mental Hygiene, New York, NY.

5:30 p.m.

**Adjournment**

5:30 p.m.

**Poster Session and Reception**

## FINAL PROGRAM

Tuesday, June 27, 2006

7:00 a.m. – 5:00 p.m.	<b>Registration</b>	<i>Waterford Lobby</i>
7:00 a.m. – 7:45 a.m.	<b>Meet the Exerts Breakfast Session</b>	<i>Waterford/Lalique Ballroom</i>
7:30 a.m.	<b>Continental Breakfast</b>	<i>Waterford Lobby</i>
	<b>Symposium 3: The Re-Emergence of <i>C. difficile</i></b> <b>CE</b>	<i>Haverford/Baccarat Ballroom</i>
	Moderator: L. Clifford McDonald, M.D. <i>Centers for Disease Control and Prevention Atlanta, GA</i>	
8:00 a.m.	<b>10. Update on Epidemiology in the U.S. and Europe</b> L. Clifford McDonald, M.D. <i>Centers for Disease Control and Prevention Atlanta, GA</i>	
8:25 a.m.	<b>Questions and Answers</b>	
8:30 a.m.	<b>11. Update on Epidemiology in Montreal and Quebec</b> Vivan G. Loo, M.D. <i>McGill University Health Center Montreal, QB, Canada</i>	
8:55 a.m.	<b>Questions and Answers</b>	
9:00 a.m.	<b>12. Antibiotic Use and Antibiotic Risk Factors for <i>Clostridium difficile</i> Associated Diarrhea</b> Jacques Pepin, M.D., M.Sc. <i>University of Sherbrooke Sherbrooke, QB, Canada</i>	
9:25 a.m.	<b>Questions and Answers</b>	
9:30 a.m.	<b>13. Clinical Management of <i>Clostridium difficile</i> Associated Diarrhea</b> Mark Miller, M.D. <i>McGill University Montreal, QB, Canada</i>	
9:55 a.m.	<b>Questions and Answers</b>	
10:00 a.m.	<b>Coffee Break</b>	<i>Waterford/Lalique Ballroom</i>

## FINAL PROGRAM

Tuesday, June 27, 2006 *(continued)*

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**Symposium 4. Pharmacological CE  
Predictors of Outcome: Can They Be Used  
to Treat or Prevent Resistance? What is  
Their Role in Drug Development**

*Haverford/Baccarat Ballroom*

Moderator: John H. Rex, M.D., F.A.C.P.  
*AstraZeneca Pharmaceuticals*  
*Cheshire, United Kingdom*

- 10:30 a.m.     **14. The Role of Pharmacological Predictors in Drug Development**  
Hartmut Derendorf, Ph.D.  
*University of Florida*  
*Gainesville, FL*
- 10:55 a.m.     **Questions and Answers**
- 11:00 a.m.     **15. Use of Pharmacologic Predictors in Prevention or Treatment of Resistance**  
Otto Cars, M.D., Ph.D.  
*Swedish Institute for Infectious Diseases*  
*Solna, Sweden*
- 11:25 a.m.     **Questions and Answers**
- 11:30 a.m.     **16. The Influence of Tissue Distribution and Protein Binding on Resistance**  
Ursula Theuretzbacher, Ph.D.  
*Center for Anti-Infective Agents*  
*Vienna, Austria*
- 11:55 a.m.     **Questions and Answers**
- 12:00 p.m.     **17. The Influence of Duration of Therapy on Resistance**  
Johan Mouton, M.D., Ph.D.  
*Med Microbiologie en Infect*  
*Nijmegen, Netherlands*
- 12:25 p.m.     **Questions and Answers**
- 12:30 p.m.     **Lunch (on your own)**

## FINAL PROGRAM

**Submitted Presentations 2:** **CME**  
**Resistant Gram Negative Bacilli:  
 Epidemiology Mechanisms and Rapid Detection**

*Haverford/Baccarat Ballroom*

Moderator: John Bradley, M.D.  
 Children's Hospital, San Diego  
 San Diego, CA

- 1:30 p.m. **S5 Drug Resistance Pattern of *Shigella sonnei*— Kansas, 1997-2005**  
 A. S. Huang<sup>1</sup>, R. Flahart<sup>2</sup>, J. Sexton<sup>2</sup>, D. C. Hunt<sup>3</sup>, G. R. Hansen<sup>3</sup>;  
<sup>1</sup>Kansas Department of Health and Environment, and Centers for Disease Control and  
 Prevention, Topeka, KS, <sup>2</sup>Kansas Department of Health and Environment Laboratory,  
 Topeka, KS, <sup>3</sup>Department of Health, Kansas Department of Health and Environment,  
 Topeka, KS.
- 1:45 p.m. **S6 Resistance Patterns of Gram Negative Rods in Community Acquired versus  
 Nosocomially Acquired Urinary Tract Infections**  
 J. Tolia, A. Roy, J. Slim;  
 St Michael's Medical Center, Newark, NJ.
- 2:00 p.m. **S7 Molecular Mechanisms Causing Imipenem Resistance among *P. aeruginosa*  
 Isolates from Intensive Care Unit (ICU) Patients**  
 S. M. Arduino;  
 Epidemiology and Preventive Medicine, University of Maryland, Baltimore, MD.
- 2:15 p.m. **S8 Development of a "Universal" DNA Microarray for Detecting Exogenous  
 Antimicrobial Resistance Genes in Diverse Bacteria**  
 J. G. Frye, C. R. Jackson, M. D. Englen, P. J. Fedorka-Cray;  
 BEAR-RU, USDA-ARS, Athens, GA.
- 2:30 p.m. **Coffee Break**

*Waterford/Lalique Ballroom*

**Symposium 5. Controversies** **CE**  
**in Antimicrobial Resistance**

*Haverford/Baccarat Ballroom*

Moderator: Stuart H. Cohen, M.D.  
 University of California, Davis Medical Center  
 Sacramento, CA

- 3:00 p.m. **18. Resistance to Topical Antiseptics: Does It Matter?**  
 Allison E. Aiello, Ph.D., M.S.  
 University of Michigan School of Public Health  
 Ann Arbor, MI
- 3:25 p.m. **Questions and Answers**

## FINAL PROGRAM

Tuesday, June 27, 2006 *(continued)*

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- 3:30 p.m.      **19. VISA and Heteroresistance**  
 Robert Daum, M.D.  
*University of Chicago*  
*Chicago, IL*
- 3:55 p.m.      **Questions and Answers**
- 4:00 p.m.      **20. Pet Animals as Reservoirs of Resistant Bacteria**  
 David H. Lloyd, B.Vet.Med., Ph.D.  
*Royal Veterinary College*  
*London, United Kingdom*
- 4:25 p.m.      **Questions and Answers**
- 4:30 p.m.      **Adjournment**

Wednesday, June 28, 2006

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- 7:00 a.m.–  
7:45 a.m.      **Meet the Experts Breakfast Session**      *Waterford/Lalique Ballroom*
- 7:30 a.m.–  
10:30 a.m.      **Registration**      *Waterford Lobby*
- 7:30 a.m.      **Continental Breakfast**      *Waterford Lobby*
- Symposium 6. Innovations and CE**      *Haverford/Baccarat Ballroom*  
**Increasing Efficiency in Clinical Trials for  
 Infectious Diseases: What Have We Learned?**
- Moderator: John H. Powers, M.D.  
*Food and Drug Administration*  
*Rockville, MD*
- 8:00 a.m.      **21. Misclassification Bias and Measurement Error in Clinical Trials for  
 Infectious Diseases: How They Affect the Efficiency of Trials**  
 Charles K. Cooper, M.D.  
*Center for Drug Evaluation and Research/FDA*  
*Silver Spring, MD*
- 8:25 a.m.      **Questions and Answers**

## FINAL PROGRAM

8:30 a.m.

- 22. Patient Reported Outcome Measures in Clinical Trials of Infectious Diseases: How They Can Help Us**  
Laurie B. Burke, R.Ph., M.P.H.  
*Center for Drug Evaluation and Research/FDA*  
*Silver Spring, MD*

8:55 a.m.

**Questions and Answers**

9:00 a.m.

- 23. Adaptive Designs in Clinical Trials of Infectious Diseases: What It Is and What It Isn't**  
Daphne TY Lin, Ph.D.  
*Center for Drug Evaluation and Research/FDA*  
*Silver Spring, MD*

9:25 a.m.

**Questions and Answers**

9:30 a.m.

- 24. Increasing the Efficiency of Clinical Trials in Infectious Diseases: Where Do We Go From Here?**  
John H. Powers, M.D.  
*Food and Drug Administration*  
*Rockville, MD*

9:55 a.m.

**Questions and Answers**

10:00 a.m.

**Coffee Break***Waterford Lobby*

**Symposium 7. Innovations and CE Solutions: Vaccines as a Strategy for Preventing and Controlling Resistance**

*Haverford/Baccarat Ballroom*

Moderator: J. Todd Weber, M.D.  
*Centers for Disease Control and Prevention*  
*Atlanta, GA*

10:30 a.m.

- 25. Pneumococcal Vaccine and the Rise of Resistance in Non-Vaccine Serotypes**  
Matthew R. Moore, M.D.  
*Centers for Disease Control and Prevention*  
*Atlanta, GA*

10:55 a.m.

**Questions and Answers**

11:00 a.m.

- 26. Current Status of TB Vaccine Development**  
Michael J. Brennan, Ph.D.  
*Centers for Drug Evaluation and Research/FDA*  
*Silver Spring, MD*

11:25 a.m.

**Questions and Answers**

## FINAL PROGRAM

Wednesday, June 28, 2006 *(continued)*

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- 11:30 a.m.      **27. Malaria Vaccine Development**  
To Be Determined
- 11:55 a.m.      **Questions and Answers**
- 12:00 p.m.      **28. Pandemic Flu Preparedness and Emerging Resistance in Flu Strains**  
Robin Robinson, Ph.D.  
*U.S. Department of Health and Human Services*  
*Washington, DC*
- 12:25 p.m.      **Questions and Answers**
- 12:30 p.m.      **Adjournment/Participant Evaluation**

\* Speakers and presentations are subject to change

## Poster Session and Reception

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**Monday, June 26, 2006, 5:30 p.m. – 6:30 p.m.**

**Waterford/Lalique Ballroom**

**(posters will be on display throughout the remainder of the conference in the Waterford/Lalique Ballroom)**

- P1 Trends in Antimicrobial Prescribing in Ambulatory Care Settings in the United States, 1993-2004**  
**L. F. McCaig<sup>1</sup>, C. R. Friedman<sup>2</sup>;**  
<sup>1</sup>National Center for Health Statistics, Centers for Disease Control and Prevention, Hyattsville, MD, <sup>2</sup>National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, GA.
- P2 *In vitro* Activity of Designer Oxazolidinones against Multi-Drug Resistant Pathogens**  
**L. E. Lawrence, P. N. Danese, J. A. Sutcliffe;**  
Microbiology, Rib-X Pharmaceuticals, New Haven, CT.
- P3 New Agents for Drug Resistant Tuberculosis (TB)**  
**R. Goldman<sup>1</sup>, B. Laughon<sup>1</sup>, S. Franzblau<sup>2</sup>, J. Krahenbuhl<sup>3</sup>, A. Lenaerts<sup>4</sup>, I. Orme<sup>4</sup>, J. Secrist<sup>5</sup>, L. Young<sup>6</sup>, K. Plumley<sup>1</sup>, C. Lambros<sup>1</sup>;**  
<sup>1</sup>Division of AIDS, NIH-NIAID, Bethesda, MD, <sup>2</sup>Institute for Tuberculosis Research, University of Illinois, Chicago, IL, <sup>3</sup>National Hansen's Disease Program, Baton Rouge, LA, <sup>4</sup>Colorado State University, Fort Collins, CO, <sup>5</sup>Southern Research Institute, Birmingham, AL, <sup>6</sup>Kuzell Institute, San Francisco, CA.

## FINAL PROGRAM

- P4 Rapid Identification of Methicillin-Resistant *Staphylococcus aureus* Using *S. aureus* EVIGENE™ and MRSA EVIGENE™**  
A. R. Larsen<sup>1</sup>, H. Westh<sup>2</sup>, M. Holt<sup>3</sup>, K. G. Madsen<sup>3</sup>;  
<sup>1</sup>Statens Serum Institut, Copenhagen, Denmark, <sup>2</sup>Department of Clinical Microbiology, Hvidovre Hospital, Hvidovre, Denmark, <sup>3</sup>AdvanDx A/S, Vedbæk, Denmark.
- P5 Investigation of Antibiotic and Antibacterial Resistance in Skin Bacteria from Users and Non-Users of Antibacterial Wash Products in Home Environments**  
E. C. Cole<sup>1</sup>, R. M. Addison<sup>2</sup>, P. D. Dulaney<sup>3</sup>, K. E. Leese<sup>4</sup>;  
<sup>1</sup>Health Science Department, Brigham Young University, Provo, UT, <sup>2</sup>Clinical Microbiology/Infectious Disease, Duke University Medical Center, Durham, NC, <sup>3</sup>Health Research Services Division, Applied Environmental, Inc., Cary, NC, <sup>4</sup>Restoration Sciences, LLC, Cary, NC.
- P6 Susceptibility of Community-Isolated Enterococci to Clinically Important Antimicrobial Agents**  
A. M. ThurdeKoos<sup>1</sup>, E. J. Barzilay<sup>2</sup>, T. Miller<sup>2</sup>, K. D. Joyce<sup>1</sup>, K. Gay<sup>1</sup>, B. Lee<sup>3</sup>, M. J. Zervos<sup>4</sup>, E. DeBess<sup>5</sup>, M. Warren<sup>6</sup>, T. Barrett<sup>2</sup>, T. M. Chiller<sup>7</sup>;  
<sup>1</sup>FDDB, CDC/AREF, Atlanta, GA, <sup>2</sup>FDDB, CDC, Atlanta, GA, <sup>3</sup>Minnesota Department of Health, St. Paul, MN, <sup>4</sup>Henry Ford Hospital, Detroit, MI, <sup>5</sup>Oregon Department of Human Resources, Portland, OR, <sup>6</sup>University of Maryland, Baltimore, MD, <sup>7</sup>FDDB, CDC/US Public Health Service, Atlanta, GA.
- P7 Community-Associated Methicillin Resistance Profiles of *Staphylococcus aureus* Isolates Collected from Human, Canine, and Equine Patients**  
J. Clarke<sup>1</sup>, C. Clarke<sup>2</sup>, J. Hilley<sup>1</sup>;  
<sup>1</sup>ICX technologies, Inc., Stillwater, OK, <sup>2</sup>Oklahoma State University, Stillwater, OK.
- P8 Proximity to the U.S.-Mexico Border and Resistant Uropathogens**  
M. Marten<sup>1</sup>, L. Hofherr<sup>2</sup>, F. E. Myers, III<sup>3</sup>;  
<sup>1</sup>Clinical Epidemiology, Scripps Mercy Hospital, San Diego, CA, <sup>2</sup>Graduate School of Public Health, San Diego State University, San Diego, CA, <sup>3</sup>Clinical Epidemiology and Safety Systems, Scripps Mercy Hospital, San Diego, CA.
- P9 Investigation of Antibiotic Resistance and Resistance Genes from *Escherichia coli* in Amphibians with Proximity to Livestock**  
R. L. Cissell, A. G. Mathew, S. Liamthong, S. Rattanabtimtong;  
Animal Science, University of Tennessee, Knoxville, TN.
- P10 Aminoglycoside Resistance Genes Found in *Enterococcus* spp. Recovered from Retail Meats**  
S. M. Bodeis-Jones<sup>1</sup>, D. G. White<sup>2</sup>, & The NARMS Team<sup>1</sup>;  
<sup>1</sup>Division of Animal and Food Microbiology, FDA, Laurel, MD, <sup>2</sup>FDA, Laurel, MD.
- P11 Antimicrobial Resistance of *Salmonella* Species from Chicken, Turkey, Cattle and Swine Slaughter Isolates**  
J. S. Bailey<sup>1</sup>, P. J. Fedorka-Cray<sup>1</sup>, J. H. Haro<sup>1</sup>, N. Anandaraman<sup>2</sup>, B. Rose<sup>2</sup>, B. Salamone<sup>2</sup>;  
<sup>1</sup>Bacteriological Epidemiology and Antimicrobial Resistance, USDA, ARS, Athens, GA, <sup>2</sup>OPHS, USDA, FSIS, Washington, DC.

## FINAL PROGRAM

- P12 Antimicrobial Resistance in Small Animals: The Scope of the Problem**  
**D. M. Boothe**, T. Smaha;  
 Anatomy, Physiology, Pharmacology, Auburn University, Auburn University, AL.
- P13 Effectiveness of Intranasal Mupirocin in the Eradication of Methicillin-Resistant *Staphylococcus aureus* (MRSA) Nasal Colonization in Premature Infants**  
**J. L. Murillo**<sup>1</sup>, P. Harmon<sup>1</sup>, T. Chan<sup>2</sup>, M. Cohen<sup>3</sup>;  
<sup>1</sup>Epidemiology, Newark Beth Israel Medical Center, Newark, NJ, <sup>2</sup>Microbiology, Newark Beth Israel Medical Center, Newark, NJ, <sup>3</sup>Neonatology, Newark Beth Israel Medical Center, Newark, NJ.
- P14 Comparison of Outcomes between Methicillin-Resistant *Staphylococcus aureus* (MRSA) versus Methicillin-Sensitive *Staphylococcus aureus* (MSSA) Bacteremia in Inpatient Setting**  
**J. L. Murillo**, P. Murillo, N. Thannikkary;  
 Epidemiology, Newark Beth Israel Medical Center, Newark, NJ.
- P15 Susceptibility of *E. coli* to Fluoroquinolones Decreases with Age in Adult Women with Uncomplicated Urinary Tract Infections in the Community Setting: A Nationwide Study in an Israeli HMO**  
**N. R. Kahan**<sup>1</sup>, D. P. Chinitz<sup>2</sup>, D. A. Waitman<sup>1</sup>, D. Dushnitzky<sup>3</sup>, E. Kahan<sup>4</sup>, M. Shapiro<sup>5</sup>;  
<sup>1</sup>Medical Division, Leumit Health Fund, Tel-Aviv, Israel, <sup>2</sup>School of Public Health, Hebrew University of Jerusalem, Jerusalem, ISRAEL, <sup>3</sup>Leumit Health Fund, Tel-Aviv, Israel, <sup>4</sup>Department of Family Medicine, Sackler Faculty of Medicine, Tel-Aviv University, Tel-Aviv, Israel, <sup>5</sup>Department of Clinical Microbiology and Infectious Diseases, Hadassah-Hebrew University Hospital, Jerusalem, Israel.
- P16 Molecular Typing and Control of Multidrug Resistant *Acinetobacter baumannii* Infections in a Community Hospital in New York**  
**A. Ramani**<sup>1</sup>, J. M. Cox<sup>2</sup>, M. Kearney<sup>2</sup>, R. Atkinson<sup>3</sup>, N. Dumas<sup>3</sup>, D. Schoonmaker-Bopp<sup>3</sup>, M. E. Sweet<sup>4</sup>;  
<sup>1</sup>Medicine, Columbia Memorial Hospital, Hudson, NY, <sup>2</sup>Microbiology, Columbia Memorial Hospital, Hudson, NY, <sup>3</sup>Wadsworth Center, Laboratories for Bacterial Diseases, NYSDOH, Albany, NY, <sup>4</sup>Infection Control, Columbia Memorial Hospital, Hudson, NY.
- P17 The Relationships of Antimicrobial Control Policies and Hospital and Infection Control Characteristics with Antimicrobial Resistance Rates**  
**D. Quiros**, T. Giblin, S. Lin, E. Larson;  
 School of Nursing, Columbia University, New York, NY.
- P18 Low Colonization Rates with Methicillin-Resistant and Methicillin-Susceptible *Staphylococcus aureus* in the Northwest Brooklyn Pediatric Population**  
**M. Somorai, M.D.**<sup>1</sup>, M. John, M.D.<sup>1</sup>, M. Doymaz, Ph.D.<sup>2</sup>, S. M. Schwarz, M.D.<sup>1</sup>;  
<sup>1</sup>Pediatrics, Long Island College Hospital, Brooklyn, NY, <sup>2</sup>Microbiology, Beth Israel Medical Center, New York, NY.
- P19 Molecular Epidemiology of Methicillin-Resistant *Staphylococcus aureus* Infections in Mexico: a Multicenter Laboratory-Based Surveillance Study**  
**J. Reyes-Mar**<sup>1</sup>, J. Sifuentes-Osornio<sup>1</sup>, J. C. Tinoco-Favila<sup>2</sup>, P. Cornejo-Juarez<sup>3</sup>, R. Morfin-Otero<sup>4</sup>, M. Magaña-Aquino<sup>5</sup>, G. Vazquez<sup>6</sup>, A. Macias-Hernandez<sup>7</sup>, O. Novoa<sup>8</sup>, D. Soriano-Becerril<sup>9</sup>, J. Molina-Gamboa<sup>10</sup>, M. Zaidi-Jacobson<sup>11</sup>, A. M. Ramirez<sup>12</sup>,

## FINAL PROGRAM

E. Rodriguez-Noriega<sup>4</sup>, A. Ponce-de-Lèon<sup>1</sup>, M. Bobadilla-del-Valle<sup>1</sup>, A. Martinez-Gamboa<sup>1</sup>, A. L. Rolon<sup>1</sup>;

<sup>1</sup>Infectious Diseases, Instituto Nacional de Ciencias Medicas y Nutricion Salvador Zubiran, Mexico City, Mexico, <sup>2</sup>Infectious Diseases, Hospital General de Durango, Durango, Dgo., Mexico, <sup>3</sup>Infectious Diseases, Instituto Nacional de Cancerologia, Mexico City, Mexico, <sup>4</sup>Infectious Diseases, Instituto de Patología Infecciosa y Experimental, Guadalajara, Jal., Mexico, <sup>5</sup>Infectious Diseases, Hospital Central Ignacio Morones Prieto, San Luis Potosi, SLP., Mexico, <sup>6</sup>Infectious Diseases, Hospital Civil de Morelia, Morelia, Mich., Mexico, <sup>7</sup>Infectious Diseases, Hospital Universitario de Leon Guanajuato, Leon, Gto., Mexico, <sup>8</sup>Infectious Diseases, Hospital Infantil de Mexico Federico Gomez, Mexico City, Mexico, <sup>9</sup>Infectious Diseases, Instituto Nacional de Perinatologia, Mexico City, Mexico, <sup>10</sup>Infectious Diseases, Hospital de Enfermedades Cardiovasculares y Torax, Monterrey, NL., Mexico, <sup>11</sup>Infectious Diseases, Hospital O'Horan, Merida, Yuc., Mexico, <sup>12</sup>Infectious Diseases, Laboratorio de Diagnóstico Microbiologico, La Paz, BCS, Mexico.

