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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 approaches and strategies to preventing the transmission of multi-drug resistant organisms

Drug Resistant *Mycobacterium tuberculosis*: Looking Back, Looking Forward

- Discuss the global epidemiology of drug resistant tuberculosis and the potential relevance of bacterial fitness to its propagation
- Review the current state-of-the-art diagnostic tools for tuberculosis, including drug resistance, and the research and development work on new technologies
- Describe the present state of the tuberculosis drug pipeline, including projects in clinical development and the longer term prospects for meaningful improvement in TB drug therapy

The Evolution of Rapid Diagnostic Technology

- Discuss how rapid diagnostic technology can accelerate early pathogen identification and detection of resistance, thereby influencing antimicrobial therapy and public health interventions
- Evaluate the need for advancing diagnostics for routine animal disease detection and early diagnosis of exotic and emerging diseases of economic and animal/public health concerns
- Review the benefits and limitations of emerging technologies, including initial infectious disease targets for diagnosis
- Discuss how rapid testing for antimicrobial resistance can impact antibiotic use, patient management, and the laboratory environment

Resistance and Public Policy

- Outline who benefits and who is harmed by different policies to address antibiotic resistance
- Discuss the life-threatening nature of lower respiratory tract infections caused by community-associated MRSA

Behavioral and Social Issues Related to Inappropriate Antibiotic Use

- Identify social and cultural influences on the inappropriate use of antibiotics and other approaches to influence antibiotic seeking behavior such as mass media campaigns
- Examine the evidence that seeks to improve appropriate antibiotic use leading to improved outcomes for patients
- Discuss the impact of different types of education-based interventions on antibiotic prescribing in emergency departments for URIs and acute bronchitis in adults

Superbugs and Severe Infections: What Do You Do?

- Review the epidemiology of hospital-associated MRSA and the clinical impact of infection caused by this pathogen
- Review the epidemiology and microbiology of emerging gram negative resistance in nosocomial gram negative bacilli in U.S. hospitals
- Discuss the contemporary epidemiology, clinical features, strain characteristics, and therapy for CA-MRSA infections in infants, children, and adolescents
- Examine the epidemiology of drug-resistant fungi, and analyze possible therapeutic approaches

Living in a Microbial World

- Examine the forces that are creating the emergence of a new group of infectious disease threats and the role of animals and their products in this biological phenomenon
- Review current knowledge of molecular mechanisms employed by bacteria to circumvent antimicrobial chemotherapy
- Discuss the activities of the FDA in monitoring antimicrobial resistance among food borne pathogens

Potential Influences of Therapy Duration on Resistance

- Demonstrate the dual influences of therapy intensity and therapy duration on the amplification of resistant bacterial subpopulations
- Discuss the influence and interrelationship of treatment duration, choice of agent, and adherence level on resistance and outcome of treatment with HIV antiretroviral therapy
- Examine the relationship between the duration of treatment and the development of drug resistance in tuberculosis and the evidence elucidating the nature of that relationship

Acknowledgments (as of June 2007)

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3M Medical
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Monitoring System (NARMS)
U.S. Food and Drug Administration
Laurel, MD*

*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 16 *AMA PRA Category 1 credits*[™]. Physicians should claim credit commensurate with the extent of their participation in the educational activity.

Continuing Nursing Education

NFID is an approved provider of continuing nursing education by the Maryland Nurses Association, an accredited approver by the American Nurses Credentialing Center's Commission on Accreditation. This educational activity has been approved for a maximum of 16 contact hours. To receive credit, each participant must attend the entire program, and complete a daily sign-in sheet and conference evaluation.

Designated Continuing Education Activities

Sessions designated with a **CE** symbol have been approved for credit. 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 daily in order to receive credit for attendance

CME Disclosures

In order for program sessions to be accredited, program presenters must disclose to the conference participants any real or apparent conflict(s) of interest related to the content of their presentations. 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 **301-657-1234**.

No Smoking Policy

The Hyatt Regency Bethesda is a non-smoking facility except for specially designated guest rooms.