**20 Increasing *Clostridium difficile* Morbidity and Mortality, Florida Hospitals, 1998-2003**

**R. A. Sanderson<sup>1</sup>**, O. Bendixsen<sup>2</sup>;

<sup>1</sup>Epidemiology, Florida Department of Health, Tampa, FL, <sup>2</sup>College of Public Health, University of South Florida, Tampa, FL.

**P21 Complicated Skin and Skin Structure Infections (cSSSI) with Community Phenotype Methicillin Resistant *Staphylococcus aureus* (CP-MRSA) in the Cubicin Outcomes Registry and Experience (CORE 2005)**

**W. J. Martone**, D. E. Katz;

Medical Affairs, Cubist Pharmaceuticals, Lexington, MA.

**P22 Complicated Skin and Skin Structure Infection (cSSSI) with Culture Confirmed *Staphylococcus aureus* Treated with Daptomycin (DAP): Cubicin Outcome Registry and Experience (CORE) 2005 Interim Analysis**

**D. E. Katz**, W. J. Martone;

Cubist Pharmaceuticals, Lexington, MA.

**P23 Epidemiological Cut-Off Values for Four Antimicrobial Agents against *Aeromonas salmonicida* Isolates Using MIC and Zone Diameter Frequency Distributions**

**R. A. Miller**, R. D. Walker, R. Reimschuessel;

Center for Veterinary Medicine, Food and Drug Administration, Laurel, MD.

**P24 Ciprofloxacin and Erythromycin Resistance in *Campylobacter*, NARMS, 1997-2004**

**F. Medalla<sup>1</sup>**, K. Gay<sup>1</sup>, J. Smith<sup>1</sup>, A. Stuart<sup>1</sup>, K. Joyce<sup>1</sup>, R. M. Hoekstra<sup>2</sup>, T. J. Barrett<sup>2</sup>, T. M. Chiller<sup>3</sup>;

<sup>1</sup>Atlanta Research and Education Foundation and Centers for Disease Control and Prevention, Atlanta, GA, <sup>2</sup>Centers for Disease Control and Prevention, Atlanta, GA, <sup>3</sup>U.S. Public Health Service and Centers for Disease Control and Prevention, Atlanta, GA.

**P25 Antimicrobial Resistance Patterns in the Puerto Rico Medical Center**

**D. Negron**, M. I. Santé;

Department of Pathology and Laboratory Medicine, University of Puerto Rico, San Juan, PR.

MEET THE EXPERT PRESENTERS

MEET THE  
EXPERT  
PRESENTERS

## MEET THE EXPERT PRESENTERS

**Hartmut Derendorf, Ph.D.**

**Meet the Experts Breakfast Session**

**Tuesday, June 27, 2006**

**7:00 am – 7:45 am**

Dr. Derendorf is Distinguished Professor and Chairman of the Department of Pharmaceutics at the University of Florida College of Pharmacy in Gainesville. He received his B.S. and Ph.D. in Pharmacy from the University of Münster in Germany and then joined the University of Florida as a Postdoctoral Fellow. He has been teaching Biopharmaceutics, Pharmacokinetics and Clinical Pharmacokinetics as a faculty member for the University. Dr. Derendorf has received several awards from the University of Florida to include the Teaching Improvement Award and the Research Foundation Professorship and International Educator of the Year Award. He has published over 260 scientific publications and given over 500 presentations at national or international meetings. He has published six textbooks and is one of the editors of the *International Journal of Clinical Pharmacology and Therapeutics*. His research interests include the pharmacokinetics and pharmacodynamics of corticosteroids, analgesics, antibiotics, as well as drug interactions. Professor Derendorf is a Fellow, former Secretary, Honorary Regent and President-elect of the American College of Clinical Pharmacology. He is a member of the American Association of Pharmaceutical Sciences, and the American Pharmaceutical Association among other organizations. He serves on the Nutrition and Therapeutics Committee of the NASA Space Medicine Program and the FDA Clinical Pharmacology Advisory Committee.

**L. Clifford McDonald, M.D.**

**Meet the Experts Breakfast Session**

**Tuesday, June 27, 2006**

**7:00 am – 7:45 am**

Dr. McDonald graduated from Northwestern University Medical School in Chicago. He completed his internal medicine residency at Michigan State University and an infectious diseases

fellowship at the University of South Alabama, followed by a fellowship in Medical Microbiology at Duke University. He is board-certified in infectious diseases by the American Board of Internal Medicine and has a special competency in medical microbiology certified by the American Board of Pathology. He completed additional post-graduate training in applied medical epidemiology at the Centers for Disease Control and Prevention where he was an Epidemic Intelligence Service Officer in the Hospital Infections Program of the National Center for Infectious Disease. Past positions have included Associate Investigator at the National Health Research Institutes in Taiwan, where he helped to develop an island-wide surveillance system for antimicrobial resistance, and Assistant Professor in the Division of Infectious Diseases at the University of Louisville, where he worked as a hospital epidemiologist in infection control. Dr. McDonald is currently a medical epidemiologist in the Division of Healthcare Quality Promotion at the Centers for Disease Control and Prevention. His research interests focus on understanding the epidemiology and mechanisms, as well as methods for prevention, of antimicrobial resistance. He is a fellow of the American College of Physicians and the Society for Healthcare Epidemiology of America, and is a member of both the Infectious Diseases Society of America and the American Society for Microbiology. He has authored and/or coauthored more than 50 research papers and book chapters on infectious disease topics.

**John H. Powers, M.D.**

**Meet the Experts Breakfast Session**

**Tuesday, June 27, 2006**

**7:00 am – 7:45 am**

Dr. Powers is the Lead Medical Officer for Antimicrobial Drug Development and Resistance Initiatives in the Office of Antimicrobial Products, Center for Drug Evaluation and Research of the U.S. Food and Drug Administration (FDA). Prior to joining the FDA, Dr. Powers was an Assistant Professor in the Division of Infectious Diseases at the University of Maryland School of Medicine. He is currently an Assistant Clinical Professor of Medicine

## MEET THE EXPERT PRESENTERS

at the University of Maryland and the George Washington University School of Medicine. Dr. Powers is an infectious diseases physician at the National Institute of Allergy and Infectious Diseases of the National Institutes of Health, where he actively sees patients and attends on infectious diseases service. Dr. Powers received his medical degree and residency training from Temple University School of Medicine, and served as Chief Resident. He completed his infectious diseases training at the University of Virginia School of Medicine. Dr. Powers is board certified in internal medicine and infectious diseases. He is a fellow of the American College of Physicians, the American Society for Internal Medicine, and the Infectious Diseases Society of America. He has been an investigator on over 50 clinical trials prior to joining the FDA. He has authored several book chapters and published several papers on clinical trial design in the study of infectious diseases. Dr. Powers has won several awards for teaching medical students, residents, and fellows. In addition, he is on the editorial board of *Antimicrobial Agents and Chemotherapy*, as well as a reviewer for several other scientific journals. He is co-chair of the U.S. government's Inter-Agency Task Force on Antimicrobial Resistance.

**Gary W. Procop, M.D.**

**Meet the Experts Breakfast Session**

**Tuesday, June 27, 2006**

**7:00 am – 7:45 am**

Dr. Procop is the Head of the Section of Clinical Microbiology at the Cleveland Clinic Foundation. He is also a staff member of the Department of Anatomic Pathology, where he specializes in infectious disease pathology. He is the Program Director for the Clinical Microbiology Fellowship and an Associate Professor of Pathology at the Cleveland Clinic Lerner College of Medicine of the Case Western Reserve University. Dr. Procop is a member of the College of American Pathologist's Clinical Microbiology Resource Committee. He received his master of science and medical degrees from Marshall University. He did his pathology residency training at Duke University Medical

Center, where he was Chief Resident, and his fellowship in clinical microbiology at the Mayo Clinic. Dr. Procop has given more than 200 poster presentations, and has authored or co-authored 86 peer-reviewed manuscripts and 17 chapters. He has three patents, two of which concern rapid and specific pathogen detection using real-time PCR. His primary interests are molecular microbiology, mycology, parasitology, and infectious disease pathology.

**Jane F. Robens, D.V.M.**

**Meet the Experts Breakfast Session**

**Tuesday, June 27, 2006**

**7:00 am – 7:45 am**

Dr. Robens is the National Program Leader for Food Safety and Health for Agricultural Research Service (ARS) of the U. S. Department of Agriculture (USDA). She successfully formulated agency-wide food safety program objectives, plans, and policies through the establishment, articulation, and support of food safety budget goals and program objectives. She directed the development of the ARS segment of Collaboration on Animal Health and Food Safety, a joint effort between three agencies of the USDA. Dr. Robens established research to improve dioxin methodology and locate contamination source for beef, and a mycotoxin research program for prevention of aflatoxin and fumonisins. She has chaired USDA interagency working groups responsible for preparing briefing materials for departmental responses to Congress on questions of food safety. Dr. Robens received her medical degree in veterinary medicine from Cornell University.

**David H. Lloyd, Ph.D., F.R.C.V.S.**

**Meet the Experts Breakfast Session**

**Wednesday, June 28, 2006**

**7:00 am – 7:45 am**

Dr. Lloyd is Professor of Veterinary Dermatology at the Royal Veterinary College in England. He leads a clinical and research group with interests focused on the biology of the skin surface, cutaneous infection

## MEET THE EXPERT PRESENTERS

and immunity, and antimicrobial resistance with special interest in staphylococci and yeasts of the genus *Malassezia*. His work covers small animals, horses, and farm animals. Dr. Lloyd is founding member and past-president of the European Society of Veterinary Dermatology, and a member of the European College of Veterinary Dermatology and the Veterinary Wound Healing Association. He was founding editor and Editor-in-Chief of the journal, *Veterinary Dermatology*. He served as president of the 5<sup>th</sup> World Congress of Veterinary Dermatology and is a board member of the World Congress of Veterinary Dermatology Association. Dr. Lloyd received his Ph.D. from the University of Glasgow in Scotland. He has authored and/or co-authored more than 150 research papers and book chapters on infectious disease topics. In addition, he serves as a reviewer for several scientific journals and proceedings.

**Robin A. Robinson, Ph.D.**

**Meet the Experts Breakfast Session**

**Wednesday, June 28, 2006**

**7:00 am – 7:45 am**

Dr. Robinson is Associate Director of the Pandemic Preparedness Program in the Office of Public Health Emergency Preparedness of the U.S. Department of Health and Human Services (DHHS). Prior to his position at DHHS, Dr. Robinson was Director of Vaccines at Novavax, Inc. Additionally, he served as an Assistant Professor of Microbiology and Immunology at the University of Texas Southwestern Medical School in Dallas, Texas. He is a member of several professional societies including the American Society for Virology, the American Society for Microbiology, and the American Association for the Advancement of Science. Dr. Robinson serves as influenza and vaccine expert on several panels and teams for the World Health Organization and as an *ad hoc* member of the Vaccine and Related Biological Products Advisory Council for the Food and Drug Administration. He received his doctoral degree in microbiology from the University of Mississippi Medical School and completed his postdoctoral fellowship in tumor

virology at Princeton University and the State University of New York at Stony Brook. Dr. Robinson has authored and/or co-authored more than 40 research papers and book chapters on viral pathogenesis, tumor viruses, and vaccines, and holds more than 30 patents on vaccines. He serves on the editorial board and as reviewer for several professional scientific and technical journals on virology, vaccines, and biotechnology.

**J. Todd Weber, M.D.**

**Meet the Experts Breakfast Session**

**Wednesday, June 28, 2006**

**7:00 am – 7:45 am**

Dr. Weber is Director, Office of Antimicrobial Resistance and Assistant to the Director in the Office of the Director of the National Center for Infectious Diseases at the Centers for Disease Control and Prevention (CDC). He is co-chair of the Federal Interagency Task Force on Antimicrobial Resistance. He has been at CDC since 1990 where he has worked in the divisions of Bacterial and Mycotic Diseases, Sexually Transmitted Disease Prevention, and the Division of HIV/AIDS Prevention. Dr. Weber is a graduate of the College of Physicians and Surgeons of Columbia University and was trained in internal medicine at Bellevue Hospital Center and Tisch Hospital in New York City. He is a fellow of the American College of Physicians and the Infectious Diseases Society of America. Dr. Weber has authored/co-authored numerous publications in scientific journals.

## ABSTRACTS OF INVITED PRESENTATIONS

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**1** Antimicrobial Resistance: The Next Pandemic

R. Moellering

Beth Israel Deaconess Medical Center  
Boston, MA**Educational Objective:**

At the conclusion of this presentation, the participant will review the clinical significance of and potential for preventing further problems related to antimicrobial resistance.

**Summary:**

The immense promise of antimicrobial chemotherapy, one of the major medical advances of the second half of the 20<sup>th</sup> Century, has been dulled by the relentless development of resistance by the very microorganisms against which the therapy has been directed. There are literally no clinically important bacteria which have not developed some type of resistance to antibiotics. Older, toxic drugs such as the polymyxins are now being called upon as drugs of last resort in a number of settings around the world because of the development of resistance to literally all other antimicrobials by gram-negative bacteria such as *Pseudomonas*, *Acinetobacter*, and others. But resistance is not limited to bacteria. Fungi and viruses have also developed significant resistance to antimicrobials. The presently circulating strains of influenza A virus are resistant to amantadine and rimantadine and the avian flu virus has already developed resistance to oseltamivir in some settings. The clinical use of antimicrobials contributes greatly to the emergence of resistance, but use of antimicrobials for veterinary, agricultural, aquacultural and industrial use of these products also plays a role. As bacteria (and other microorganisms) develop increasing resistance, especially in the hospital setting, the clinician is tempted to use antibiotics in growing numbers of combinations to make certain that he or she has "adequate coverage." This leads to a vicious cycle of increasing resistance and increased antimicrobial utilization. Potential solutions to the problem of developing antimicrobial resistance are complex but must be implemented if we are to prevent a pandemic of infections due to resistant microorganisms.

**Reference:**

1. Wood MJ, Moellering RC, Sr. Microbial Resistance, Bacteria and More. *Clin Infect Dis* 2003; 36 (Suppl 1): S2-S3.

**2** Using Diagnostic Testing to Reduce the Overuse of Antibiotics in Nosocomial Pneumonia

M. Niederman

Winthrop University Hospital  
Mineola, NY**Educational Objective:**

At the conclusion of this presentation, the participant will review the usage patterns of antibiotics in critically ill patients with nosocomial pneumonia and describe approaches to the effective use of therapy that pay attention to the need to avoid overuse of antibiotics.

**Summary:**

The management of nosocomial pneumonia and other severe infections requires a strategy for antibiotic use that is designed to achieve prompt and accurate empiric therapy, without overusing antibiotics. Although efforts at antibiotic restriction have been attempted, they have not eliminated the problem. A more effective strategy may include the combination of a "de-escalation" approach in conjunction with rapidly collected, accurate diagnostic data. This approach should be geared to improved patient outcome in the setting of responsible antibiotic usage. The centerpiece of this approach is to initiate empiric therapy with a broad-spectrum treatment regimen, based on a knowledge of the most likely etiologic pathogens for the given infection, modified by awareness of local patterns of microbiology and antimicrobial resistance. Prior to therapy, patients require collection of a lower respiratory tract sample for diagnostic testing. Traditional culture approaches require

2-3 days before information can be obtained to narrow and focus therapy. If rapid diagnostic testing can be used on these samples, focused and effective therapy may be accomplished earlier. The key, and remaining controversy is whether such diagnostic testing, based on sensitive molecular diagnostic methods, should be used to modify therapy on the basis of positive or negative findings. This presentation will argue that the data have their greatest value when negative, since the absence of a pathogen can allow more focused and responsible antibiotic usage. If de-escalation is based on this type of information, it could lead to using a more narrow spectrum agent, reducing the number of antibiotics, stopping therapy altogether in patients not likely to have infection, as well as making efforts to reduce duration of therapy.

**References:**

1. Niederman MS. The importance of de-escalating antimicrobial therapy in patients with ventilator-associated pneumonia. *Seminars in Respiratory and Critical Care Medicine* 2006; 27: 45-50.
2. Niederman MS. Use of broad-spectrum antimicrobials for the treatment of pneumonia in seriously ill patients: maximizing clinical outcomes and minimizing selection of resistant organisms. *Clin Infect Dis* 2006; 42: S 72-81.

**3**

## Rapid Assays for Drug Resistant Tuberculosis and Their Application to Developing and Developed Countries

D. Alland

New Jersey Medical School  
Newark, NJ**Educational Objective:**

At the conclusion of this presentation, the participant will discuss the scope of the tuberculosis drug-resistance problem and the types of rapid assays available to detect drug resistance.

**Summary:**

Each year, approximately 3 million people die from *Mycobacterium tuberculosis* infections. Standard techniques to identify and determine the antibiotic susceptibility of *M. tuberculosis* infections are insensitive and slow. More rapid PCR techniques have been developed to identify some types of antibiotic resistance. However, most are labor intensive and require technical sophistication. PCR inhibitors, the risk of sample cross-contamination, and the limited ability to concentrate samples also hinders PCR applicability. We have developed a new method to overcome these limitations. A low-cost plastic cartridge automatically concentrates all bacilli present in a sputum sample, removes PCR inhibitors, lyses the cells, and flushes the resulting *M. tuberculosis* DNA into a built-in PCR reaction tube. Nested PCR is performed automatically using a well-established, multiplexed molecular beacon assay that detects 95% of all mutations associated with rifampin resistance. The system isolated and detected as few as 100 bacilli per milliliter of sputum in one hour. Thus, this method is as rapid as sputum microscopy, but is more sensitive. Testing of clinical samples is now underway.

**Reference:**

1. El-Hajj H, Marras SAE, Tyagi S, Kramer FR, Alland D. Detection of Rifampin Resistance in *Mycobacterium tuberculosis* in a Single Tube with Molecular Beacons. *Journal of Clinical Microbiology* 39:4131-4137, 2001.

## ABSTRACTS OF INVITED PRESENTATIONS

4

**Preventing Antimicrobial Resistance with Nuclear Acid Diagnostics: A Strategy for Success**  
 P. Dailey  
 Roche Molecular Systems, Inc.  
 Alameda, CA

**Educational Objective:**

At the conclusion of this presentation, the participant will review the current status of the use of molecular diagnostic assays to assist in directing specific antimicrobial therapy for major microbial diseases, and discuss the challenges that remain before the more widespread use of such assays.

**Summary:**

Molecular (nucleic acid) diagnostic assays have had a major impact in the treatment of chronic viral diseases (HIV/AIDS, Hepatitis C, and Hepatitis B) and the screening for sexually-transmitted infections. Despite major advances in nucleic acid amplification technology, automation, and instrumentation, molecular testing has failed to have a major impact on the treatment of most common microbial diseases such as community-acquired pneumonia, meningitis, ventilator-associated pneumonia, and healthcare-associated infections. Molecular testing is actually only performed in approximately 5% of hospitals in the developing world. "Targeted therapy" based on molecular diagnostic testing remains a wish—not a reality. The reasons for this failure will be discussed. Successful development of effective assays requires a change in their design so that they directly and clearly impact clinical management. Unless molecular testing can affect empiric, broad-spectrum antimicrobial therapy, it will continue to have limited usefulness in increasing diagnostic accuracy, enabling more prudent antimicrobial use, and slowing the development of antimicrobial resistance. Success may require a fundamental change in the way that molecular assays are designed and developed.

**References:**

- Peterson LR, and Dalhoff, A. Towards targeted prescribing: will the cure for antimicrobial resistance be specific, directed therapy through improved diagnostic testing? *J. Antimicrobial Chemotherapy* 53: 902-905 (2004).
- Harbarth S, and Samore MH. Antimicrobial resistance determinants and future control. *Emerg. Infect. Dis.* 11:794-801 (2005).

5

**Diagnostics in Agriculture**  
 R. Oberst  
 Kansas State University  
 Manhattan, KS

**Educational Objective:**

At the conclusion of this presentation, the participants will discuss the needs for advancing diagnostics for routine animal disease detection and early diagnosis of exotic and emerging diseases of economic and animal/public health concerns, and the challenges of defining the diagnostic capacity and capabilities for these investigations as they relate to response, control, and eradication programs.

**Summary:**

Traditional animal health diagnostics in the U.S. for identifying enzootic, exotic and emerging pathogens is confronted with numerous challenges. U.S. animal health infrastructure has not significantly deployed the necessary technologies needed to accommodate the anticipated response, control and eradication programs predicted in the event of the intentional or unintentional introduction of foreign or high consequence biological agents in our national herds/flocks. Deploying better diagnostic tests for identifying all animal diseases should be made a priority. Authorization of the National Animal Health Laboratory Network (NAHLN) by the U.S. Congress in 2002 was a major change in policy and shifted the responsibility of foreign animal disease diagnostics to a shared responsibility between federal and state-funded veterinary diagnostic facilities.

The full implementation of the NAHLN mission will require defining the agents to be tested; the development/validation of standardized assays for these agents; proficiency

training of lab personnel/equipment; developing sufficient containment facilities to handle routine testing and surge capacity; coordinating/installing communication linkages between veterinary laboratories within NAHLN and other laboratory networks that serve as national, reference or sentinel labs, such as the CDC's Laboratory Response Network (LRN), FDA's Food Emergency Response Network (FERN), and other Federal, State, military, and international laboratories.

**Reference:**

- Animal Health at the Crossroads: Preventing, Detecting, and Diagnosing Animal Diseases. Committee on Assessing the Nation's Framework for Addressing Animal Diseases, National Research Council. National Academy of Sciences; 2005. Available at: <http://www.nap.edu/catalog/11365.html>. Accessed May 12, 2006.

6

**Treatment Options and Trends**  
 V. Fowler  
 Duke University Medical Center  
 Durham, NC

**Educational Objective:**

At the conclusion of the presentation, the participant will know the available treatment alternatives for infections caused by Methicillin-resistant *S. aureus* in the community and the healthcare setting, as well as potential new agents in development.

**Summary:**

The problem of MRSA is large and growing. Already a leading cause of infection in the hospital, MRSA is now one of the most common causes of community-acquired infection, as well.

Because of the diversity of disease caused by MRSA, treatment hinges upon the extent of infection. MRSA infection limited to the skin (e.g., small abscesses, etc) may be treated with simple abscess drainage and/or short courses of oral antibiotics, while more severe forms of MRSA infections necessitate extensive surgical debridement and extended courses of intravenous therapy. Several options exist for both oral and parenteral therapy of MRSA.

Challenges to treatment of MRSA include the increasing complexity of infections cause by this pathogen, the increasing problem of antimicrobial resistance, and a dwindling number of new antibiotics under development.

**Reference:**

- Stryjewski ME, Chu VH, Cabell CH, Fowler VG, Jr. Issues in the management of endocarditis due to resistant gram positive organisms. *Current Infectious Disease Reports* 2004; 6:283-291.

7

**Rapid Diagnostics of Bacterial Pathogens and Mechanisms of Resistance**  
 G. Procop  
 The Cleveland Clinic Foundation  
 Cleveland, OH

**Education Objective:**

At the conclusion of this presentation, participants will review rapid molecular methods that may be used for the identification of bacterial pathogens, and the detection of genetic factors that confer resistance to antimicrobial agents and select virulence factors.

**Summary:**

The initial step in therapy begins with the appropriate diagnosis, whether achieved at the bedside or through laboratory testing. Cultures that become positive are often the first definitive proof of a serious bacterial infection, although the clinical signs and

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symptoms that prompted the culture clearly precede the positive culture, and are often linked to empiric antimicrobial coverage. However, sometimes the empiric antimicrobial coverage, even with broad-spectrum agents, may fail to cover the infecting pathogen.

Rapid molecular diagnostic methods, such as *in situ* hybridization and species-specific real-time PCR assays afford the definitive identification of the infecting microorganism. The results from such testing may be available 24-72 hours sooner than results from traditional methods. This allows for more targeted antimicrobial coverage, which may be modified based on local antibiogram data. In addition, real-time PCR techniques may be used to detect genetic elements associated with resistance, such as the *mecA* or *vanA* and *vanB* genes. These methods may also be used to detect virulence factors, such as the PVL gene, or to subtype the *mec* cassette to provide epidemiologic information (e.g., CAMRSA).

Finally, multiplex technology and post-amplification analysis following broad-range PCR hold promise as methods of rapidly identifying virtually all microorganisms of clinical importance, and with time and further development perhaps even the characterization of complex mechanisms of resistance, such as the numerous genes that confer ESBL and AmpC resistance profiles.

**References:**

1. Ibrahim EH, et al. The influence of inadequate antimicrobial treatment of bloodstream infections on patient outcomes in the ICU setting. *Chest*, 2000. 118(1): p. 146-55.
2. Jansen GJ, et al. Rapid identification of bacteria in blood cultures by using fluorescently labeled oligonucleotide probes. *J Clin Microbiol*, 2000. 38(2): p. 814-7.
3. Kempf VA, K. Trebesius, I.B. Autenrieth. Fluorescent In situ hybridization allows rapid identification of microorganisms in blood cultures. *J Clin Microbiol*, 2000. 38(2): p. 830-8.

## 8

**Community MRSA: Epidemiology**  
H. Chambers  
San Francisco General Hospital  
San Francisco, CA

**Educational Objective:**

At the conclusion of this presentation the participant will identify the characteristic features of the molecular and clinical epidemiology for community MRSA clones found in the United States.

**Summary:**

Methicillin resistant *Staphylococcus aureus* (MRSA) is no longer an exclusively nosocomial pathogen. Multiple outbreaks and some limited population-based prevalence data indicate that MRSA has arrived as a community pathogen. The clinical and molecular epidemiology of community MRSA is distinctive. They tend to be susceptible to most antibiotics other than beta-lactams and they tend to occur in outbreak settings, at least thus far. Initially associated with skin and soft tissue infections primarily, as the prevalence of these community MRSA strains increases, the spectrum of disease broadens. Two predominant community MRSA clones, USA300 and USA400 (MW2), are responsible for most of the disease in the US; both contain PVL genes, encoding a virulence factor strongly associated with emergence of community MRSA, as well as a unique resistance cassette element, type IV SCCmec (staphylococcal chromosomal cassette). The USA300 clone is particularly virulent and fit, displacing other clones both in communities and in the hospital. As the burden of MRSA disease increases inside and outside of the hospital, particularly if there is also an increase in disease severity, management of staphylococcal infections will be significantly and adversely impacted.

**Reference:**

1. Zetola N, Francis JS, Nuermberger EL, Bishai WR. Community-acquired methicillin-resistant *Staphylococcus aureus*: an emerging threat. *Lancet Infect Dis* 5:275-86, May 2005. PMID: 15854883

## 9

**The Community Angle: Biology and Epidemiology**  
F. Lowy  
Columbia University  
New York, NY

**Educational Objective:**

At the conclusion of this presentation, the participant will review the recent emergence of *Staphylococcus aureus* as a community-based pathogen; and discuss the molecular and epidemiologic features of the new patterns of staphylococcal disease that are occurring throughout the United States and elsewhere.

**Summary:**

In the 1990s a change in the epidemiology of methicillin resistant *Staphylococcus aureus* (MRSA) was noted when serious, sometimes fatal, infections began to occur among healthy members of the community without the traditional hospital-associated risk factors. These MRSA infections have for the most part involved the skin and soft tissues although 6-8% of infections have been more invasive. They have been reported among healthy children, the urban poor and homeless, military personnel, prisoners, injection drug users and members of athletic teams. Features common to these outbreaks have included close contact, minor abrasions, poor hygienic conditions and shared materials. Increasingly these strains are being reported in the hospital setting. They are therefore establishing themselves as nosocomial as well as community-based pathogens. The widespread nature of these outbreaks is reminiscent of the phage 80/81 *S. aureus* outbreaks observed in the 1950s.

A limited number of MRSA clones have been responsible for these infections. In contrast with hospital-associated MRSA, these strains are often susceptible to other families of antibiotics (although this too is evolving). A feature common to these community-associated MRSA clones is the presence of unique genetic transposable elements [staphylococcal chromosomal cassette *mec* (SCC*mec*)] that appear more genetically mobile than other SCC*mec* elements.

**References:**

1. Baba T, Takeuchi F, Kuroda M, et al. Genome and virulence determinants of high virulence community-acquired MRSA. *Lancet* 2002;359(9320):1819-27.
2. Herold BC, Immergluck LC, Maranan MC, et al. Community-acquired methicillin-resistant *Staphylococcus aureus* in children with no identified predisposing risk. *JAMA* 1998; 279(8):593-8.
3. Chambers HF. The Changing Epidemiology of *Staphylococcus aureus*? *Emerg Infect Dis* 2001;7(2):178-82.
4. Miller LG, Perdreau-Remington F, Rieg G, et al. Necrotizing fasciitis caused by community-associated methicillin-resistant *Staphylococcus aureus* in Los Angeles. *N Engl J Med* 2005;352(14):1445-53.

## 10

**Update on Epidemiology in the U.S. and Europe**  
L. McDonald  
Centers for Disease Control and Prevention  
Atlanta, GA

**Educational Objective:**

At the conclusion of this presentation, the participant will discuss how the epidemiology of *Clostridium difficile*-associated disease (CDAD) is changing and possible reasons for this change.

**Summary:**

Several lines of evidence suggest a changing epidemiology of CDAD. First, there have been increased reports of individual hospital outbreaks, in many instances associated with increased deaths and colectomies. Second, there has been a sharp increase since 2000 in the number and rate of U.S. acute care hospital discharges coded for CDAD. Finally, national surveys conducted over the past two years suggest that 30-40% of U.S. infectious disease physicians have perceived increases in the incidence, severity, and likelihood of CDAD recurrence. Possible reasons for this increase in incidence and disease severity could involve trends in antimicrobial or other drug (i.e., stomach acid

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suppressing medication) usage, changes in infection control practices (i.e., hand hygiene or environmental surface disinfection), or the emergence of one or more strains of *C. difficile* with increased antimicrobial resistance and/or virulence. Indeed just such a novel strain has emerged and appears responsible for outbreaks in the United States, Canada, and Europe. This strain possesses somewhat unique toxin gene variations, including a deletion in a putative negative regulator (*tcdC*) for toxins A and B and genes for an additional toxin known as binary toxin. Although this strain has been isolated infrequently from U.S. patients over the past 20 years, it has recently (since 2000) appeared as a cause of major outbreaks; one reason for this may be the emergence of increased resistance to fluoroquinolones in this strain, possibly providing a selective advantage over other strains. There is also evidence to suggest that this strain produces much greater quantities of both toxins A and B and that this strain produces these toxins earlier during log phase growth. Experiences to date suggest that control of hospital outbreaks caused by this strain can be difficult to achieve and will likely require multifaceted interventions including careful attention to infection control practices as well as some form of antimicrobial usage restrictions. Finally, the most recent development in the changing epidemiology of CDAD is what appears to be increasingly severe disease in previously low risk populations including individuals with little or no exposure to either healthcare settings or antimicrobials. Improved surveillance will be necessary to more fully understand the magnitude of community-acquired CDAD and possible reasons for recent increases in its incidence.

**Reference:**

1. McDonald LC, Killgore GE, Thompson A, Owens RC, Kazakova SV, Sambol SP, Johnson S, Gerding DN. Emergence of an epidemic, toxin gene variant strain of *Clostridium difficile* responsible for outbreaks in the United States between 2000 and 2004. *New Eng J Med* 2005 Dec; 353: 2433-41.

**11** Update on Epidemiology in Montreal and Quebec  
V. Loo  
McGill University Health Center  
Montreal, QB, Canada

**Educational Objective:**

At the conclusion of this presentation, the participant will discuss the current status of the epidemiology of *Clostridium difficile* in Montréal and other areas of Québec.

**Summary:**

*Clostridium difficile* is an important cause of nosocomial diarrhea. In late 2002, several hospitals in Québec, Canada noted a marked increase in the incidence of *C. difficile* associated diarrhea (CDAD) with increased morbidity and mortality. Hospitals in Québec had a higher incidence of CDAD compared with other Canadian provinces. Similar outbreaks of CDAD have been reported in the United States and recently in the United Kingdom and the Netherlands.

A predominant strain of *C. difficile* (NAP1/027) that is resistant to fluoroquinolones, binary toxin positive and has a deletion in the regulatory component of toxins A and B is responsible for the geographically dispersed outbreaks of CDAD. This strain produces 16 times more toxin A and 23 times more toxin B in vitro compared with control strains.

Hospitals need to be vigilant and should conduct surveillance for CDAD. Early diagnosis and treatment are essential. Effective infection control measures coupled with judicious use of antibiotics need to be in place to prevent CDAD outbreaks.

**Reference:**

1. Loo VG, Poirier L, Miller MA, et al. A predominantly clonal multi-institutional outbreak of *Clostridium difficile*-associated diarrhea with high morbidity and mortality. *New Engl J Med* 2005; 353: 2442-49.

**12** Antibiotic Use and Antibiotic Risk Factors for *Clostridium difficile* Associated Diarrhea  
J. Pepin  
University of Sherbrooke  
Sherbrooke, QB, Canada

**Educational Objective:**

At the conclusion of this presentation, the participant will discuss the risk associated with various antibiotics in the context of an emerging, toxin-hyperproducing, strain of *Clostridium difficile*.

**Summary**

During an epidemic of *Clostridium difficile*-associated diarrhea (CDAD) in a tertiary care hospital of Quebec, two thirds of nosocomial cases were caused by the hypervirulent NAP1/027 toxinotype III strain. A cohort study showed that fluoroquinolones were the highest-risk antibiotics; the adjusted relative risk (RR) of ciprofloxacin (3.7) was higher than that of levofloxacin (2.5). Intermediate-risk antibiotics included cephalosporins, macrolides, clindamycin and  $\beta$ -lactam/ $\beta$ -lactamase inhibitors (RR: 1.6-1.9). Aminoglycosides, cotrimoxazole, metronidazole and IV vancomycin were not associated with CDAD after adjustment for confounders. For fluoroquinolones, the risk increased in parallel with duration of use (RR 2.4, 3.0, 4.4 with 1-3, 4-6 and  $\geq 7$  days of use), while for  $\beta$ -lactam/ $\beta$ -lactamase inhibitors RR did not vary (1.8, 2.0, 1.8). When the epidemic was recognized in mid-2003, infection control measures were strengthened: nevertheless, incidence more than doubled over the following 6 months. CDAD incidence began to decrease in the spring of 2004, when recommendations about use of antibiotics were disseminated to all physicians. Comparing FY 2005-06 to FY 2003-04, there was a 26% reduction in the use of all antibiotics among hospitalised patients. The reduction was more marked for cefuroxime (-97%), ceftriaxone (-86%), IV ciprofloxacin (-48%) and oral ciprofloxacin (-25%). There were important increases in the use of piperacillin/tazobactam (+62%) and respiratory fluoroquinolones (+105%). During the 2005-06 winter, CDAD incidence was about one third of the 2003-04 winter. Although mathematical modelling will be necessary to sort out the impact of various interventions, our results suggest that when CDAD incidence reaches epidemic levels, the hospital environment might be a more important source of infection than the hands of personnel. More selective use of antibiotics was temporally associated with a reduction in CDAD incidence. Most of the 26% reduction in overall use of antibiotics was achieved through a shortening of the duration of antimicrobial therapy of common infections.

**Reference:**

1. Bignardi G. Risk factors for *Clostridium difficile* infection. *J Hosp Infect* 1998; 40(1):1-15

**13** Clinical Management of *Clostridium difficile*  
M. Miller  
McGill University  
Montreal, QB, Canada

**Educational Objective:**

At the conclusion of this presentation, the participant will review the various antibiotic and non-antibiotic means of controlling and treating CDAD, as well as the new developments and approaches in managing this disease.

**Summary:**

*Clostridium difficile*-associated diarrhea (CDAD) remains the single most frequent and important nosocomial enteric infection. Recent epidemiologic studies and molecular characterization of infecting isolates have demonstrated the appearance of a "hyper-virulent" strain which is associated with severe disease and higher lethality. Community-acquired cases are also increasing in frequency and severity. The approach to effectively managing CDAD includes:

- meticulous attention to Infection Prevention and Control issues
- reduction in antibiotic use (the single most important inciting factor)

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- knowledge of the various clinical syndromes (e.g. profound leukocytosis, ileus)
- prompt diagnosis
- prompt institution of therapy
- knowledge of expected complications (e.g. ileus, sepsis) and their management
- understanding the role of surgery (i.e. colectomy) for severe disease
- effective management of relapsing disease

We are in need of a validated severity-of-illness scoring system for patients with CDAD, in order to better conduct clinical trials and improve our therapeutic strategies. Newer therapies (antibiotic-based, non-antibiotic-based, and immune-based) are on the horizon, and are desperately needed for CDAD prevention as well as for treating patients with severe disease and multiple relapses.

**References:**

1. Loo VG, Poirier L, Miller MA, et al. A predominantly clonal multi-institutional outbreak of *Clostridium difficile*-associated diarrhea with high morbidity and mortality. *NEJM* 2005;353:2442-9
2. Johnson S, Gerding DN. *Clostridium difficile*-associated diarrhea. *Clin Infect Dis* 1998;26:1027-36

**14** The Role of Pharmacological Predictors in Drug Development  
H. Derendorf  
University of Florida  
Gainesville, FL

**Educational Objective:**

At the conclusion of this presentation, the participant will review the current status of pharmacokinetic and pharmacodynamic approaches used in drug development to streamline dose optimization strategies with greatest likelihood of therapeutic success and minimum chance for resistance development.

**Summary:**

Pharmacokinetic/pharmacodynamic (PK/PD) modeling in recent years has become an established approach in optimizing dosing of drugs. In the anti-infective field, this has mainly been done using serum concentration as the source for PK information and the minimum inhibitory concentration (MIC) as a measure for PD properties. These measures then have been integrated in PK/PD-indices such as  $C_{max}/MIC$ ,  $AUC/MIC$  and  $time > MIC$  which have been applied for the different classes of anti-infective agents. Although these indices have had a significant impact in a rational dose selection process, there are still major shortcomings. On the PK side, it is important that only free, unbound concentrations are considered in the calculation of these indices. Furthermore, unbound serum concentration should only be used if they are not significantly different from the actual drug concentration at the site of the infection. Unbound drug concentrations at the site of infection can frequently be measured using microdialysis. On the PD side it can be shown that MIC is a suboptimal measure for anti-infective potency. Kill-curve analysis allows a much more detailed data analysis and provides a more solid input in the dose selection process. Examples for all of these issues will be provided.