Poster Session

The Poster Session/Reception will be held on Monday, June 25, 6:00p.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.

Syllabus and Handouts

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. The conference is unable to replace misplaced programs.

Handouts of the plenary presentations will also be available as provided by the speaker. Due to the advance printing of the handouts, speaker presentations are subject to change. Please be sure to take advantage of the notes section to indicate any pertinent revisions. The conference is unable to provide revised copies of handouts.

Registration Fees and Hours

The onsite registration fee: **US \$500.00**

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 24	7:00 p.m. – 8:30 p.m.
Monday, June 25	8:00 a.m. – 5:00 p.m.
Tuesday, June 26	7:00 a.m. – 5:00 p.m.
Wednesday, June 27	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, 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 26, 2007

Conference on Antimicrobial Resistance Organizing and Scientific Program Committee Meeting

(Closed meeting)

5:00 p.m. – 8:00 p.m., *Old Georgetown Room*

Wednesday, June 27, 2007

Interagency Task Force on Antimicrobial Resistance

Sponsored by the Centers for Disease Control and Prevention, U.S. Food and Drug Administration, and the National Institutes of Health

11:30a.m.-12:30p.m., *Haverford/Baccarat Ballroom*

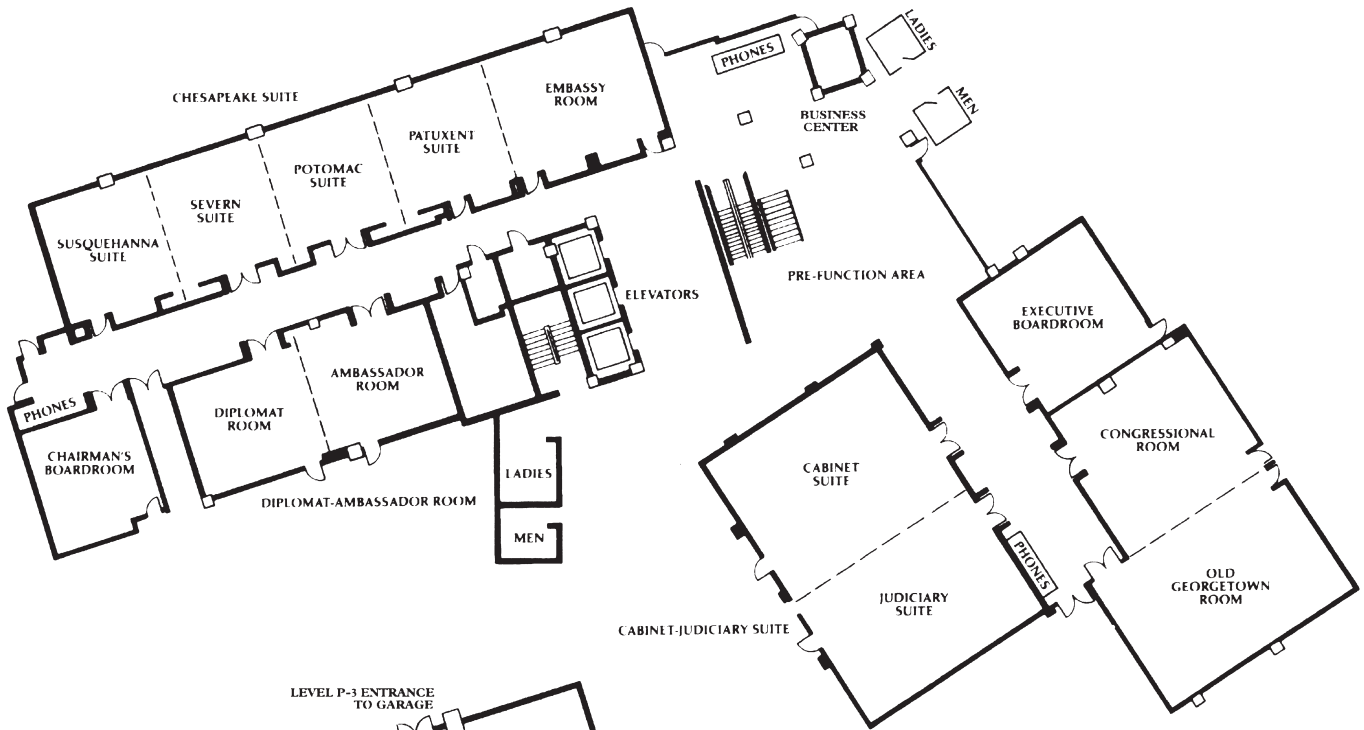
The Centers for Disease Control and Prevention (CDC), Food and Drug Administration (FDA), and National Institutes of Health (NIH), co-chairs of the Interagency Task Force on Antimicrobial Resistance, will hold an open meeting to present the annual report of progress by Federal agencies in “A Public Health Action Plan to Combat Antimicrobial Resistance (Part I: Domestic Issues)” and solicit comments from the public regarding the annual report. The Action Plan and Annual Report are available at <http://www.cdc.gov/drugresistance>.