**References:**

1. Müller M, de la Pena A, Derendorf H. Issues in pharmacokinetics and pharmacodynamics of anti-infective agents: kill curves versus MIC. *Antimicrob Agents Chemother.* Feb 2004;48(2):369-377.
2. Müller M, de la Pena A, Derendorf H. Issues in pharmacokinetics and pharmacodynamics of anti-infective agents: distribution in tissue. *Antimicrob Agents Chemother.* May 2004;48(5):1441-1453.

**15** Use of Pharmacologic Predictors in Prevention or Treatment of Resistance  
O. Cars  
Swedish Institute for Infectious Diseases  
Solna, Sweden

**Educational Objective:**

At the conclusion of this presentation, the participant will discuss the current pharmacological concepts related to prevention of bacterial resistance.

**Summary:**

The rapid evolution of antibiotic resistance in pathogenic bacteria, combined with a decreasing interest from the pharmaceutical industry in developing new antibiotics, has created a major public health problem. As a result, strategies to maintain the effects of existing antibiotics and thereby prolong their useful life span have a high priority, among them strategies to amend dosage regimens. Historically, the focus on optimal antibiotic dosage has been on efficacy; little attention has been given to the possibility of optimizing dosing regimens to prevent or minimize resistance development. Pharmacodynamic breakpoints, which are predictive of clinical and/or microbiological success in the treatment of infection, have been determined for many classes of antibacterials, including the fluoroquinolones, aminoglycosides and beta-lactams. Although exceeding these values may predict efficacy, it may not prevent the development of resistance. A number of in vitro and animal studies indicate that suboptimal dosage regimens will facilitate resistance development and may be a significant risk factor for emergence of resistance. For drugs where resistance development occurs stepwise through chromosomal mutations, such as the fluoroquinolones, the mutant prevention concentration (MPC) has been defined as the lowest antibiotic concentration that prevents growth of the least susceptible first-step mutant within (MSW) is the concentration interval (between MIC and MPC) in which resistant subpopulations can be selectively enriched. Among other antibacterial classes, data are still scarce. Besides the pharmacokinetic/pharmacodynamic properties, the mutation rate and biological fitness cost of mutants will influence the selection process. Characterization of the pharmacodynamic properties for a new drug in development, including those for prevention of resistance development, can help direct the design of the best dosing strategy for clinical trials.

**References:**

1. DeRyke CA, SuYoung Lee S, Kuti JL, Nicolau D. Optimizing dosing strategies of antibacterials utilizing pharmacodynamic principles: impact on development of resistance. *Drugs* 2006; 66:1-14
2. Olofsson SK, Marcusson LL, Komp Lindgren P, Hughes D, Cars O. Selection of ciprofloxacin resistance in *Escherichia coli* in an in vitro kinetic model: relation between drug exposure and mutant prevention concentration. *J. Antimicrob Chemother.* Advanced Access published online, April 19, 2006

**16** The Influence of Tissue Distribution and Protein Binding on Resistance  
U. Theuretzbacher  
Center for Anti-Infective Agents  
Vienna, Austria

**Educational Objective:**

At the conclusion of this presentation, the participant will discuss the relevance of tissue concentrations and protein binding, and the influence of active concentrations at the site of infection on resistance selection pressure and its clinical implication.

**Summary:**

Most infections occur in the tissues of the body rather than in the blood. The site of infection is usually the extracellular compartment of tissues or body fluids such as epithelial lining fluid, bronchial secretion or middle ear fluid. Antibiotic concentrations at the site of infection may be reduced due to high protein binding or patient-related factors. The exposure of active (unbound) drug at the site of infection, where high numbers of bacteria multiply, is not only responsible for efficacy but also drives the selection pressure for resistance. To predict the propensity of antibiotic

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concentrations to select resistant subpopulations, pharmacokinetic and pharmacodynamic (PK/PD) parameters have been adapted. In general, higher PK/PD indices are needed to suppress resistant subpopulations than reduce the general population. The information derived from PK/PD modeling allows to optimize dosage regimens and minimize the preferential killing of the susceptible majority, leaving a selected drug-resistant subpopulation intact. Better understanding about the influence of protein binding, PK/PD principles at tissue sites versus blood, and interaction between antibiotic treatment and commensal flora is needed to improve dosing regimens that may be less likely to promote resistance selection pressure at the site of infection.

**Reference:**

1. Liu P, Derendorf H. Antimicrobial tissue concentrations. *Infect Dis Clin North Am* 2003; 17:599-613

**17** The Influence of Duration of Therapy on Resistance

J. Mouton

Canisius Wilhelmina Hospital  
Nijmegen, Netherlands**Educational Objective:**

At the conclusion of this presentation, the participant will explain the factors that determine emergence of resistance over time in relation to prolonged exposure, both at the population level as well as the level of the individual.

**Summary:**

Emergence of resistance has been related to a number of factors. The common feature in most of these is total exposure to drug, both in the population and in the individual. On a population level, the total exposure of drug is related to the number of prescriptions (thus, the indications) and the duration of therapy. It is not exactly clear however which of these two factors are predominant in determining emergence of resistance in the population, and may depend on the mechanism of resistance, epidemiology, setting and spreading. Ultimately, selection of the resistant micro-organism occurs at the level of the individual (or environment). Prolonged exposure increases the probability of selecting less-susceptible or resistant micro-organisms. The way this happens depends on the mechanism of resistance. If resistance occurs stepwise in small entities, prolonged exposure is the ideal means of selecting it. If resistance is more of an on/off phenomenon, it will primarily be determined by the mutation frequency and number of micro-organisms present over time. However, little data on the effect of prolonged treatment exist. Only a few studies have been performed in animals treated for more than a week. In humans, most data include case reports and are observational, comparative studies are impractical because of the low frequency of events. Data from specific patient groups requiring long term treatment, such as patients with cystic fibrosis, clearly show a clear relation between duration of therapy and emergence of resistance. Treatment strategies should be aimed at reducing the probability of emergence of resistance by reducing duration of therapy wherever applicable, without compromising efficacy. It also includes optimizing therapy by reducing the number of micro-organisms as speedy as possible when initiating therapy, for instance by applying high initial doses.

**Reference:**

1. Lipsitch M, Samore MH. Antimicrobial use and antimicrobial resistance: A population perspective. *Emerg Infect Dis* 2002; 8(4):347-354.

**18**

## Resistance to Topical Antiseptics: Does It Matter?

A. Aiello

University of Michigan School of Public Health  
Ann Arbor, MI**Educational Objective:**

At the conclusion of this presentation, the participant will be able to list the antiseptic product ingredients that have been implicated in studies of resistance; describe mechanisms that may confer bacterial resistance to antiseptics; and discuss the potential implications for cross-resistance with antibiotics.

**Summary:**

Hand hygiene has a measurable impact on infections in clinical and community settings in the U.S. While antiseptic soaps are increasingly being used as a hygiene measure within the household setting, there is little evidence that liquid hand soaps marketed as "antibacterial" afford any benefit over their non-antibacterial counterparts. In-vitro studies have provided evidence that exposure to ingredients in such products, particularly triclosan, can contribute to the escalating problem of antimicrobial resistance. First, a brief overview of the studies that have examined the effectiveness of antiseptic products marketed for consumer use will be presented. Next, the results from several studies and specific mechanisms that may confer resistance to various antiseptics will be described. Last, issues regarding the use of antiseptics and cross-resistance with antibiotics will be discussed.

**References:**

1. Aiello AE, Larson, E.L. Antibacterial cleaning and hygiene products as an emerging risk factor for antibiotic resistance in the community. *Lancet Infect Dis* 2003;3:31-36.
2. Sheldon AT, Jr. Antiseptic "resistance": real or perceived threat? *Clin Infect Dis* 2005;40:1650-1656.

**19**

## VISA and Heteroresistance

R. Daum

University of Chicago  
Chicago, IL**Educational Objective:**

At the conclusion of this presentation, participants will review the role of heteroresistance in clinical infections.

**Summary:**

Glycopeptides such as vancomycin licensed in the US, and teicoplanin licensed elsewhere, until recently, have been considered the antibiotics of last resort for the therapy of *S. aureus* infections. Until recently, it was believed that *S. aureus* would never become resistant to glycopeptides because such resistance would necessitate a lethal mutation. Proving again its remarkable adaptability, *S. aureus* has developed 2 resistance mechanisms. The first, sometimes called intermediate resistance, and abbreviated VISA (or GISA) for vancomycin (or glycopeptide) intermediate (resistant) *S. aureus*, involves cell wall thickening, decreased autolysis, one of a variety of peptidoglycan structural changes and, usually, rapid reversion of the resistance phenotype upon withdrawal of antibiotic environmental pressure. Unselected *S. aureus* isolates line up on a continuum of decreased susceptibility with VISA strains at the tip of the pyramid. The second mechanism, sometimes called vancomycin-resistant *S. aureus* (VRSA, rhymes with MRSA) involves piracy of a genetic mechanism employed by *Enterococcus spp* to alter the biochemical structure of its peptidoglycan stem peptide precursor. Here the D-ala-D-ala terminus is replaced by D-ala-D-lac. The mutant stem peptide precursor binds vancomycin with greatly lowered affinity, thus providing the *S. aureus* cell with resistance. Curiously, routine methods employed by clinical microbiology laboratories are not reliable to detect resistance associated with either mechanism. The optimal laboratory method to detect these isolates, vancomycin-resistance population analysis, is labor intensive and beyond the capability of most clinical microbiology laboratories. Glycopeptide resistance is probably more common than realized and may be one

## ABSTRACTS OF INVITED PRESENTATIONS

mechanism by which therapy with these agents often appears to be suboptimal.

**Reference:**

1. Liu C, Chambers HF. Staphylococcus aureus with heterogenous resistance to vancomycin: epidemiology, clinical significance, and critical assessment of diagnostic methods. *Antimicrob Agents Chemother* 2003; 47(10):3040-3045

20

**Pet Animals as Reservoirs of Resistant Bacteria****D. Lloyd**

Royal Veterinary College  
London, United Kingdom

**Educational Objective:**

At the conclusion of this presentation, participants will discuss the roles of pet animals as reservoirs of resistant bacteria transferable to humans, and the need to study risk factors associated with their transfer to humans.

**Summary:**

Increasing amounts of antimicrobials are used on pets, including substances used in human medicine, particularly broad-spectrum agents (clavulante-potentiated aminopenicillins, cephalosporins, fluoroquinolones). There is evidence that resistance to antimicrobials is growing amongst bacteria causing infection in pets. These include *Staphylococcus intermedius* and *Escherichia coli*, and organisms of clinical importance in man such as methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci and multiresistant *Salmonella* Typhimurium DT104. Transmission of such organisms, particularly pathogenic staphylococci, occurs between pets, owners and veterinary staff, and pets can act as reservoirs of such bacteria, which may have an impact on the use of antimicrobials in human medicine. There is a need to generate data on levels of carriage of such bacteria in pets and risk factors associated with their transfer to in-contact humans.

**Reference:**

1. Guardabassi L, Schwarz S, Lloyd DH. (2004) Pet animals as reservoirs of antimicrobial-resistant bacteria. *Journal of Antimicrobial Chemotherapy* 2004; 54: 321-32.

21

**Misclassification Bias and Measurement Error in Clinical Trials for Infectious Diseases: How They Affect the Efficiency of Trials****C. Cooper**

Center for Drug Evaluation and Research/FDA  
Silver Spring, MD

**Educational Objective:**

At the conclusion of this presentation, participants will define, discuss, and review an example of clinical trial misclassification bias and also to show how it may decrease the efficiency of a clinical trial.

**Summary:**

Misclassification bias in a clinical trial occurs when errors in outcome assessment are made, for example, when a patient who truly is cured is considered a failure of treatment in the analysis or vice versa. Misclassification bias decreases the efficiency of clinical trials and may result in inappropriate conclusions of trial results. The potential for misclassification bias potentially is increased when outcome assessment is a measure of subjective findings, such as symptoms experienced by the patient. This problem may be magnified further when assessment is made by a third party, such as when a clinician determines outcomes of patient symptoms. Overall assessment of outcome based on a global clinician assessment of outcome may not always be in concordance with the individually recorded symptoms. Non-differential misclassification bias occurs when there are similar rates of errors in both treatment groups within a given trial. In a non-inferiority trial, such misclassification can either reduce or increase the power of a study for determining non-inferiority, depending on

whether misclassification increase or decreases the point estimates of outcomes. Differential misclassification occurs when the number of errors made between treatment groups is not similar. This has an even greater potential to reach an incorrect conclusion regarding the assessment of trial results. An example of a disease for which misclassification may occur when assessing outcomes is acute exacerbations of chronic bronchitis (AECB). In AECB trials there are no standard definitions for clinician assignment of outcomes of patient symptoms, nor standardized criteria for how questions should be asked of patients by clinicians. Inter-clinician variability in assessing outcomes may introduce bias into trials that in turn may affect trial results. We examined the degree of concordance of clinician assessment of outcomes with patient symptoms as recorded by those same clinicians in a clinical trial of antimicrobial therapy for AECB. This analysis shows that clinicians tended to assess patients as successes while concomitantly documenting lack of improvement of symptoms in case report forms, with differential misclassification between treatment groups. Optimistic misclassification of outcomes may affect the results of trials by minimizing treatment differences. This may result in false-positive conclusions in non-inferiority trials or false-negative conclusions in superiority trials. Validated direct patient reported outcome symptom measurement tools might be a more accurate way to assess outcomes in symptomatic diseases. The number of misclassification errors that overestimated the treatment effect was higher in both treatment arms than the number of errors that underestimated the treatment effect. This finding supports the observation that blinding may be less effective in active-controlled trials in controlling for bias, because it is known to investigators beforehand that all patients enrolled in the trial are receiving an active therapy. Overoptimistic misclassification may be particularly problematic when disease symptoms are self-limited. Thus, misclassification bias may interact with other biases in a clinical trial to influence overall conclusions of trial results.

**Reference:**

1. Kim MY et al. The effects of outcome misclassification and measurement error on the design and analysis of therapeutic equivalence trials. *Statistics in Medicine* 2001; 20:2065-2078.

22

**Patient Reported Outcome Measures in Clinical Trials of Infectious Diseases:****How They Can Help Us****L. Burke**

Center for Drug Evaluation and Research/FDA  
Silver Spring, MD

**Educational Objective:**

At the conclusion of this presentation, the participant will discuss when patient-reported outcome (PRO) measures may offer advantages over traditional clinical trial measures and how to determine whether a PRO measure is adequate to support claims about treatment benefit.

**Summary:**

PRO measures offer the advantage of directly measuring treatment benefit, defined as how a patient feels or functions with respect to disease or a health condition. Historically, assessment of symptom or function improvement was made by physicians who observed and interacted with patients, even when the concepts of assessment were non-observable, known only to the patient. Increasingly, however, such non-observable assessments, as well as some observable assessments, are based on PRO instruments. This trend results from recognition that, not only are some treatment effects known only to the patient, but also patients provide a unique perspective on treatment effectiveness. For example, clinically meaningful improvements in lung function as measured by spirometry may not correlate well with improvements in asthma-related symptoms and their impact on a patient's ability to perform daily activities. In addition, self-completed questionnaires that capture directly the patient's perceived response to treatment without a third party's interpretation may be more reliable than observer-reported measures because they are not affected by inter-observer variability. Furthermore, if observer-reported measures are necessary, clinical assessments formalized using a structured interview technique minimizes

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measurement error and ensures consistency. The adequacy of a PRO instrument as a measure to support medical product claims depends on its developmental history and demonstrated measurement properties. FDA encourages sponsors to specify what claims they seek, determine what concepts underlie those claims, and document the basis for instrument selection, modification, development and validation according current best practices. By explicitly addressing the review issues identified in the draft guidance referenced below, sponsors can increase the efficiency of their endpoint discussions with FDA during the product development process, streamline FDA's review of PRO endpoint adequacy, and provide optimal information about treatment benefit measured from the patient perspective at the time of product approval.

**Reference:**

1. Food and Drug Administration, Draft Guidance for Industry on Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims, posted as Clinical/Medical Draft at <http://www.fda.gov/cder/guidance/index.htm>, February 2006.

**23** Adaptive Designs in Clinical Trials of Infectious Diseases: What It Is and What It Isn't  
D. Lin  
Center for Drug Evaluation and Research/FDA  
Silver Spring, MD

**Educational Objectives:**

At the conclusion of this presentation, the participant will review fundamental concepts of the adaptive clinical trials and discuss how they differ from the traditional clinical trials, especially the classical group sequential trials.

**Summary:**

The concepts and several methods for adaptive designs have been discussed and developed since early 1990. It received much more attention after the FDA published the critical path report in March, 2004. Even though many papers were published regarding the adaptive design, there is no clear definition of this type of design in the literature. Adaptive design is used loosely to capture the entire process of taking an interim look/analysis at the accumulating data of an ongoing clinical trial, modify aspects of the trial design, conduct, and/or analysis in midstream of the trial based on feedback or learning from the interim results. The question is how to improve expected trial outcomes during the experiment while still able to protect the validity and integrity of the trial and reach good statistical decision in a timely fashion?

In this presentation, some fundamental concepts of the adaptive clinical trials will be discussed. The misconception of adaptive designs as a remedy for inadequate planning will be clarified. How the adaptive clinical trials differ from the traditional clinical trials, especially the classical group sequential trials will be compared. Challenges and issues of the adaptive designs will also be discussed. Finally, the applicability of the adaptive designs in clinical trials of infectious diseases will be covered.

**References:**

1. Cui L, Hung HMJ, Wang S-J. Modification of sample size in group sequential trials. *Biometrics* 1999; 55: 853-857.
2. Jennison C, Turnbull BW. Mid-course sample size modification in clinical trials based on the observed treatment effect. *Statist. Med.* 2003; 22:971-993.
3. Shih WJ. Group sequential, sample size re-estimation and two-stage adaptive designs in clinical trials: A comparison. *Statist. Med.* 2006; 25:933-941.

**24** Increasing the Efficiency of Clinical Trials in Infectious Disease: Where Do We Go From Here?

J. Powers

Center for Drug Evaluation and Research/FDA  
Silver Spring, MD

**Educational Objective:**

At the conclusion of this presentation, participants will discuss how advances in clinical trial design and analysis can help increase the efficiency of drug development.

**Summary:**

The emergence of new diseases and the potential for increased treatment failure and death due to antibacterial resistance in serious and life threatening diseases points to a need for novel therapies in infectious diseases. For ethical, scientific and economic reasons, it is appropriate to develop drugs in the most efficient way possible. Efficiency implies acquiring the same or more information regarding the safety and effectiveness of drugs with the least possible expenditure of resources. Spurring new antimicrobial development should be addressed on several fronts, including legislative efforts to provide incentives for drug development.

Substantial evidence of safety and effectiveness for drugs is defined by meeting the criteria set forth for adequate and well-controlled trials that provide the evidence upon which to base evaluations of therapies. The definition of adequate and well controlled trials includes meeting the following criteria: 1) having a clear objective for the trial, 2) having a meaningful quantitative comparison with a control drug, 3) ensuring patients have the disease in a treatment trial or patients are at risk of the disease in a prevention trial, 4) ensuring baseline comparability of patients, 5) minimizing bias during the trial 6) having endpoints that are well defined and reliable, and 7) using appropriate analyses.

Appropriate planning of a trial based on the natural history of the disease under study may maximize the chances of acquiring useful information. A meaningful comparison with a control drug either in the setting of a superiority trial or a noninferiority trial is necessary to draw adequate conclusions about drug effectiveness and provide the information necessary to balance the risks of the drug. Noninferiority trials are appropriate when the magnitude of the treatment of the control drug is well known, reproducible, and constant from trial to trial. Using new diagnostic tools and biomarkers to ensure patients have the disease under study will increase the likelihood of demonstrating positive treatment effects. Novel endpoints may provide clinicians with information on the superiority of one therapy over another in terms that are clinically meaningful for patients. Finally, appropriate analysis of trial results will allow meaningful conclusions and generation of hypotheses for future trials.

**Reference:**

1. Powers JH. Antimicrobial drug development – the past, the present, and the future. *Clin Microbiol Infect* 2004; 10(suppl 4):23-31.

**25** Pneumococcal Vaccine and the Rise of Resistance in Non-Vaccine Serotypes

M. Moore

Centers for Disease Control and Prevention  
Atlanta, GA

**Educational Objective:**

At the conclusion of this presentation, the participant will discuss the role of pneumococcal vaccines in controlling infections caused by antimicrobial resistant *Streptococcus pneumoniae* as well as the impact of serotype replacement on the prevalence of antimicrobial resistance.