PROGRAM-AT-A-GLANCE

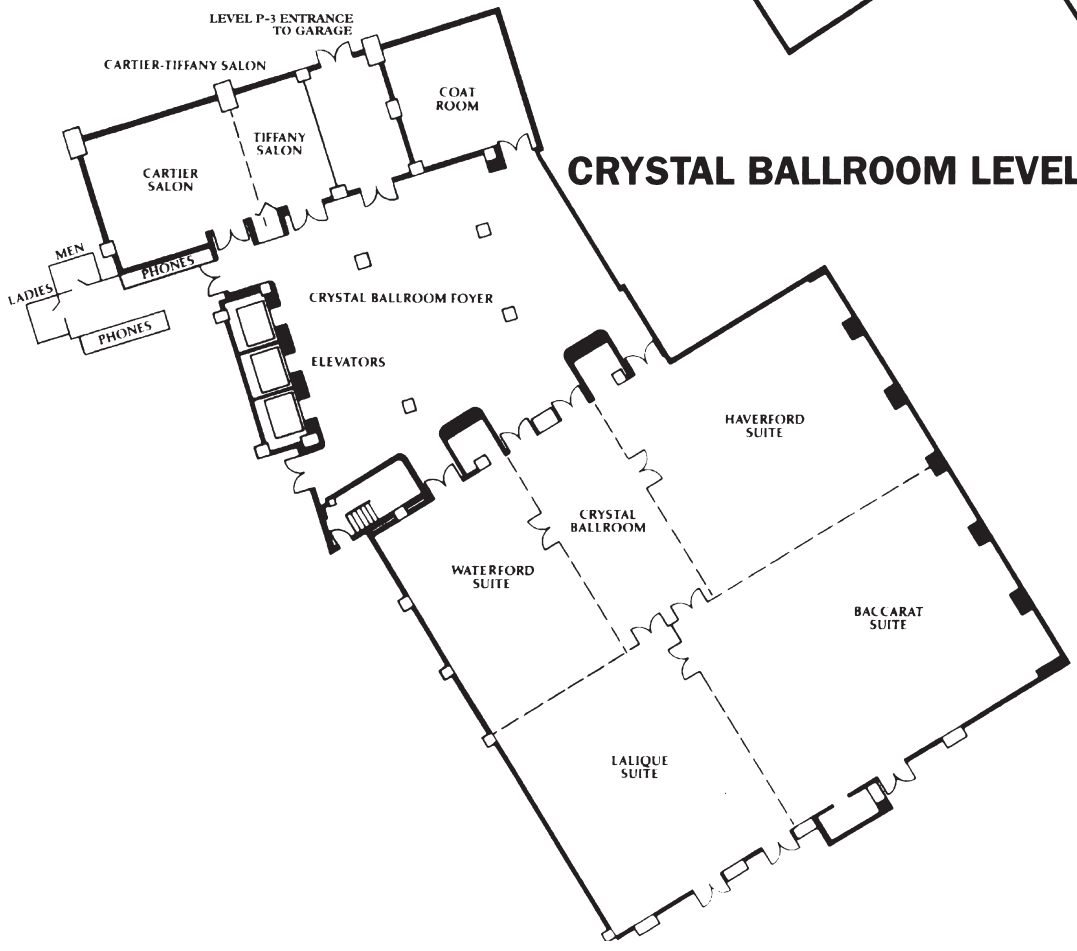
	SUNDAY, JUNE 24	MONDAY, JUNE 25	TUESDAY, JUNE 26	WEDNESDAY, JUNE 27
7:00am-5:00pm			Registration	Registration
7:00am-10:30am				Meet the Experts Breakfast Session
7:15am-7:45am			Meet the Experts Breakfast Session	Meet the Experts Breakfast Session
7:30am-8:00am			Continental Breakfast	Continental Breakfast
8:00am		Poster Set-up		
8:00am-9:30am			Symposium 4: Behavioral and Social Issues Related to Inappropriate Antibiotic Use	
8:00am-10:00am		Registration		Symposium 7: Potential Influences of Therapy Duration on Resistance
8:00am-5:00pm				
8:30am-9:20am		Continental Breakfast		
9:20am-9:30am		Welcome and Introductions		
9:30am-10:00am			Coffee Break	
9:30am-10:30am		Keynote Address		
10:00am-10:30am				Coffee Break
10:00am-12:00pm			Symposium 5: Superbugs and Severe Infections: What Do You Do?	
10:30am-11:00am		Coffee Break		
10:30am				Submitted Presentations
11:00am-1:00pm		Symposium 1: Drug Resistant <i>Mycobacterium tuberculosis</i> : Looking Back, Looking Forward		
11:30am				Adjournment/Participant Evaluation
12:00pm-1:30pm			Lunch (on your own)	
1:00pm-2:00pm		Lunch (on your own)		
1:30pm-2:30pm			Submitted Presentations	
2:00pm-4:00pm		Symposium 2: The Evolution of Rapid Diagnostic Technology		
2:30pm-3:00pm			Coffee Break	
3:00pm-4:30pm			Symposium 6: Living in a Microbial World	
4:00pm-4:30pm		Coffee Break		
4:30pm			Adjournment	
4:30pm-6:00pm		Symposium 3: Resistance and Public Policy		
6:00pm		Poster Session and Reception		
7:00pm-8:30pm	Registration			

HOTEL FLOOR PLAN

CONFERENCE LEVEL



CRYSTAL BALLROOM LEVEL



FINAL PROGRAM

Sunday, June 24, 2007

7:00 p.m.–
8:30 p.m.

Registration

Crystal Ballroom Foyer

Monday, June 25, 2007

8:00 a.m.–
5:00 p.m.

Registration

Crystal Ballroom Foyer

8:00 a.m.

Poster Set-Up

Waterford/Lalique Ballroom

8:45 a.m.

Continental Breakfast

Crystal Ballroom Foyer

9:20 a.m.

Opening Remarks

Susan J. Rehm, M.D.

*National Foundation for Infectious Diseases
Bethesda, MD*

Haverford/Baccarat Ballroom

Keynote Address 

Haverford/Baccarat Ballroom

Moderator: Susan J. Rehm, M.D.

*National Foundation for Infectious Diseases
Bethesda, MD*

9:30 a.m.

1. Brave New World: Preventing Emergence and Transmission of Resistant Organisms

Trish M. Perl, M.D., M.Sc.

*Johns Hopkins School of Medicine
Baltimore, MD*

10:20 a.m.

Questions and Answers

10:30 a.m.

Coffee Break

Crystal Ballroom Foyer

FINAL PROGRAM

Monday, June 25, 2007 *(continued)*

Symposium 1. Drug Resistant CE
Mycobacterium tuberculosis:
Looking Back, Looking Forward

Haverford/Baccarat Ballroom

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

- 11:00 a.m. **2. Epidemiology of Multi-drug Resistant and Extensive Drug Resistant *Mycobacterium tuberculosis*: Transmission Dynamics and Fitness**
 Peter Small, M.D.
Bill & Melinda Gates Foundation
Seattle, WA
- 11:25 a.m. **Questions and Answers**
- 11:30 a.m. **3. Diagnostic Tools: Present and Future**
 Mark Perkins, M.D.
Foundation for Innovative New Diagnostics
Geneva, Switzerland
- 11:55 a.m. **Questions and Answers**
- 12:00 p.m. **4. Current Therapy for Tuberculosis: What Do You Do When the Going Gets Tough?**
 Joia S. Mukherjee, M.D., M.P.H.
Brigham and Women's Hospital
Boston, MA
- 12:25 p.m. **Questions and Answers**
- 12:30 p.m. **5. TB Drug Pipeline: Are There Meaningful New Drugs on the Event Horizon?**
 Mel Spigelman, M.D.
Global Alliance for TB Drug Development
New York, NY
- 12:55 p.m. **Questions and Answers**
- 1:00 p.m. **Lunch (on your own)**

FINAL PROGRAM

Symposium 2. The Evolution  of Rapid Diagnostic Technology*Haverford/Baccarat Ballroom*

Moderator: Susan J. Rehm, M.D.
*National Foundation for Infectious Diseases
 Bethesda, MD*

2:00 p.m.