**Summary:**

The 7-valent pneumococcal conjugate vaccine (PCV7) was introduced into the U.S. pediatric immunization schedule in 2000. We determined the impact of increasing uptake of PCV7 on invasive pneumococcal disease (IPD) caused by antibiotic resistant strains. We used population-based surveillance for IPD, defined as isolation of pneumococcus from a sterile site, in 8 Active Bacterial Core surveillance (ABCs) sites, to

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compare IPD rates among children in 2004 to baseline (1998/1999 average). Reference laboratories performed antimicrobial susceptibility testing and serotyping. Rates of IPD caused by all serotypes and by PCV7-types decreased from baseline to 2004 in all age groups. Among young children, rates of IPD caused by penicillin-nonsusceptible strains declined by 57% between 1998 and 2004. The incidence of IPD caused by non-PCV7 serotypes, or replacement disease, is increasing, although the magnitude of this increase is small in comparison to the overall decline in IPD. Serotype 19A has emerged as the predominant replacement serotype in the U.S. and the most common serotype to cause antibiotic resistant IPD. Despite only modest increases in vaccine coverage and evidence of replacement disease, PCV7 remains highly beneficial.

**Reference:**

1. Pai, R., et al., Postvaccine genetic structure of *Streptococcus pneumoniae* serotype 19A from children in the United States. *J Infect Dis*, 2005; 192(11): 1988-95.

26

**Current Status of TB Vaccine Development**

M. Brennan

Centers for Biologics Evaluation and Research/FDA  
Atlanta, GA**Educational Objective:**

At the conclusion of this presentation, the participant will identify the major challenges confronting tuberculosis (TB) vaccine developers including identification of important vaccine candidates, preclinical screening, manufacturing, targets of clinical trials, and the potential of introducing the newly developed TB vaccines into developing nations.

**Summary:**

The design of new TB vaccines has been based on a two-fold strategy, [1] to replicate the immune response following natural infection with *Mycobacterium tuberculosis* (Mtb) which is known to protect the majority of infected individuals from active disease or [2] to elicit a novel immune response in individuals that thwarts infection with Mtb or controls disease. A number of whole cell vaccines are under development to address these strategies including live recombinant BCG vaccines over-expressing Mtb antigens, live attenuated Mtb lacking certain genes and killed whole cell vaccines. A live vaccinia-vectored vaccine expressing an Mtb antigen, subunit protein-based vaccines formulated with novel adjuvants and adenovirus-vectored vaccines are also under study. Six new TB vaccines will be in various stages of clinical development by the end of 2006. Clinical study of these new TB vaccines presents with a number of unique, as well as familiar, challenges including issues of vaccine safety, immunization strategies, target populations, clinical trial design, and registration of new TB vaccines in developing countries.

**Reference:**

1. Brennan MJ., Sizemore C., Morris SL. Tuberculosis vaccine development: research, regulatory and clinical strategies. *Expert Opinion in Biological Therapy* 4:1493-1504, 2004.

27

**Malaria Vaccine Development**

S. Hoffman

Sanaria, Inc.  
Rockville, MD

TO BE DETERMINED

28

**Pandemic Flu Preparedness and Emerging Resistance in Flu Strains**

R. Robinson

U.S. Department of Health and Human Services  
Washington, DC**Educational Objective:**

At the conclusion of this presentation, the participant will discuss the current status of U.S. efforts to develop new vaccines and antivirals and their domestic manufacturing capacities for an influenza pandemic; and identify the underlying challenges to establish and maintain U.S. infrastructures for pandemic medical countermeasures

**Summary:**

Preparedness for public health threats is a major goal of the U.S. Department of Health and Human Services (HHS). An influenza pandemic has a great potential to cause large numbers of deaths and illnesses over a short time period. A pandemic occurs when there is an antigenic shift in influenza A virus and transmission of a new strain to which most or all of the world's population is susceptible. Three pandemics occurred during the 20th century, the most severe of which, in 1918, caused over 500,000 U.S. deaths and more than 20 million deaths worldwide. Recent outbreaks of human disease caused by highly pathogenic avian H5N1 influenza virus strains in Asia, Europe, and Africa highlight the vulnerability of global preparedness for a pandemic. Estimates for the next pandemic, extrapolating from those of the 20<sup>th</sup> century, range from about 100,000 to over 2 million deaths in the U.S. alone.

Influenza antiviral drugs and influenza vaccines are considered primary means to decrease the mortality and morbidity associated with the next pandemic. With vaccination comes major implications including the need for a two dose vaccination regimen due to the immunological naivety to the pandemic virus strain, the emergence of a pandemic at any time of the year, persistence longer than a single season, and reappearance over several years, and well-matched vaccine stockpiles cannot be prepared in advance. Global demand during a pandemic will outstrip global influenza vaccine manufacturing capacity. Antiviral drugs form an important part of a strategy for dealing with an influenza pandemic with a new influenza virus of any origin, including avian influenza. In the event of a pandemic outbreak the infection will spread very quickly and the effective vaccine production and availability could be delayed several months, furthermore the current classes of marketed products have limitations, contraindications and possible viral resistance development.

HHS is pursuing multiple and parallel strategies to close the gap between current antiviral drug and influenza vaccine supplies and the HHS goal of stockpiling licensed and new antiviral drugs and pre-pandemic vaccines as part of the strategic plan for pandemic preparedness. The U.S. has set out to rebuild an influenza vaccine infrastructure by fostering advanced development of modern cell culture and other influenza vaccines, building domestic vaccine manufacturing capacity, and preparation of pre-pandemic vaccine stockpiles that may protect the critical workforce needed for continuity of a constitutional government and medical treatment. Concomitantly, HHS sees the advanced development of new influenza antivirals agents designed to affect different targets of influenza virus infection or to enhance effects of present classes of influenza antiviral drugs as necessary steps to counteract the limited supply and efficacy, limited domestic production capacity, and rising possibility of resistant virus strains to licensed antivirals in the event of a pandemic outbreak.

**Reference:**

1. HHS Pandemic Influenza Plan, Nov. 2, 2005. <http://www.hhs.gov/pandemicflu/plan>

# ABSTRACTS OF SUBMITTED ORAL PRESENTATIONS

## ABSTRACTS OF SUBMITTED ORAL PRESENTATIONS

S1

**Prevalence, Profile, and Predictors of Community-Associated Methicillin-Resistant *Staphylococcus aureus* (CA-MRSA) Colonization among Pregnant Women**K. T. Chen<sup>1</sup>, R. C. Huard<sup>2</sup>, P. Della-Latta<sup>2</sup>, H. Campbell<sup>3</sup>, L. Borrell<sup>4</sup>, P. M. Schlievert<sup>5</sup>, L. Saiman<sup>6</sup>;<sup>1</sup>Ob/Gyn and Epidemiology, Columbia University, New York, NY, <sup>2</sup>Pathology, Columbia University, New York, NY, <sup>3</sup>Ob/Gyn, Columbia University, New York, NY, <sup>4</sup>Epidemiology, Columbia University, New York, NY, <sup>5</sup>Microbiology, University of Minnesota, Minneapolis, MN, <sup>6</sup>Pediatrics, Columbia University, New York, NY.

**Background:** The increase of CA-MRSA infections poses a serious public health threat. The aims of this study were 1) to determine the prevalence and profile of CA-MRSA vaginal-rectal colonization among pregnant women by conducting a prospective surveillance study on group B *Streptococcus* (GBS) screening cultures submitted to a single clinical laboratory over 6 months and 2) to assess the predictors of CA-MRSA colonization by performing a case-control study.

**Methods:** A sample of 2,963 GBS screening cultures was analyzed for the presence of MRSA by conventional microbiologic methods and by PCR analysis. CA-MRSA isolates were defined as those possessing the staphylococcal chromosomal cassette *mec* IV or V and usually lacking a multidrug-resistant phenotype. The presence of the toxin, Panton-Valentine Leukocidin (PVL), was determined by PCR.

**Results:** 1) We identified 493 (16.6%) methicillin-sensitive *S. aureus* (MSSA) and 14 (0.5%) MRSA isolates. Of the MRSA isolates, 13 were CA-MRSA of which 8 contained PVL. 2) In a 1:4 ratio, we compared 13 CA-MRSA-colonized pregnant women to 52 randomly selected MSSA-colonized and 52 *S. aureus*-negative controls. Cases were 12 times significantly less likely to be GBS-colonized as compared with MSSA controls in multivariable analyses.

**Conclusions:** We present the first report of CA-MRSA vaginal-rectal colonization of pregnant women and associated parameters. Future studies with increased numbers of CA-MRSA colonized pregnant women are needed.

**Reference:**

1. Saiman L, O'Keefe M, Graham P, et al. Hospital transmission of community-acquired methicillin-resistant *Staphylococcus aureus* among postpartum women. *Clin Infect Dis* 2003; 37:1313-1319.

S2

**Cluster of Neonatal Methicillin-Resistant *Staphylococcus aureus* (MRSA) Infections due to Unrecognized MRSA Colonization at Birth**J. L. Murillo<sup>1</sup>, P. Harmon<sup>1</sup>, W. Cruz<sup>1</sup>, T. Chan<sup>2</sup>, M. Cohen<sup>3</sup>, M. Koraboina<sup>4</sup>, B. Kreiswirth<sup>4</sup>;<sup>1</sup>Epidemiology, Newark Beth Israel Medical Center, Newark, NJ, <sup>2</sup>Microbiology, Newark Beth Israel Medical Center, Newark, NJ, <sup>3</sup>Neonatology, Newark Beth Israel Medical Center, Newark, NJ, <sup>4</sup>Public Health Research Institute, Newark, NJ.

**Background:** The epidemiology of MRSA in the neonatal intensive care unit (NICU) is not completely understood and how MRSA is introduced into the NICU remains a subject of controversy.

**Methods:** A retrospective chart review of a cluster of infected and colonized infants with MRSA was followed by prospective surveillance cultures of all new admissions to the NICU. Control measures included contact isolation, cohorting and nasal decolonization with topical mupirocin. Data was compared with 2002 and 2003 experience. Pulse field gel electrophoresis (PFGE) was performed on MRSA isolates to determine clonal relationships.

**Results:** 29 babies (6 infected, 23 colonized) with MRSA were identified from July to November 2005. 4 babies were bacteremic and 2 had skin and soft tissue infection; none died. The mean onset of infection or colonization was significantly

shorter (mean=14.9 days, 95% CI 7.1-22.8) compared to 2003 (mean=41.0 days, 95% CI 27.7-54.3, p<0.01) or 2002 (mean=73.5days, 95% CI 60.3-86.7, p<0.001). Prospective screening identified 6 babies who had nasal colonization with MRSA at the time of delivery. PFGE showed a predominantly hospital-associated strain combined with a few community-associated strains.

**Conclusions:** MRSA was introduced into the NICU by babies unrecognized to have nasal colonization at birth resulting in earlier onset of MRSA infection compared to previous years.

**References:**

1. Nambiar S, Herwaldt LA, Singh N. Outbreak of invasive disease caused by methicillin-resistant *Staphylococcus aureus* in neonates and prevalence in the neonatal intensive care unit. *Pediatr Crit Care Med* 2003; 4:220-226.
2. Shiojima T, Ohki Y, Nako Y, et al. Immediate control of a methicillin-resistant *Staphylococcus aureus* outbreak in a neonatal intensive care unit. *J Infect Chemother* 2003; 9:243-247.

S3

**Dominant Clones of Methicillin Resistant *Staphylococcus aureus* (MRSA) in Asuncion, Paraguay**M. van Westreenen;  
Med Microbiology and Infectious Diseases, Erasmus Medical Center, Rotterdam, The Netherlands.

**Background:** In Paraguay data on the epidemiological and clinical characteristics of antibiotic resistant bacteria, in particular MRSA, are scarce and incomplete. We present data on the community and nosocomial endemicity of MRSA genotypes in the region of Asuncion, Paraguay.

**Methods:** Twelve laboratories collected 124 community and 121 nosocomial isolates of *S. aureus*, including clinical data, during an 8-week period. Pulsed-field gel electrophoresis (PFGE) and SCC*mec* typing were used for identifying the major clones. The Panton-Valentine leukocidin (PVL) genes (*lukS-PV/lukF-PV*) were detected by PCR.

**Results:** Fifty-six phenotypically identified MRSA isolates were confirmed *mecA* positive, of which 45 were hospital-acquired and 11 community-acquired. PFGE analysis of 45 MRSA isolates and 35 MSSA isolates revealed 17 different genotypes of which there were 4 major types (A/C/G/H). The G-type DNA pattern was the most prevalent clone and represented 20% of the HA-MRSA isolates. This major type circulated in 4 different hospitals. Among the MSSA isolates the C-type pattern was predominant. The G and H-type showed acquisition of SSC*mec* type I, the A and C-type showed SCC*mec* type IV. Fourteen (6%) of the 245 isolates yielded positive PVL amplification.

**Conclusion:** The prevalence of MRSA in healthy Paraguayan carriers is 8%, and in patients 38%. There is clonal distribution of 4 main PFGE-types. The CA-MRSA do not have the same properties compared to the epidemic nosocomial clones. Only sporadic community isolates showed a high degree of similarity with HA-MRSA.

**References:**

1. van Westreenen M, Paaau A, Fluit AC, Brisse S, van Dijk W, Verhoef J. Occurrence and spread of SHV extended-spectrum beta-lactamase-producing *Klebsiella pneumoniae* isolates in Curacao. *J Antimicrob Chemother* 2003; 52:530-532.
2. van Belkum A. High-throughput epidemiologic typing in clinical microbiology. *Clin Microbiol Infect* 2003; 9:86-100.

## ABSTRACTS OF SUBMITTED ORAL PRESENTATIONS

S4

**Identifying Target Groups for Prevention of Community-Associated Methicillin Resistant *Staphylococcus aureus* Infection, New York City**  
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**Background:** Men who have sex with men (MSM) are thought to be at risk of community-associated methicillin resistant *Staphylococcus aureus* (CA-MRSA). Because CA-MRSA reporting is not mandated in New York City (NYC), local risk factors have not been identified. This investigation aims to compare demographics and risk behaviors of CA-MRSA patients to the NYC population.

**Methods:** In April 2005, we began receiving antibiotic resistance profiles and demographics of patients diagnosed with MRSA from a commercial laboratory. To elicit symptoms and behaviors, we administered structured questionnaires by phone to eligible patients (NYC residents with skin infections). We attempted to reach patients for 120 days after specimen collection before closing interview periods. Case characteristics were compared with census and local survey data.

**Results:** Of 716 *S. aureus* skin infections diagnosed through October 2005, 446 (62%) were susceptible and 270 (38%) were resistant to oxacillin. Of 155 eligible patients whose interview periods were closed, 115 (74%) were reached, 99 (64%) agreed to be interviewed. Of these, 79 (80%) MRSA patients who did not have hospital or dialysis exposure were categorized as CA-MRSA. Compared to NYC residents, a higher proportion of CA-MRSA cases were male (64% vs. 47%,  $p < 0.01$ ), white (68% vs. 37%,  $p < 0.01$ ), and college educated (76% vs. 25%,  $p < 0.01$ ). Compared to adult NYC men, a higher proportion of adult male CA-MRSA cases reported sex with men (70% vs. 10%,  $p < 0.01$ ) and HIV (27% vs. 1%,  $p < 0.01$ ).

**Conclusions:** Patients with CA-MRSA skin infections who accessed outpatient care were disproportionately MSM and HIV-positive. Further analyses should aim to determine behaviors associated with CA-MRSA infection.

**References:**

1. Lee NE, Taylor MM, Bancroft E, Ruane PJ, et al. Risk factors for community-associated methicillin-resistant *Staphylococcus aureus* skin infections among HIV-positive men who have sex with men. *Clin Infect Dis* 2005; 40:1529-1534.
2. Naimi, TS, LeDell KH, Como-Sabetti K, et al. Comparison of community and health-care associated methicillin-resistant *Staphylococcus aureus* infection. *JAMA* 2003; 290:2976-2984.

S5

**Drug Resistance Pattern of *Shigella sonnei*— Kansas, 1997-2005**  
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**Background:** Approximately 20,000 cases of shigellosis are reported in the United States annually. When indicated, the Centers for Disease Control and Prevention recommend trimethoprim-sulfamethoxazole for susceptible organisms acquired in the United States. During recent decades, *Shigella sonnei* has developed resistance to this antibiotic worldwide. Data from the National Antimicrobial Resistance Monitoring System (NARMS) indicate an increase in ampicillin and trimethoprim-sulfamethoxazole resistance. Understanding the antimicrobial resistance patterns of *S. sonnei* is important for empiric treatment recommendations and to prevent increases in antibiotic-resistant infections.

**Methods:** Kansas laboratories are required to submit all *Shigella* spp. isolates to the Kansas Department of Health and Environment Laboratory (KDHEL). KDHEL identifies and analyzes resistance to multiple antibiotics. Data collected for January 1997-December 2005 were analyzed.

**Results:** Of 743 *Shigella* isolates submitted, 663 (89%) were *S. sonnei*; 80 (11%) were *S. flexneri*; and 3 (<1%) *S. boydii*. This analysis focuses on *S. sonnei*, which causes the majority of cases in Kansas. For *S. sonnei*, 376 (57%) were resistant to trimethoprim-sulfamethoxazole; 517 (78%) to ampicillin; 181 (27%) to ampicillin-sulbactam; and 302 (46%) to both trimethoprim-sulfamethoxazole and ampicillin. No isolates were resistant to ciprofloxacin.

**Conclusions:** Resistance to trimethoprim-sulfamethoxazole occurs in >50% of *S. sonnei* isolates in Kansas. This differs from the NARMS result. Therefore, empiric antibiotic recommendation for Kansas should be based on the state-specific antibiogram. To effectively minimize further development of antimicrobial resistance, judicious use of antibiotics and increased awareness of changing antibiotic resistance patterns of *S. sonnei* is needed.

**References:**

1. Sivapalasingam S, Nelson JM, Joyce K, Hoekstra M, Angulo FJ, Mintz ED. High prevalence of antimicrobial resistance among *Shigella* isolates in the United States tested by the National Antimicrobial Resistance Monitoring System from 1999 to 2002. *Antimicrob Agents Chemother* 2006;50:49-54.
2. National Antimicrobial Resistance Monitoring System for Enteric Bacteria (NARMS): 2002 Human Isolates Final Report. Atlanta, Georgia: U.S. Department of Health and Human Services, CDC, 2004.

S6

**Resistance Patterns of Gram Negative Rods in Community Acquired versus Nosocomially Acquired Urinary Tract Infections**

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**Background:** Urinary tract infections (UTIs) in hospitalized patients are an important contributor to morbidity. Recent studies show increasing antibiotic resistance in gram negative rods (GNRs) causing UTIs (1). We studied the resistance pattern of GNRs in our population.

**Methods:** A retrospective study at an inner-city hospital in New Jersey. All positive urine cultures (>100,000 copies/mL) of GNRs from 6-12/05 were included. Infections were classified as either community acquired (CA) or nosocomial (NOS) based on the CDC definition (2). Chart review revealed if the patient was admitted from home (H) or a nursing home (NH). Three subgroups of patients were compared. Data was analyzed using Chi-Square analysis.

**Results:**

	Levofloxacin			Ampicillin			Ceftriaxone			Trimethoprim/Sulfamethoxazole		
	CA-H	NH	NOS	CA-H	NH	NOS	CA-H	NH	NOS	CA-H	NH	NOS
EC	27	79	34	50	83	50	6	21	19	13	29	16
KP	38	90	78	86	100	93	24	81	70	32	81	68

We identified 389 total positive cultures: 142 *Escherichia coli* (EC), 98 *Klebsiella pneumoniae* (KP). The table shows the percentage of resistant organisms classified by mode of acquisition of infection and antibiotic used. Statistical significance, shown in bold, was demonstrated for EC and KP for several antibiotic agents when CA-H was compared with CA-NH and when CA-H was compared with NOS.

**Conclusions:** Our study confirms that *E. coli* and *Klebsiella pneumoniae* UTIs have significant resistance against commonly used antibiotics and empirical therapy with a single agent may lead to a high level of treatment failure.

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especially for infections acquired nosocomially or in nursing homes.

**References:**

1. Gupta K, Hooton TM, Stamm WE. Increasing antimicrobial resistance and the management of uncomplicated community-acquired urinary tract infections. *Ann Intern Med* 2001; 135:41-50.
2. Hooton TM, Besser R, Foxman B, Fritsche TR, Nicolle LE. Acute uncomplicated cystitis in an era of increasing antibiotic resistance: a proposed approach to empirical therapy. *Clin Infect Dis* 2004; 39:75-80.

## S7 Molecular Mechanisms Causing Imipenem Resistance among *P. aeruginosa* Isolates from Intensive Care Unit (ICU) Patients

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**Background:** Imipenem resistant (IMP<sup>R</sup>) *Pseudomonas aeruginosa* are important nosocomial pathogens. IMP<sup>R</sup> can result from alterations in the *oprD* porin, *ampC* overexpression or acquisition of metallo-, -lactamases. In this study, we investigated the molecular mechanisms responsible for IMP<sup>R</sup> in *P. aeruginosa* colonizing ICU patients.

**Methods:** We studied 50 isolates (16 IMP<sup>R</sup> & 34 IMP<sup>S</sup>) from perirectal surveillance cultures of ICU patients during 2001-2002. Metallo- $\beta$ -lactamases were assessed based on the MIC (mg/l) of IMP with or without EDTA. Chromosomal *ampC*  $\beta$ -lactamases were evaluated by disk diffusion with ceftazidime, piperacillin-tazobactam and IMP with and without cloxacillin. The *oprD* coding region and the *ampC* negative regulator *ampD* were amplified by PCR, sequenced and compared to those of PAO1.

**Results:** Nine isolates had deletions in *oprD*. Six that only had an *oprD* mutation had intermediate resistance (MIC=6-8). The remaining 3 showed overexpression of *ampC* by the cloxacillin assay. Seven additional isolates had *ampC* overexpression. 1 isolate, AH559 (MIC=32) had deletions of both *ampD* and *oprD*. 3 isolates (MIC=16) had an amino acid substitution (Ile-117-Ser) in *ampD* and 1 isolate (MIC=8) had a 200 bp N-terminal deletion in *ampD*. Complementation with a plasmid carrying functional *ampD* partially (AH559) or completely restored susceptibility. EDTA did not change the IMP MICs indicating an absence of metallo- $\beta$ -lactamases.

**Conclusion:** In our hospital, no metallo- $\beta$ -lactamases were seen; *oprD* deletions alone produced only low-level resistance (MIC=6-8). High-level resistance (MIC $\geq$ 16 mg/l) to IMP was only seen with *ampC* overexpression.

**Reference:**

1. Pagani L, Colinson C, Migliavacca R, et al. Nosocomial outbreak caused by multidrug-resistant *Pseudomonas aeruginosa* producing IMP-13 metallo-beta-lactamase. *J Clin. Microbiol.* 2005; 43:3824-3828.

## S8

Development of a "Universal" DNA Microarray for Detecting Exogenous Antimicrobial Resistance Genes in Diverse Bacteria  
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**Background:** The horizontal transfer of exogenous antimicrobial resistance genes between bacteria is one of the factors leading to the spread of antimicrobial resistance. To study the epidemiology of this spread, it is necessary to identify the genes responsible for resistance. Currently, each gene must be screened individually in order to identify the gene responsible for the observed resistance expressed by a bacterium. The inability to rapidly identify these genes limits research progress.

**Methods:** A DNA microarray was constructed to simultaneously detect all sequenced antimicrobial resistance genes. Antimicrobial resistance gene sequences were downloaded from the National Center for Biotechnology Information database; 70mer oligonucleotide probes were designed to detect them, they were then synthesized and arrayed onto glass slides. Total DNA from control and test strains were labeled with fluorescent dye and hybridization, scanning and analysis were done following standard methods.

**Results:** The microarray successfully detected resistance genes in a variety of diverse bacteria, including *Salmonella*, *E. coli*, *Campylobacter* and *Enterococcus*. Hybridization results were validated by positive controls and confirmed by PCR and Southern blotting. The microarray reliably tested for hundreds of genes per assay and detected dozens of genes in resistant isolates.

**Conclusions:** The microarray can be used to rapidly screen for almost all exogenous resistant genes in one assay. This technique will facilitate monitoring the spread of antimicrobial resistance and improve our understanding of the epidemiology of the genes causing resistance.

**Reference:**

1. Frye JG, Jesse T, Long F, et al. DNA microarray detection of antimicrobial resistance genes in diverse bacteria. *Int J Antimicrob Agents* 2006; 27:138-151.

# ABSTRACTS OF SUBMITTED POSTER PRESENTATIONS

## ABSTRACTS OF SUBMITTED POSTER PRESENTATIONS

**P1** Trends in Antimicrobial Prescribing in Ambulatory Care Settings in the United States, 1993-2004L. F. McCaig<sup>1</sup>, C. R. Friedman<sup>2</sup>;<sup>1</sup>National Center for Health Statistics, Centers for Disease Control and Prevention, Hyattsville, MD, <sup>2</sup>National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, GA.

**Background:** Antimicrobial resistance is an ongoing problem in the US. From 1992-2001, the overall antimicrobial prescribing rate in ambulatory care settings declined by 23%; for persons 15-24 years old, the rate decreased by 13%.<sup>1</sup> However, no trend in adult prescribing in emergency departments (EDs) was found; an increasing trend was observed in outpatient department (OPDs).

**Methods:** Data from the 1993-2004 National Ambulatory Medical Care Survey (NAMCS) and National Hospital Ambulatory Medical Care Survey (NHAMCS), annual national probability surveys of US office-based physicians and hospital OPDs and EDs, respectively, were examined to assess changes in antimicrobial prescribing. Two years of data were combined to provide more reliable estimates. Each year, ~2500 physicians and ~500 hospitals were in the NAMCS and NHAMCS samples, respectively, including ~30,000 patient visits in each setting.

**Results:** From 1993-2004, the overall antimicrobial prescribing rate in ambulatory care settings decreased by 19% (from 154 antimicrobials per 1000 visits to 124). While rates continue to decline for children and adults seen in physician offices (down by 27% and 22%, respectively) and children visiting EDs (down by 11%), rates are increasing for adults seen in OPDs (up by 26%) and EDs (up by 8%). No trend was observed for persons 15-24 years old seen in any of the ambulatory care settings.

**Conclusions:** The decline in antimicrobial prescribing rates observed during the 1990's continues in physician offices. For adults, rates continue to increase in OPDs and for the first time, are rising in EDs. In addition, rates are no longer decreasing for persons 15-24 years old. Further investigation of these differences is warranted.

**Reference:**

1. McCaig L. Decline in antimicrobial prescribing in ambulatory care settings in the United States, 1992-2001. Presented at the 2003 Annual Conference on Antimicrobial Resistance, Bethesda, MD, June 26-28, 2003.

**P2** *In vitro* Activity of Designer Oxazolidinones against Multi-Drug Resistant Pathogens

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**Background:** R<sup>-</sup>-101 and R<sup>-</sup>-103 are members of a series of designer oxazolidinones that target prokaryotic ribosomes with extended spectrum of activity and enhanced potency compared to linezolid, the only commercialized oxazolidinone. The development of this series was guided by proprietary crystallographic and computational methods that exploited common interactions shared by linezolid and sparsomycin at the A-site of the 50S subunit.

**Methods:** MICs against multi-drug resistant strains were determined by the microdilution method according to CLSI approved standard M7-A5.

**Results:** Members of this series inhibited *in vitro* translation up to 100-fold more than linezolid, and consequently had enhanced antibacterial activity against streptococci, and community-associated MRSA (CA-MRSA) and most notably *H. influenzae*. Recent characterization of R<sub>X</sub>-101 and R<sub>X</sub>-103 against *S. pneumoniae* and *S. pyogenes* strains with defined macrolide-resistance mechanisms demonstrated at least 10-fold better activity compared to linezolid regardless of resistance mechanism. MIC<sub>90</sub>s for R<sub>X</sub>-101 and R<sub>X</sub>-103 against

*S. pneumoniae* *mef*(A), *S. pneumoniae* *erm*(B), *S. pneumoniae* *mef*(A) + *erm*(B), and *S. pyogenes* *mef*(A) were 0.25 µg/ml, <=0.25 µg/ml, <=0.25 µg/ml and 0.125 - 0.25 µg/ml, respectively. R<sub>X</sub>-101 and R<sub>X</sub>-103 also had MICs of <=0.25 - 0.5 µg/ml against 2 strains of linezolid-resistant *S. pneumoniae*. Against CA-MRSA R<sub>X</sub>-101 and R<sub>X</sub>-103 were 4-fold to 8-fold more active than linezolid, and they displayed MIC<sub>90</sub>s of 1 - 4 µg/ml against *H. influenzae*.

**Conclusions:** The designer oxazolidinones showed potent *in vitro* activity against multi-drug resistant bacteria that cause respiratory tract infections including streptococci, CA-MRSA, and *H. influenzae*.

**References:**

1. Clinical and Laboratory Standards Institute. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically*. Clinical and Laboratory Standards Institute, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2004.
2. Franceschi F, Duffy EM. Structure-based drug design meets the ribosome. *Biochem Pharmacol* 2006; 71(7):1016-1025

**P3** New Agents for Drug Resistant Tuberculosis (TB)R. Goldman<sup>1</sup>, B. Laughon<sup>1</sup>, S. Franzblau<sup>2</sup>, J. Krahenbuhl<sup>3</sup>, A. Lenaerts<sup>4</sup>, I. Orme<sup>4</sup>, J. Secrist<sup>5</sup>, L. Young<sup>6</sup>, K. Plumley, C. Lambros<sup>1</sup>;<sup>1</sup>Division of AIDS, NIH-NIAID, Bethesda, MD, <sup>2</sup>Institute for Tuberculosis Research, University of Illinois, Chicago, IL, <sup>3</sup>National Hansen's Disease Program, Baton Rouge, LA, <sup>4</sup>Colorado State University, Fort Collins, CO, <sup>5</sup>Southern Research Institute, Birmingham, AL, <sup>6</sup>Kuzell Institute, San Francisco, CA.

**Background:** The MDR-TB pandemic has heightened efforts to discover new drugs active against resistant strains. The Tuberculosis Antimicrobial Acquisition and Coordination Facility (TAACF) is a testing service supported and directed by the NIAID, providing compound suppliers with confidential preclinical drug screening data and *in vivo* efficacy data. Southern Research Institute (SRI) coordinates the medicinal chemistry program and compound acquisition (over 80,000 to date) The National Hansen's Disease Program evaluates *in vitro* activity of submitted compounds received from SRI. Colorado State University receives compounds that show promising *in vitro* activity and screens for *in vivo* efficacy in animal models.

**Methods:** MIC: 90% growth inhibition using the microplate Alamar Blue assay in BACTEC 12B medium. Cytotoxicity: (IC<sub>50</sub>) for VERO cells after 72 hours exposure. *In vivo* efficacy: Screening model (interferon-γ knockout mice) and standard mouse model using low-dose aerosol infection and monitoring of CFUs in the lung and spleen. *In vitro* 'latent' TB: Activity against TB grown under low oxygen.

**Results:** Several compound classes, including quinolones, nitroimidazoles, quinolinemethanols, amidinohydrazones, isoxyls, and other novel classes, were active in mouse models and active against resistant strains *in vitro*. Some were active *in vitro* against 'latent' TB. Combining isoniazid (INH) with quinolones produced some culture-negative mice, while combination with nitroimidazoles appeared antagonistic.

**Conclusions:** Several novel anti-TB agents are active *in vivo*. Alteration of the intracellular redox potential, by INH depletion of NADH, could explain the antagonism between INH and nitroimidazoles. There have been over 170 TAACF-derived publications.

**Reference:**

1. Danelishvili L, Wu M, Young L, Bermudez L. Genomic approach to identifying the putative target of and mechanisms of resistance to mefloquine in mycobacteria. *Antimicrob Agents Chemother* 2005; 49:3707-3714.

## ABSTRACTS OF SUBMITTED POSTER PRESENTATIONS

**P4** Rapid Identification of Methicillin-Resistant *Staphylococcus aureus* Using *S. aureus* EVIGENE™ and MRSA EVIGENE™A. R. Larsen<sup>1</sup>, H. Westh<sup>2</sup>, M. Holt<sup>3</sup>, K. G. Madsen<sup>3</sup>;<sup>1</sup>Statens Serum Institut, Copenhagen, Denmark, <sup>2</sup>Department of Clinical Microbiology, Hvidovre Hospital, Hvidovre, Denmark, <sup>3</sup>AdvanDx A/S, Vedbæk, Denmark.

**Background:** Identification of methicillin-resistant *Staphylococcus aureus* (MRSA) is of major concern since MRSA is emerging worldwide. *S. aureus* EVIGENE™ and MRSA EVIGENE™ (AdvanDx Inc, Woburn, MA; For Research Use Only) are qualitative, signal amplified sandwich hybridization assays for rapid identification of MRSA by detection of the *nuc* and *mecA* gene, specific for *S. aureus* and of methicillin-resistance, respectively.

**Methods:** In this study, we evaluated the combination of *S. aureus* EVIGENE™ and MRSA EVIGENE™ in a Danish setting using clinical isolates representing 15 of the most common *spa* types present in Denmark, the SCCmec cassette types (I-V), all 39 *Staphylococcus* species (ATCC strains) as well as 91 *Staphylococcus* isolates from clinical samples [70 *S. aureus* and 21 coagulase-negative staphylococci (CNS)] with PCR as the gold standard.

**Results:** *S. aureus* EVIGENE™ and MRSA EVIGENE™ correctly identified all MRSA isolates comprising the different *spa* types and SCCmec cassette types. Of the 39 different *Staphylococcus* species, *S. aureus* as well as *S. capitis*, *S. caprae* and *S. saccharolyticus* were tested positive for the *nuc* gene by *S. aureus* EVIGENE™. The sensitivity and specificity on clinical isolates were 100% (70/70) and 95.2% (20/21) for *S. aureus* EVIGENE™. For MRSA EVIGENE™ the sensitivity and specificity were 100% (40/40) and 100% (30/30) for determination of MRSA and 100% (11/11) and 100% (10/10) for determination of methicillin-resistant CNS. A very high signal-to-noise ratio between positive and negative test results allowed the results to be read by eye.

**Conclusion:** *S. aureus* EVIGENE™ and MRSA EVIGENE™ are rapid and accurate tests for identification of MRSA isolates.

**References:**

1. Hackbarth CJ, Chambers HF. Methicillin-resistance staphylococci: genetics and mechanisms of resistance. *Antimicrob Agents Chemother*.1989; 33:991-994.
2. Boyce J. Patterns of methicillin-resistant *Staphylococcus aureus* prevalence. *Infect Control Hosp Epidemiol*.1991; 2:79-82.

**P5** Investigation of Antibiotic and Antibacterial Resistance in Skin Bacteria from Users and Non-Users of Antibacterial Wash Products in Home EnvironmentsE. C. Cole<sup>1</sup>, R. M. Addison<sup>2</sup>, P. D. Dulaney<sup>3</sup>, K. E. Leese<sup>4</sup>;<sup>1</sup>Health Science Department, Brigham Young University, Provo, UT, <sup>2</sup>Clinical Microbiology/Infectious Disease, Duke University Medical Center, Durham, NC, <sup>3</sup>Health Research Services Division, Applied Environmental, Inc., Cary, NC, <sup>4</sup>Restoration Sciences, LLC, Cary, NC.

**Background:** Antibacterial wash products have come under scrutiny as potential contributors to the problem of antibiotic resistance. This study investigated antibiotic resistance in skin bacterial isolates from users of antibacterial wash products, compared to isolates from non-users.

**Methods:** Participants (n=210) comprised groups of 70 each: 1) those that frequently used wash products containing triclosan (TCS); 2) those that frequently used products containing triclocarban (TCC); 3) those that used no antibacterial wash products (control). A skin swab was collected from each participant for coagulase-negative *Staphylococcus* species and *S. aureus* (SA). Antibiotic and antibacterial MIC testing was performed on all isolates (n=317).

**Results:** There was no increased antibiotic resistance in *Staphylococcus* isolates from groups regularly using wash products containing TCC or TCS, compared with participants using wash products containing no TCC or TCS. None of the study isolates was resistant to vancomycin, and the rate of methicillin resistant *S. aureus* detected was less than that reported for both hospital inpatient and outpatient isolates. The data showed a lack of antibiotic/antibacterial cross-resistance when comparatively assessed across the groups.

**Conclusion:** This community study of resident skin staphylococci confirms similar findings from studies of antibiotic/antibacterial resistance in home environments, and discounts the use of antibacterial wash products contributing to the selection of drug-resistant bacteria on human skin.

**References:**

1. Cole E, Addison R, Rubino J, et al. *J Appl Microbiol* 2003; 95:664-676.
2. Aiello A, Marshall B, Levy S, Della-Latta P, Lin S, Larson E. Antibacterial cleaning products and drug resistance. *Emerg Infect Dis* 2005; 10:1565-1570.

**P6** Susceptibility of Community-Isolated Enterococci to Clinically Important Antimicrobial AgentsA. M. ThurdeKoos<sup>1</sup>, E. J. Barzilay<sup>2</sup>, T. Miller<sup>2</sup>, K. D. Joyce<sup>1</sup>,K. Gay<sup>1</sup>, B. Lee<sup>3</sup>, M. J. Zervos<sup>4</sup>, E. DeBess<sup>5</sup>, M. Warren<sup>6</sup>, T. Barrett<sup>2</sup>, T. M. Chiller<sup>7</sup>;<sup>1</sup>FDDB, CDC/AREF, Atlanta, GA, <sup>2</sup>FDDB, CDC, Atlanta, GA, <sup>3</sup>Minnesota Department of Health, St. Paul, MN, <sup>4</sup>Henry Ford Hospital, Detroit, MI, <sup>5</sup>Oregon Department of Human Resources, Portland, OR, <sup>6</sup>University of Maryland, Baltimore, MD, <sup>7</sup>FDDB, CDC/US Public Health Service, Atlanta, GA.

**Background:** Emergence of multi-drug resistant Gram-positive pathogens has led to development of new antimicrobial agents with enhanced activity. Antimicrobial agents developed for treatment of enterococcal infections include daptomycin, linezolid, and quinupristin-dalfopristin (Q/D). We report the susceptibility profiles of community-isolated enterococci from stool to these antimicrobials.

**Methods:** Stool samples were collected from outpatients with diarrhea, reporting no hospitalization in the previous two weeks. Three sites (MD, MI, and MN) submitted 10 stool specimens per month, 2004. From each stool specimen, one enterococcal isolate was sent to CDC. Isolates were cultured for identification. Susceptibility testing to antimicrobials was performed by broth microdilution. Participants were asked questions concerning antimicrobial use, travel and other exposures in the previous 6 months.

**Results:** Of 330 stools collected, 280 (85%) enterococci were isolated. Of these, 127 (45%) were tested. A total of 126 (99%) were susceptible to daptomycin, 123 (97%) were susceptible to linezolid, and 14 (52%) of *E. faecium* were susceptible to Q/D. Among participants whose enterococci were not susceptible to daptomycin or linezolid, there were no associations with risk factors. In participants whose *E. faecium* were not susceptible to Q/D, there was an increased association with farm exposure that was not statistically significant.

**Conclusion:** Some enterococci isolated from community stool samples are not susceptible to daptomycin, linezolid, and Q/D. This was not associated with recent hospitalization or antimicrobial use. It will be important to understand sources of resistant commensal bacteria, especially as they relate to transferring resistance of newly approved and critical antibiotics. This may indicate acquisition and transmission of these bacteria from food animal sources.

**References:**

1. Coque T, Tomayko J, Ricke S, Okhyusen P, Murray B. Vancomycin-resistant enterococci from nosocomial, community, and animal sources in the United States. *Antimicrob Agents Chemother* 1996; 40:2605-2609.
2. Endtz H, van den Brack N, van Belkam A, et al. Fecal carriage of vancomycin-resistant enterococci in hospitalized patients and in those living in the community in the Netherlands. *J Clin Microbiol* 1997; 35:3026-3031.

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**P7** Community-Associated Methicillin Resistance Profiles of *Staphylococcus aureus* Isolates Collected from Human, Canine, and Equine Patients  
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**Background:** Close contact between humans and companion animals creates the potential for transfer of resistant bacteria between species. The goal of this study was to compare *Staphylococcus aureus* isolates collected from human, canine, and equine patients, with respect to methicillin resistance and presence of the Panton-Valentine leukocidin (PVL) gene.