- 6. Role of Rapid Diagnostics**
 Nabin K. Shrestha, M.D.
*The Cleveland Clinic Foundation
 Cleveland, OH*

2:25 p.m.

Questions and Answers

2:30 p.m.

- 7. Rapid Diagnostics in Veterinary Medicine**
 Richard D. Oberst, D.V.M., Ph.D.
*Kansas State University
 Manhattan, KS*

2:55 p.m.

Questions and Answers

3:00 p.m.

- 8. Current and Emerging Technologies**
 Lance R. Peterson, M.D.
*Evanston Northwestern Healthcare
 Evanston, IL*

3:25 p.m.

Questions and Answers

3:30 p.m.

- 9. Impact of Rapid Testing for Antimicrobial Resistance**
 Frederick S. Nolte, Ph.D.
*Emory University School of Medicine
 Atlanta, GA*

3:55 p.m.

Questions and Answers

4:00 p.m.

Coffee Break*Crystal Ballroom Foyer***Symposium 3: Resistance  and Public Policy***Haverford/Baccarat Ballroom*

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

4:30 p.m.

- 10. Introduction**
 John H. Powers, M.D.
*Scientific Applications International Corporation
 Bethesda, MD*

FINAL PROGRAM

Monday, June 25, 2007 *(continued)*

- 4:45 p.m. **11. Fundamental Economic Tradeoffs in Addressing the Problem of Resistance**
Anup Malani, J.D., Ph.D.
University of Chicago Law School
Chicago, IL
- 5:10 p.m. **Questions and Answers**
- 5:15 p.m. **12. Case Presentation: The Challenges of Life-Threatening CA-MRSA Infection**
John S. Bradley, M.D.
Children's Hospital, San Diego
San Diego, CA
- 5:30 p.m. **Round Table Discussion: Policy Approaches to Infectious Diseases Public Health Importance**
- 6:00 p.m. **Adjournment**
- 6:00 p.m. **Poster Session and Reception**

Tuesday, June 26, 2007

- 7:00 a.m. -
5:00 p.m. **Registration** *Crystal Ballroom Foyer*
- 7:15 a.m. -
7:45 a.m. **Meet the Experts Breakfast Session** *Waterford/Lalique Ballroom*
- Table One:**
What Would Accelerate New Agent Discovery and Development?
John H. Rex, M.D., F.A.C.P.
- Table Two:**
What is the Gates Foundation?
Peter M. Small, M.D.
- Table Three:**
TBA
Stuart H. Cohen, M.D.
- 7:30 a.m. **Continental Breakfast** *Crystal Ballroom Foyer*

FINAL PROGRAM

Symposium 4. Behavioral  and Social Issues Related to Inappropriate Antibiotic Use

Haverford/Baccarat Ballroom

Moderator: Cindy R. Friedman, M.D.
*Centers for Disease Control and Prevention
Atlanta, GA*

8:00 a.m.

13. Why Do Consumers Pursue Antibiotics? Cultural Influences on Antibiotic Seeking Behavior

Kitty K. Corbett, Ph.D., M.P.H.
*Simon Fraser University
British Columbia, Canada*

8:25 a.m.

Questions and Answers

8:30 a.m.

14. Physicians and Inappropriate Prescribing: What Can Be Done to Change Their Behavior

Jeffrey A. Linder, M.D., M.P.H.
*Brigham and Women's Hospital
Boston, MA*

8:55 a.m.

Questions and Answers

9:00 a.m.

15. Interventions to Improve Antibiotic Use in Acute Care Treatment: Results of the IMPAACT

Ralph Gonzales, M.D., M.S.P.H.
*University of California, San Francisco
San Francisco, CA*

9:25 a.m.

Questions and Answers

9:30 a.m.

16. Is There a Relationship Between Health Care Quality and Appropriate Antibiotic Use?

Joshua Metlay, M.D., Ph.D.
*University of Pennsylvania School of Medicine
Philadelphia, PA*

9:55 a.m.

Questions and Answers

10:00 a.m..

Coffee Break

Waterford/Lalique Ballroom

Symposium 5. Superbugs and  Severe Infections: What Do You Do?

Haverford/Baccarat Ballroom

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

FINAL PROGRAM

Tuesday, June 26, 2007 (continued)

- 10:15 a.m. **17. Severe Infections Due to Hospital-Associated MRSA**
 Adolf W. Karchmer, M.D.
Beth Israel Deaconess Medical Center
Boston, MA
- 10:40 a.m. **Questions and Answers**
- 10:45 a.m. **18. Severe Infections Caused by Hospital Associated Gram-negative Bacteria**
 John P. Quinn, M.D.
Rush Medical School
Chicago, IL
- 11:10 a.m. **Questions and Answers**
- 11:15 a.m. **19. CA-MRSA: Birth Through Adolescence**
 Carol J. Baker, M.D.
Baylor College of Medicine
Houston, TX
- 11:40 a.m. **Questions and Answers**
- 11:45 a.m. **20. Drug Resistance in Fungal Infections**
 John H. Rex, M.D.
AstraZeneca Pharmaceuticals
Cheshire, United Kingdom
- 12:10 p.m. **Questions and Answers**
- 12:15 p.m. **Lunch (on your own)**
- Submitted Presentations 1: ** *Haverford/Baccarat Ballroom*
***Staphylococcus aureus* and**
Trends in Oral Antimicrobial Drug Use
- Moderator: Barry I. Eisenstein, M.D.
Cubist Pharmaceuticals, Inc.
Lexington, MA
- 1:30 p.m. **S1 Changes in *Staphylococcus aureus* Nasal Colonization in the United States, 2001-2004**
R. J. Gorwitz, D. Kruszon-Moran, S. K. McAllister, G. McQuillan, L. K. McDougal,
 G. E. Fosheim, B. E. Jensen, G. Killgore, F. C. Tenover, M. J. Kuehnert;
 Centers for Disease Control and Prevention, Atlanta, GA.

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1:45 p.m.

S2 Risk Factors for Community-Associated Methicillin-Resistant *Staphylococcus aureus* Skin Infection in New York City

A. Yeung¹, D. Kapell¹, D. Krieger¹, R. Murayama¹, E. Delgiacco¹, J. Russell¹, L. Amoroso¹, Y. Lue², R. Aquino², J. Kornblum¹, J. Mediavilla³, B. Kreiswirth³, D. Weiss¹, M. Marx¹;

¹New York City Department of Health and Mental Hygiene (NYC DOHMH), New York, NY, ²Quest Diagnostics Inc., Teterboro, NJ, ³Public Health Research Institute, Newark, NJ.

2:00 p.m.