**Methods:** Clinical isolates submitted to animal and human diagnostic laboratories were characterized for methicillin-resistance by disk diffusion, E-test, MIC analysis, latex agglutination, and PCR using *mecA* primers. Additional analyses were performed to identify genetic profiles indicative of community-associated (CA) strains. These involved multiplex PCR to distinguish SCC<sub>mec</sub> type I, II, III, and IV, and further investigation of type IV isolates to identify the presence of the Panton-Valentine leukocidin (PVL) gene.

**Results:** Of the 136 *S. aureus* isolates collected, 43 were methicillin resistant and 19 had community-associated profiles (17 equine, 1 canine, and 1 human). The PCR products of the PVL genes in all animals produced smaller gel electrophoresis bands (~ 380bp) than those of the human isolates (433bp). Cloning and sequencing of these PVL genes revealed that there was consensus between the human clinical and ATCC positive control sequences, but that all animal isolates varied from the human strains mainly by a ~50bp deletion.

**Conclusion:** Isolation of MRSA in both humans and companion animals suggests that there is a risk of transfer of resistant bacteria between species. While MRSA strains in both humans and companion animals contained the PVL gene, it is not clear yet whether these genes are functionally similar.

**References:**

1. Oliveira D, de Lencastre H. Multiplex PCR strategy for rapid identification of structural types and variants of the *mec* element in methicillin-resistant *Staphylococcus aureus*. *Antimicrob Agents Chemother* 2002; 46:2155-2161.
2. Lina G, Piemont Y, Godail-Gamot F, et al. Involvement of Panton-Valentine leukocidin-producing *Staphylococcus aureus* in primary skin infections and pneumonia. *Clin Infect Dis* 1999; 29:1128-1132.

**P8** Proximity to the U.S.-Mexico Border and Resistant Uropathogens  
M. Marten<sup>1</sup>, L. Hofherr<sup>2</sup>, F. E. Myers, III<sup>3</sup>;  
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**Background:** Urinary tract infections (UTIs) are common bacterial infections resulting in excess physician visits and hospital admissions. *E. coli* accounts for 75 to 95% of UTIs. San Diego, California is a geographically unique southwestern city that experiences high antibiotic resistance rates for *E. coli*. This study was designed to identify risk factors for drug resistant *E. coli* uropathogens.

**Methods:** Outpatient medical records from an acute care facility in San Diego were examined and resulted in 196 patients with *E. coli* positive urine cultures. Descriptive statistics and univariate analysis of covariates against resistance were performed. Logistic regression was performed to identify confounders and to estimate odds ratios for living near the border and having resistant isolates.

**Results:** Univariate associations between living near the U.S.-Mexico border and having a resistant *E. coli* uropathogen were evaluated for the following

antibiotics: ampicillin [n=83; OR=2.83; 95% CI (0.69, 11.66); p=0.136], ciprofloxacin [n=11; OR=7.1; 95% CI (1.3, 40.8); p=0.011], trimethoprim-sulfamethoxazole [n=60; OR=1.8; 95% CI (0.46, 6.9); p=0.389], and tetracycline [n=61; OR=4.6; 95% CI (1.11, 19.1); p=0.022]. After adjusting for other variables, there was a significant association between living near the border and tetracycline resistance [n=61; OR=4.46; 95% CI (1.1, 18.8); p= 0.0413].

**Conclusions:** This study found living near the border may increase the risk of acquiring a resistant *E. coli* uropathogen.

**References:**

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2. Karlowsky J, Thornsberry C, Jones M, Sahn D. Susceptibility of antimicrobial resistance urinary *Escherichia coli* isolates to fluoroquinolones and nitrofurantoin. *Clin Infect Dis* 2003; 26:183-187.

**P9** Investigation of Antibiotic Resistance and Resistance Genes from *Escherichia coli* in Amphibians with Proximity to Livestock  
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Cattle with proximity to aquatic environments can harbor bacteria which may acquire antibiotic resistant genes as a result of routine antibiotic use (Schroeder et al., 2001). This may lead to possible contamination of adjacent aquatic environments and wildlife. We investigated the prevalence of class 1 integrons and antibiotic resistance in *E. coli* from bullfrog (*Rana catesbeiana*) and green frog (*Rana clamitans*) larvae from ponds within and adjacent to cow-calf beef production systems. Bacteria were isolated from frog larvae, cow manure, and pond water, using standard procedures. Integron prevalence was determined by multi-plex PCR. Resistance to tetracyclines, florfenicol, and sulfisoxazole was determined by standard microdilution broth techniques (NCCLS, 2002), and a selected subset of isolates were subjected to the NARMS veterinary Gram-negative panel (#CMV1AGNF). A Chi-Square analysis and Fisher's Exact Test were used to determine differences between categorical data (sensitive versus resistant) across sample sources. We detected class 1 integrons in 2% of isolates (n = 112) from pond water and in 0.7% of isolates (n = 123) from cow manure. Integrons were not detected in isolates (n = 1014) from frog larvae. The percentage of isolates resistant to tetracycline from water of cattle-access ponds was greater (P = .017) compared to isolates from cattle-excluded ponds. Florfenicol and tetracycline resistance was more prevalent (P < .005) in frog larvae isolates from cattle-access ponds compared to cattle-excluded ponds. Multi-resistance patterns were observed to differ between sample sources. These data show that resistance genes may move from cattle production systems into aquatic environments and wildlife.

**References:**

1. NCCLS. Performance standards for antimicrobial disk and dilution susceptibility tests for bacteria isolated from animals; Approved Standard-Second Edition. NCCLS document M31-A2 (ISBN 1-56238-461-9). NCCLS, Wayne, PA 19087-1898, USA 2002.
2. Schroeder C, Zhao C, DeRoy C, et al. Antimicrobial resistance of *Escherichia coli* O157 isolated from humans, cattle, swine, and food. *Appl Environ Microbiol* 2002; 68:576-581.

## ABSTRACTS OF SUBMITTED POSTER PRESENTATIONS

**P10** Aminoglycoside Resistance Genes Found in *Enterococcus* spp. Recovered from Retail MeatsS. M. Bodeis-Jones<sup>1</sup>, D. G. White<sup>2</sup>, & The NARMS Team<sup>1</sup>;<sup>1</sup>Division of Animal and Food Microbiology, FDA, Laurel, MD,<sup>2</sup>FDA, Laurel, MD.

**Background:** Enterococci exhibiting high-level aminoglycoside resistance (HLAR, MIC > 500 µg/ml) have been reported as a cause of nosocomial infections in the U.S. and are usually mediated by aminoglycoside-modifying enzymes. Although earlier studies have reported the isolation of HLAR enterococci in food-producing animals, little information is available on the prevalence of HLAR enterococci among retail foods of animal origin.

**Methods:** HLAR enterococci (n=568) were previously isolated from meat samples purchased from grocery stores in 4 participating FoodNet states (GA, MD, OR, TN) via the NARMS retail meat program in 2002. The polymerase chain reaction (PCR) was utilized to examine each isolate for the presence of six different genes associated with aminoglycoside resistance in enterococci.

**Results:** The majority of HLAR enterococci were either *E. faecium* (n=338) or *E. faecalis* (n=214). The *aac(6')-Ie-aph(2'')-Ia* (n=113) and *aph(3')-IIIa* genes (n=108) were the most common aminoglycoside resistance genes identified among recovered enterococci. The *aac(6')-Ie-aph(2'')-Ia* gene was most often identified in *E. faecalis* isolates (n=102/113) and from ground turkey samples (n=69/113). Whereas, the *aph(3')-IIIa* gene was found in both *E. faecalis* (n=60) and *E. faecium* (n=45) isolates primarily from ground turkey samples (n=62/108). None of the isolates contained the *aph(2'')-Ic* or *aph(2'')-Ib* genes.

**Conclusions:** This study shows the presence of a reservoir of HLAR enterococci among retail foods of animal origin, predominately ground turkey. Additionally, the finding that many HLAR enterococci failed to generate a PCR product for any of the genes tested suggests the presence of new and unidentified aminoglycoside resistance genes.

**References:**

1. Vakulenko S, Donabedian S, Voskresenskiy M, Zervos S, Chow J. Multiplex PCR for detection of aminoglycoside resistance genes in enterococci. *Antimicrob Agents Chemother* 2003; 47:1423-1426.
2. Donabedian SM, Thal LA, Hershberger E, et al. Molecular characterization of gentamicin-resistant Enterococci in the United States: evidence of spread from animals to humans through food. *J Clin Microbiol* 2003; 41:1109-1113.

**P11** Antimicrobial Resistance of *Salmonella* Species from Chicken, Turkey, Cattle and Swine Slaughter IsolatesJ. S. Bailey<sup>1</sup>, P. J. Fedorka-Cray<sup>1</sup>, J. H. Haro<sup>1</sup>, N. Anandaraman<sup>2</sup>, B. Rose<sup>2</sup>, B. Salamone<sup>2</sup>;<sup>1</sup>Bacteriological Epidemiology and Antimicrobial Resistance, USDA, ARS, Athens, GA, <sup>2</sup>OPHS, USDA, FSIS, Washington, DC.

**Background:** The rate of food-associated enteritis due to *Salmonella* sp. has remained consistently higher than related to other bacterial pathogens. Public health and regulatory agencies have therefore made reduction of *Salmonella*, including multiple antibiotic resistant strains, from chicken and other animal products a major priority.

**Methods:** From 1999 through 2004, the prevalence and antimicrobial resistance profiles of *Salmonella* isolates from FSIS slaughter establishments submitted to the national antimicrobial resistance monitoring system (NARMS) were determined. More than 40,000 isolates of *Salmonella* from FSIS slaughter plants were analyzed for antimicrobial resistance profiles using NARMS protocols and procedures.

**Results:** In recent years, *Salmonella* recovery from chickens has increased from about 10% to about 16% while in cattle, swine and turkeys recovery has

remained constant or has been slightly reduced. Single antibiotic or multiple-drug resistance in *Salmonella* is primarily associated with the serovar of *Salmonella* and secondarily associated with the *Salmonella* from a particular animal host species. Examples include: more antimicrobial resistance is seen in *S. typhimurium* var 5- (formerly var Copenhagen) than from any other *Salmonella* serovar no matter the animal source,

**Conclusions:** *S. typhimurium* from turkeys carries more resistance than *S. typhimurium* from other animals; very little antimicrobial resistance is seen in *S. enteritidis* regardless of source. Single and multiple antimicrobial resistance characteristics of *Salmonella* serovar from all animal sources will be discussed.

**Reference:**

1. U.S. Department of Agriculture, Agricultural Research Service, Bacterial Epidemiology and Antimicrobial Resistance. Annual NARMS Reports, 1999-2004 [Online.] <http://www.ars.usda.gov/Main/docs.htm?docid=6750> Accessed 03 March 2006.

**P12** Antimicrobial Resistance in Small Animals: The Scope of the Problem

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**Background:** Antimicrobial resistance in small animals impacts both the pet (as a patient) and the pet owner (pet as reservoir). Previous data from our laboratory indicates a disconcertingly high incidence of multidrug resistant *E. coli* uropathogens in our canine patients. We hypothesize that the incidence of resistant *E. coli* canine and feline pathogens is greater in patients at teaching hospitals (predominantly medically-complicated infections) compared to private practitioners (generally uncomplicated infections) and that resistance varies geographically.

**Methods:** *E. coli* isolates (n=350) were collected from four veterinary teaching hospitals: Alabama, Mississippi, North Carolina, Kansas and Washington; and five veterinary commercial laboratories: Indiana, Massachusetts, Wisconsin, and California. MICs were determined using Epsilon Testing for 7 drugs: amoxicillin (AC), amoxicillin-clavulanic acid (XL), cefpodoxime (PX) doxycycline (DC), enrofloxacin (EN), gentamicin (GF) and trimethoprim-sulfadimethoxine (TS). Percent resistance and pharmacodynamic indices were compared among laboratories (region and type).

**Results:** Percent resistance ( $p \leq 0.05$ ) was higher in teaching compared to commercial labs (Table 1). Within lab sources, the highest and lowest rates were Alabama (47%) versus Washington (27%) for teaching labs and Massachusetts (20%) versus California (11%) for commercial labs.

**Conclusions:** The incidence of *E. coli* resistance in small animals varies geographically and with laboratory source.

Table 1: Overall Percent Resistance of Small Animal *E. coli* Pathogens to Selected Drugs.

Drug	AC	XL	PX	DC	EN	GF	TS
Commercial	39±6	28±7	12±6	16±5	10±6	6±5	10±8
Teaching	56±11	51±11	33±11	31±9	31±12	19±11	26±13

**References:**

1. Guardabassi L, Schwarz S, Lloyd DH. Pet animals as reservoirs of antimicrobial-resistant bacteria. *J Antimicrob Chemother* 2004; 54:321-332.
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## ABSTRACTS OF SUBMITTED POSTER PRESENTATIONS

**P13** Effectiveness of Intranasal Mupirocin in the Eradication of Methicillin-Resistant *Staphylococcus aureus* (MRSA) Nasal Colonization in Premature InfantsJ. L. Murillo<sup>1</sup>, P. Harmon<sup>1</sup>, T. Chan<sup>2</sup>, M. Cohen<sup>3</sup>;<sup>1</sup>Epidemiology, Newark Beth Israel Medical Center, Newark, NJ,<sup>2</sup>Microbiology, Newark Beth Israel Medical Center, Newark, NJ,<sup>3</sup>Neonatology, Newark Beth Israel Medical Center, Newark, NJ.

**Background:** MRSA is an organism of epidemic potential in the neonatal intensive care unit (NICU). Control measures include decolonization of nasal carriers with topical mupirocin. We describe our experience with intranasal mupirocin during an MRSA outbreak in the NICU.

**Method:** Nasal cultures were obtained from all infants hospitalized during a 16 week period from July to November 2005 after a cluster of 6 patients were identified with MRSA infection. Positive patients were treated with intranasal mupirocin applied twice daily for 7 days. Post-treatment cultures were obtained and repeated at one month.

**Results:** 26 out of 418 (6.2%) nasal cultures from 248 infants were found positive for MRSA. Of 23 infants treated with intranasal mupirocin, 2 (8.7%) required 14 days of treatment. Two patients relapsed at 52 days and one patient at 42 days requiring a second course of treatment. Two patients with MRSA nasal colonization progressed to bacteremia. Six out of 175 (3.4%) NICU healthcare workers also had nasal colonization with MRSA and all cleared after one course of mupirocin treatment.

**Conclusion:** Intranasal mupirocin was effective in eradicating nasal colonization with MRSA in premature infants. Some patients required a longer course or a second course of treatment. Patients with MRSA nasal colonization not treated with mupirocin may progress to bacteremia.

**References:**

1. Hitomi S, Kubota M, Mori N, et al. Control of a methicillin-resistant *Staphylococcus aureus* outbreak in a neonatal intensive care unit by unselective use of nasal mupirocin ointment. *J Hosp Infect* 2000; 46:123-129.
2. Semret M, Miller MA. Topical mupirocin for eradication of MRSA colonization with mupirocin-resistant strains. *Infect Control Hosp Epidemiol* 2001; 22:578-580.

**P14** Comparison of Outcomes between Methicillin-Resistant *Staphylococcus aureus* (MRSA) versus Methicillin-Sensitive *Staphylococcus aureus* (MSSA) Bacteremia in Inpatient Setting

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**Background:** MRSA bacteremia among inpatients has been typically associated with high morbidity and mortality. The introduction of the less lethal community-acquired MRSA into the inpatient setting could reduce the morbidity and mortality of MRSA.

**Method:** Outcome measures of 134 patients with MRSA and MSSA bacteremia from January 1, 2004 to December 31, 2004 were reviewed to determine mortality and length of stay (LOS). Community-acquired or community-onset bacteremia was defined as any positive blood culture identified within 3 days of hospitalization. Mortality rates, LOS and proportion of community-acquired bacteremias were compared between MRSA and MSSA.

**Results:** 81 patients with MSSA bacteremia and 57 patients with MRSA bacteremia were identified for comparison. There was no difference in the mortality rates between the two groups (1.2% versus 3.8%). However, mean LOS for MRSA bacteremia (27.1 days, 95% C.I. 21.8-32.4) was significantly longer

than MSSA (13.6 days, 95% C.I. 9.4-17.9)  $p < 0.0001$ . There was no difference in the proportion of community-acquired or onset bacteremia between MRSA and MSSA (71.7% versus 82.7%,  $p = 0.20$ ) and in the number of hospital encounters prior to the onset of bacteremia between the two groups.

**Conclusion:** There was no difference in the mortality rates between MRSA and MSSA bacteremia but the LOS remained significantly longer for MRSA.

**References:**

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2. Cosgrove SE, Sakoulas G, Perencevich EN, et al. Comparison of mortality associated with methicillin-resistant and methicillin-susceptible *Staphylococcus aureus* bacteremia: a meta-analysis. *Clin Infect Dis* 2003; 36:53-59.

**P15** Susceptibility of *E. coli* to Fluoroquinolones Decreases with Age in Adult Women with Uncomplicated Urinary Tract Infections in the Community Setting: A Nationwide Study in an Israeli HMON. R. Kahan<sup>1</sup>, D. P. Chinitz<sup>2</sup>, D. A. Waitman<sup>1</sup>, D. Dushnitsky<sup>3</sup>, E. Kahan<sup>4</sup>, M. Shapiro<sup>5</sup>;<sup>1</sup>Medical Division, Leumit Health Fund, Tel-Aviv, ISRAEL, <sup>2</sup>School of Public Health, Hebrew University of Jerusalem, Jerusalem, Israel, <sup>3</sup>Leumit Health Fund, Tel-Aviv, Israel, <sup>4</sup>Department of Family Medicine, Sackler Faculty of Medicine, Tel-Aviv University, Tel-Aviv, Israel, <sup>5</sup>Department of Clinical Microbiology and Infectious Diseases, Hadassah-Hebrew University Hospital, Jerusalem, Israel.

**Background:** Guidelines for the treatment of uncomplicated cystitis in women recommend empiric therapy with antibiotics for which resistance rates do not exceed 10%-20%. The growing prevalence of *Escherichia coli* resistant to fluoroquinolones (FQs) has therefore raised concern. We hypothesized that due to increased utilization, resistance to FQs may have surpassed this level in older women in the Israeli community setting. The purpose of this study was to identify age groups of women in which FQs may no longer be appropriate for empiric treatment of cystitis.

**Methods:** This study was conducted the Leumit Health Fund, an Israeli HMO. Five year age interval stratum-specific resistance rates (% and 95% CI) for ofloxacin were calculated for all cases of women aged 41-75 with a urine culture found positive for *E. coli*, diagnosed with non-recurrent, uncomplicated cystitis during the first five months 2005 without putative risk factors for FQ resistance.

**Results:** The data from 1,291 urine cultures were included. The crude resistance rate was 8.7% (95% CI: 7.1-10.2). Resistance was lowest amongst younger women (3.2%; 95% CI: 1.1-5.2) and highest amongst older women (19.9%; 95% CI: 13.2-26.5). Resistance rates increased with age with a linear trend ( $\chi^2$  for linear trend 18.8;  $P < 0.001$ ), approaching 10% in women aged 51-55 (7.1%; 95% CI: 3.4-10.9).

**Conclusions:** Physicians opting to empirically treat cystitis in postmenopausal women should consider prescribing drugs other than FQs.

**Reference:**

1. Warren JW, Abrutyn E, Hebel JR, Schaeffer AJ, Stamm WE. Guidelines for antimicrobial treatment of uncomplicated acute bacterial cystitis and acute pyelonephritis in women. *Clin Infect Dis* 1999;29:745-758.

## ABSTRACTS OF SUBMITTED POSTER PRESENTATIONS

**P16** Molecular Typing and Control of Multidrug Resistant *Acinetobacter baumannii* Infections in a Community Hospital in New York

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**Background:** Multidrug resistant *Acinetobacter baumannii* (MDRAB) strains are recognized as pathogens and hospital outbreaks are an emergent problem owing to its ability to acquire multiple antibiotic resistance genes. Control of nosocomial outbreaks caused by *Acinetobacter baumannii* (AB) is challenging especially in a community hospital. In this study, we controlled a nosocomial outbreak due to *Acinetobacter* confirmed by pulsed-field gel electrophoresis (PFGE).

**Methods:** Ninety-one isolates of AB from 39 patients admitted to Columbia Memorial Hospital, a 192-bed community hospital in Hudson, NY from Jan 1, 2005 to Feb 28, 2006 were analyzed. Fifty-nine isolates were resistant to multiple agents and were examined in detail. Seven isolates (from 6 patients), three from March 2005 and four isolates from Nov 2005 to Jan 2006 were examined using PFGE. Strict control initiatives included amplified contact precautions, hand washing, education, infection control compliance, colonization surveillance, and environmental surveillance were implemented after March 2005. After 7 months a number of MDRAB strains were again isolated and four isolates with the same antibiogram pattern were tested using PFGE.

**Results:** The initial three isolates examined in March 2005 outbreak had patterns that were indistinguishable and were considered to be related. Three isolates in the second outbreak revealed patterns that differed by >3 bands and therefore unlikely to be related, one was 3 or less different and interpreted maybe related.

**Conclusions:** Though the incidence of MDRAB strains is increasing, a program focused on preventing transmission by the implementation of a strict infection control policy is effective even in a small community hospital with limited resources.

**References:**

1. Marchione S, Koll B, Raucher B, Yampierre C, Protic J. The importance of molecular typing and environmental culturing in the control of *Acinetobacter* sp. American Society of Microbiology Annual Meeting, May 24-27, 2004.
2. Wang J, McDonald L, Chang S, Ho M. Community-acquired *Acinetobacter baumannii* bacteremia in adult patients in Taiwan. *J. Clin. Microbiol.* 2002; 40:1526-1529.

**P17** The Relationships of Antimicrobial Control Policies and Hospital and Infection Control Characteristics with Antimicrobial Resistance Rates

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**Background:** Antibiotic misuse and noncompliance with infection control (IC) precautions have contributed to increasing levels of antimicrobial resistance (AR) in hospitals. We assessed the extent to which IC programs monitored AR and correlated resistance rates with characteristics of antimicrobial control policies, provider attitudes and practices, and implementation of the CDC hand hygiene guideline.

**Methods:** During site visits to 33 U.S. hospitals, IC directors provided data on antimicrobial control policies and rates during the previous 12 months of three resistant organisms: methicillin-resistant *S. aureus* (MRSA), vancomycin-resistant enterococci (VRE), and ceftazidime-resistant *K. pneumoniae* and level of implementation of the CDC guideline. ICU staff completed questionnaires regarding their attitudes toward practice guidelines and observations of staff

hand hygiene were made. Variables associated with resistance rates were examined for independent effects using logistic regression.

**Results:** MRSA, VRE and ceftazidime-resistant *K. pneumoniae* rates were 52.5%, 18.2%, and 16.0%, respectively. Ten (30.3%) hospitals had an antibiotic control policy. Hospitals with high guideline implementation scores had significantly lower levels of MRSA ( $p < 0.05$ ) and VRE ( $p = 0.001$ ). No statistically significant correlation was observed between staff attitudes toward practice guidelines, observed hand hygiene behavior or having an antibiotic use policy and resistance rates. In logistic regression analysis, only implementation score was a significant predictor of higher rates of MRSA and VRE.

**Conclusions:** The presence of an antibiotic control policy does not necessarily guarantee its effectiveness. In this study hospital-wide prevention efforts were associated with less antimicrobial resistance.

**References:**

1. Diekema DJ, BootsMiller BJ, Vaughn TE, et al. Antimicrobial resistance trends and outbreak frequency in United States hospitals. *Clin Infect Dis* 2004; 38:78-85.
2. Gould IM. Antibiotic policies and control of resistance. *Curr Opin Infect Dis* 2002;15:395-400.

**P18** Low Colonization Rates with Methicillin-Resistant and Methicillin-Susceptible *Staphylococcus aureus* in the Northwest Brooklyn Pediatric Population

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<sup>2</sup>Microbiology, Beth Israel Medical Center, New York, NY.

**Background:** Community-acquired methicillin-resistant *Staphylococcus aureus* (MRSA) is an emerging pathogen in pediatrics. In the US, nasal MRSA colonization rates in children were reported to have increased from 0.4-2.2% to 9.2% over the last 5 years. In New York City, available data suggests low pediatric MRSA carriage rate. Accordingly, the present study examines MRSA prevalence and potential colonization risk factors in a northwest Brooklyn pediatric cohort.

**Methods:** In two ambulatory pediatric settings anterior nares cultures were obtained. Parents completed a questionnaire to assess risk factors. *S. aureus* was isolated using standard microbiological methods. Antibiotic susceptibility testing was performed by the Vitek System (bioMérieux) and confirmed by disk-diffusion method. Statistical analyses employed Fisher's exact test.

**Results:** Cultures were obtained in 327 children, and only one child (0.3%), with mild-intermittent asthma but no other identifiable risk factors, was MRSA positive. Fifty-four cultures (16.5%) grew methicillin-susceptible *S. aureus* (MSSA). MSSA positive children tended to be older (mean 6.2y vs. 4.4y) and attended elementary ( $p < 0.001$ ) and middle schools ( $p < 0.03$ ). MSSA colonization was more frequent in the hospital-based clinic (25% vs. 8% in private office,  $p < 0.006$ ) and in the spring (29% vs. 9% in summer,  $p < 0.01$ ).

**Conclusions:** 1. Despite increasing numbers of reported MRSA infections, nasal carriage in children in New York City remains low; 2. MSSA colonization occurs more frequently in the spring, among older children attending grade school, and in a hospital-based clinic setting.

**References:**

1. Creech C, Kernodle D, Alsentzer A, Wilson C, Edwards KM. Increasing rates of nasal carriage of methicillin-resistant *Staphylococcus aureus* in healthy children. *Pediatr Infect Dis J* 2005; 24:617-621.
2. Shopsin B, Mathema B, Martinez J, et al. Prevalence of methicillin-resistant and methicillin-susceptible *Staphylococcus aureus* in the community. *J Infect Dis* 2000; 182:359-362.

## ABSTRACTS OF SUBMITTED POSTER PRESENTATIONS

**P19** Molecular Epidemiology of Methicillin-Resistant *Staphylococcus aureus* Infections in Mexico: a Multicenter Laboratory-Based Surveillance Study

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**Background:** Methicillin-resistant *Staphylococcus aureus* (MRSA) infections have been confined as cause of hospital-acquired infections (HAI), however MRSA has been recently isolated from community-acquired infections (CAI) worldwide. Therefore, we conducted a laboratory-based surveillance study in 12 Mexican centers to determine the rate of MRSA among both CAI and HAI during 2004.

**Methods:** All clinical isolates were recovered from invasive infections and only one isolate per patient was processed. Isolates were identified by standard procedures, tested for MIC determination, tested for *mecA* gene by PCR amplification and genotyped by PFGE.

**Results:** We included 828 isolates recovered from blood (221), soft tissue (202), surgical wound (139), respiratory-tract (116), IV catheters (34) and others (116); 77% came from HAI. The global rate of MRSA was 36%; it was higher among HAI (37.8%) than in CAI (29.3%). It was higher among ICU-patients (44.2%) than in other hospital areas (34.2%) ( $p=0.025$ ), and in adults than in children (41% vs. 14.5%,  $p<0.01$ ); the rate of resistance to quinolones, macrolides and lincosamides was >40%, but in MRSA was  $\geq 95\%$ . No resistance to vancomycin, streptogramin and linezolid was found. Forty percent of MSSA ( $n=531$ ) and 71% of MRSA ( $n=297$ ) isolates belonged to a cluster by PFGE. Outbreaks were identified in 10 of 12 participating centers and included CAI and HAI isolates; in some cases even mixed clusters were identified.

**Conclusions:** The high rate of MRSA (29.3%) in CAI was completely unexpected. PFGE analysis showed outbreaks in hospitals and in the community. The nationwide emergence of multidrug-resistant *S. aureus* may indicate a dissemination of a dangerous nosocomial pathogen into the community.

**References:**

- Zetola N, Francis JS, Nuernberger EL, Bishai WR. Community-acquired methicillin-resistant *Staphylococcus aureus*: an emerging threat. *Lancet Infect Dis* 2005; 5:275-286.
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**P20** Increasing *Clostridium difficile* Morbidity and Mortality, Florida Hospitals, 1998 -2003

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**Background:** Florida has had increasing reports of morbidity and mortality caused by *Clostridium difficile*. Florida is one of 16 states with confirmed cases of the newly described North American Pulsed Field Type 1 strain.

**Methods:** A public use file of Florida hospital discharges (1998-2003) was analyzed for *Clostridium difficile* enteritis (ICD-9-CM code (0008.45) and discharge status (dead versus alive).

**Results:** During a 6-six year period, discharges coded as *C. difficile* increased from 34.0/100,000 in 1998 to 70.2/100,000 in 2003; the biggest increase was in 2000-2001 with a change from 35.0 to 46.9. Deaths among patients coded as a *C. difficile* discharge increased from 94.8/1000 (1998) to 106.7/1000 (2003), and more than 80% of deaths occurred among patients  $\geq 75$  years or older.

**Conclusions:** The recently described *C. difficile* variant may be responsible for the increased incidence and mortality in Florida. Between 1998-2003, rates of *C. difficile* discharges and deaths both increased. Further characterization of risk factors associated with *C. difficile* hospitalization and deaths is needed.

**Reference:**

- McDonald LC, Killgore GE, Thompson M, et al. An epidemic, toxin gene-variant strain of *Clostridium difficile*. *N Engl J Med* 2005; 353:2433-2441.

**P21** Complicated Skin and Skin Structure Infections (cSSSI) with Community Phenotype Methicillin Resistant *Staphylococcus aureus* (CP-MRSA) in the Cubicin Outcomes Registry and Experience (CORE 2005)

W. J. Martone, D. E. Katz;

Medical Affairs, Cubist Pharmaceuticals, Lexington, MA.

**Background:** Community onset MRSA infections are increasing; little information about treatment of these infections with daptomycin (DAP) is available.

**Methods:** CORE 2005 is a retrospective chart review of patients (pts) who received DAP. 100 pts had cSSSI with MRSA; pts with concomitant MRSA infection sites (eg., blood) were excluded. CP-MRSA was defined as MRSA susceptible to clindamycin (CLM) and trimethoprim-sulfamethoxazole (TMS). All other isolates, including 3 with CLM and TMS resistance, were classified as indeterminate (IND-MRSA).

**Results:** 28 pts had CP-MRSA and 72 had IND-MRSA cSSSI infections. 22 (79%) CP-MRSA pts were located in the community in the 48 hours prior to DAP therapy vs. 41 (58%) of IND-MRSA pts ( $\chi^2$ -square  $p=.052$ ). CP-MRSA pts were younger (61% vs 33% < 50 yrs), had fewer underlying diseases (mean = 1.5 vs. 2.3), and received fewer concomitant antibiotics than IND-MRSA pts. The most common DAP dosages were 4 mg/kg (51%) and 6 mg/kg (25%). 74% of the pts received other antibiotics before DAP. Outcomes were similar in CP-MRSA (93% success) and IND-MRSA (83% success); however days to clinical response (3.2d vs. 7.8d) and duration of therapy (8.3d vs. 20d) were shorter in CP-MRSA.

**Conclusion:** DAP was used first line in 26% of pts. Outcomes were similar in CP-MRSA and IND-MRSA. CP-MRSA pts received fewer concomitant antibiotics, had fewer days to clinical response, and shorter duration of therapy.

**Reference:**

- Arbeit RD, Maki D, Tally FP, et al. The safety and efficacy of daptomycin for the treatment of complicated skin and skin structure infections. *Clin Inf Dis* 2004; 38:1673-1681.

## ABSTRACTS OF SUBMITTED POSTER PRESENTATIONS

**P22** Complicated Skin and Skin Structure Infection (cSSSI) with Culture Confirmed *Staphylococcus aureus* Treated with Daptomycin (DAP): Cubicin Outcome Registry and Experience (CORE)\_2005 Interim Analysis

D. E. Katz, W. J. Martone;  
Cubist Pharmaceuticals, Lexington, MA.

**Background:** DAP (Cubicin®) is indicated for treatment of cSSSIs caused by certain susceptible Gram-positive pathogens, including methicillin resistant *Staphylococcus aureus* (MRSA) and methicillin susceptible *S. aureus* (MSSA). CORE was developed in 2004 to capture data on post-approval clinical experience with DAP.

**Methods:** CORE is a retrospective, multicenter registry, designed to collect data on patients (pts) who received DAP. For this analysis, concomitant MRSA infection sites were excluded. 130 records of pts with cSSSI due to culture confirmed MRSA and MSSA were analyzed. As of January 31, 2005, 43 clinical sites in the U.S. submitted data.

**Results:** 100 pts had MRSA and 30 pts had MSSA. Demographics of pts were: 71 (55%) female, 83 (64%) located in the community two days prior to DAP therapy, 76 (58%) > 50 years of age, hypertension (41%), and diabetes (33%). On average, 71% of pts received other Gram-positive antibiotics before DAP treatment (74% MRSA and 63% MSSA). Common DAP dosages were 4 mg/kg/d (46%), 6 mg/kg/d (22%), and 5 mg/kg/d (8%). Clinical success was reported in 86% of pts (41% cure and 45% improved), failure in 5%, and nonevaluable in 10%. Outcomes were similar for MRSA (86% success) and MSSA (83% success). Mean days to clinical response for MRSA and MSSA were 6.5 and 6.0, respectively.

**Conclusions:** DAP was used first-line in 29% of pts with cSSSI. Outcomes were similar in pts with MRSA and MSSA. Overall outcomes were similar to pivotal clinical trials<sup>1</sup>; however, success in MRSA pts appeared higher in CORE 2005.

**References:**

1. Arbeit RD, Maki D, Tally FP, et al. The safety and efficacy of daptomycin for the treatment of complicated skin and skin structure infections. *Clin Inf Dis* 2004;38:1673-1681.
2. Martone WJ, Lamp KC. Complicated skin and skin structure infections (cSSSI) treated with daptomycin (DAP) in the Cubicin Outcomes Registry and Experience (CORE), Poster Presentation, NFID 2004 Conference on Antimicrobial Resistance, June 28-30, 2004.

**P23** Epidemiological Cut-Off Values for Four Antimicrobial Agents Against *Aeromonas salmonicida* Isolates Using MIC and Zone Diameter Frequency Distributions

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**Background:** Breakpoints for antimicrobial agents may be clinical or epidemiological. The objective of this study was to develop epidemiological cut-off values for four antimicrobial agents when tested against a representative population of the major aquaculture pathogen, *Aeromonas salmonicida*.

**Methods:** Species identification of 223 submitted, geographically distributed *A. salmonicida* isolates was completed using polymerase chain reaction (PCR). Oxytetracycline, ormetoprim/sulfadimethoxine, florfenicol, and oxolinic acid minimum inhibitory concentrations (MICs) and zone diameters were determined for each isolate in accordance with the standardized antimicrobial susceptibility testing methods for bacterial isolates from aquatic animals, recently approved by the CLSI. Susceptibility data was tabulated in a scattergram and analyzed using error rate-bounding.

**Results:** Susceptibility tests on oxytetracycline, ormetoprim/sulfadimethoxine, and oxolinic acid revealed two distinct populations of bacteria. Isolates tested against florfenicol clustered in a single population. Oxolinic acid susceptibility data revealed higher MICs in the non-USA *A. salmonicida* isolates. Slower growing atypical isolates were generally more susceptible than typical isolates for all drugs except oxolinic acid.

**Conclusions:** The use of population distributions sometimes used with antimicrobial susceptibility testing of mammalian isolates to develop epidemiological cut-off values appears to be appropriate for use in aquatic medicine. This type of data, considered with pharmacokinetic and efficacy data may be useful for developing clinical breakpoints in aquaculture in the future.

**Reference:**

1. Miller RA, Walker RD, Carson J, et al. Standardization of a broth microdilution susceptibility testing method to determine minimum inhibitory concentrations of aquatic bacteria. *Dis Aquat Organ* 2005; 64:211-222.

**P24** Ciprofloxacin and Erythromycin Resistance in *Campylobacter*, NARMS, 1997-2004

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**Background:** *Campylobacter* is the most common cause of bacterial gastroenteritis in the US. Most infections are self-limited, but antibiotic treatment is essential for serious illness. Fluoroquinolones (e.g., ciprofloxacin) and macrolides (e.g., erythromycin) are the most frequently used antibiotics. Poultry is the major source for human infections. In 2005, FDA banned fluoroquinolone use in poultry due to human antibiotic resistance concerns.

**Methods:**

Since 1997, participating states forwarded one *Campylobacter* isolate each week to the National Antimicrobial Resistance Monitoring System for Enteric Bacteria (NARMS) at CDC. In 1997, 5 states submitted isolates; since 2003, 10 states participated. Isolates were speciated and susceptibility tested using E-test. Ciprofloxacin resistance was defined as minimum inhibitory concentration (MIC)  $\geq 4$   $\mu\text{g/mL}$ . Erythromycin resistance, defined as MIC  $\geq 32$   $\mu\text{g/mL}$ , was based on new Clinical and Laboratory Standards Institute (CLSI) breakpoints for erythromycin.

**Results:** From 1997-2004, 2,649 *Campylobacter* isolates were tested: 2,484 (94%) were *C. jejuni*, 140 (5%) were *C. coli*, and 25 (1%) were other/unknown species. Ciprofloxacin resistance was detected in 457 (17%) isolates and erythromycin resistance in 34 (1%). Among *C. jejuni*, 416 (17%) were ciprofloxacin-resistant and 25 (1%) were erythromycin-resistant. Among *C. coli*, 36 (26%) were ciprofloxacin-resistant and 8 (6%) were erythromycin-resistant. Ciprofloxacin resistance increased from 13% (28/217) in 1997 to 18% (76/415) in 2004 among all *Campylobacter* isolates; it was 20% in 2002 and 18% in 2003. No increase in erythromycin resistance was found.

**Conclusions:** Ciprofloxacin resistance in *Campylobacter* has increased since 1997, peaking in 2002 and remaining unchanged in 2003-2004. To determine the impact of the withdrawal of fluoroquinolone use in poultry, national monitoring for resistance in *Campylobacter* needs to be continued.

**Reference:**

1. Gupta A, Nelson JM, Barrett TJ, et al. Antimicrobial resistance among *Campylobacter* strains, US, 1997-2001. *Emerg Infect Dis* 2004; 10:1102-1109.
2. Nelson JM, Smith KE, Vugia DJ, et al. Prolonged diarrhea due to ciprofloxacin-resistant *Campylobacter*. *J Infect Dis* 2004; 190: 1150-1157.

## ABSTRACTS OF SUBMITTED POSTER PRESENTATIONS

**P25** Antimicrobial Resistance Patterns in the Puerto Rico Medical Center  
D. Negron, M. I. Santé;  
Department of Pathology and Laboratory Medicine,  
University of Puerto Rico, San Juan, PR.

**Background:** Increasing antimicrobial resistance among hospital and community acquired pathogens is a major therapeutic challenge. Infections caused by resistant bacteria have higher rates of morbidity and mortality, with associated increased healthcare costs. The purpose of this study is to evaluate the trends in antibiotic resistance at the Puerto Rico Medical Center and compare the data with the international literature.

**Methods:** Organism occurrence and antimicrobial susceptibility data was extracted from the Vitek® DCS-R5 System (bioMerieux, Inc, Hazelwood, MO). These data comprised all the clinical isolates from blood, urine and miscellaneous sites processed by the clinical laboratory of the Medical Services Administration in the Puerto Rico Medical Center, during the period of January 2004 to December 2004.

**Results:** A total of 15,399 isolates were collected during the study period. Coagulase negative staphylococci were the most common pathogens isolated from blood. *Escherichia coli* accounted for most urinary tract infections. *Pseudomonas aeruginosa* was the most common isolate in the miscellaneous cultures. Fifty-four percent of *Staphylococcus aureus* were methicillin resistant. There were no cases of resistance to either vancomycin or linezolid. Of all the *Enterococcus faecalis* isolates, 21% and 94% were resistant to vancomycin and quinupristin/dalfopristin, respectively. Twenty-five percent of *Klebsiella pneumoniae* demonstrated extended spectrum beta-lactamases. *Pseudomonas aeruginosa* had higher rates of resistance to all first line antimicrobial agents, when compared with the international literature.

**Conclusions:** The elevated resistance rates to antimicrobial agents indicate the need to establish urgent measures of infectious disease control in order to reduce the emergence and spread of these pathogens.

**References:**

1. National Nosocomial Infections Surveillance System. National Nosocomial Infections Surveillance (NNIS) System Report, data summary from January 1992 through June 2004, issued October 2004. *Am J Infect Control* 2004; 32:470-485.
2. Jones RN. Global epidemiology of antimicrobial resistance among community-acquired and nosocomial pathogens: a five-year summary from the SENTRY antimicrobial surveillance program (1997-2001). *Semin Respir Crit Care Med* 2003; 24:121-131.

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