S3 Prevention of Nosocomial Transmission of Methicillin-Resistant *Staphylococcus aureus* (MRSA) Infections in the Neonatal Intensive Care Unit using Admission Screening

J. L. Murillo¹, M. Cohen², P. Harmon¹, W. Cruz¹, P. Murillo¹, T. Chan³;

¹Epidemiology, Newark Beth Israel Medical Center, Newark, NJ, ²Neonatology, Newark Beth Israel Medical Center, Newark, NJ, ³Microbiology, Newark Beth Israel Medical Center, Newark, NJ.

2:15 p.m.

S4 Update on National Outpatient Utilization of Oral Antimicrobial Drugs, 1995-2006

R. Johann-Liang¹, C. Pamer¹, L. Gouvernale¹, T. Valappil¹, S. Iyasu¹, J. H. Powers, III²;

¹Office of Surveillance and Epidemiology, Food and Drug Administration Center for Drug Evaluation and Research, Silver Spring, MD, ²Scientific Applications International Corporation, in support of Collaborative Clinical Research Branch, NIAID, Bethesda, MD.

2:30 p.m.

Coffee Break*Waterford/Lalique Ballroom***Symposium 6. Living  in a Microbial World***Haverford/Baccarat Ballroom*

Moderator: Susan J. Rehm, M.D.

*National Foundation for Infectious Diseases
Bethesda, MD*

3:00 p.m.

21. The Convergence of Animal and Human Health

Lonnie J. King, D.V.M.
*Centers for Disease Control and Prevention
Atlanta, GA*

3:25 p.m.

Questions and Answers

3:30p.m.

22. Molecular Mechanisms in the Emergence of Resistance

David G. White, Ph.D.
*U.S. Food and Drug Administration
Laurel, MD*

3:55 p.m.

Questions and Answers

FINAL PROGRAM

Tuesday, June 26, 2007 *(continued)*

- 4:00 p.m. **23. The Role of NARMS in Detecting and Tracking Antimicrobial Resistance**
Patrick F. McDermott, Ph.D.
U.S. Food and Drug Administration
Laurel, MD
- 4:25 p.m. **Questions and Answers**
- 4:30 p.m. **Adjournment**

Wednesday, June 27, 2007

- 7:15 a.m.-7:45 a.m. **Meet the Experts Breakfast Session** *Waterford/Lalique Ballroom*
Table One:
Gram Negative Resistance
John P. Quinn, M.D.
- Table Two:**
Pediatric Infectious Diseases: Issues Surrounding Lack of Controlled Data on New Antibiotics and Clinical Trial Design in Otitis Media in Children
John S. Bradley, M.D.
- Table Three:**
Extensively Drug-Resistant Tuberculosis (XDR TB)
Peter Cegielski, M.D., M.P.H.
- 7:00 a.m.-
10:30 a.m. **Registration** *Crystal Ballroom Foyer*
- 7:30 a.m. **Continental Breakfast** *Crystal Ballroom Foyer*

Symposium 7. Potential Influences of Therapy Duration on Resistance CE *Haverford/Baccarat Ballroom*

Moderator: John H. Powers, M.D.
Scientific Applications International Corporation
Bethesda, MD

- 8:00 a.m. **24. Review of the History of Antibiotic Duration Studies for Various Bacterial Infections**
John H. Powers, M.D.
Scientific Applications International Corporation
Bethesda, MD
- 8:25 a.m. **Questions and Answers**

FINAL PROGRAM

- 8:30 a.m. **25. Pharmacokinetic/Pharmacodynamic Modeling of Appropriate Duration of Antibiotic Treatment**
George Drusano, M.D.
Ordway Research
Albany, NY
- 8:55 a.m. **Questions and Answers**
- 9:00 a.m. **26. Influence and Interrelationship of Duration of Treatment, Choice of Agent, and Adherence on Resistance in HIV Therapy**
Sharon Mannheimer, M.D.
Columbia University
New York, NY
- 9:25 a.m. **Questions and Answers**
- 9:30 a.m. **27. Duration of Therapy and Drug Resistance in Tuberculosis**
J. Peter Cegielski, M.D.
Centers for Disease Control and Prevention
Atlanta, GA
- 9:55 a.m. **Questions and Answers**
- 10:00 a.m. **Coffee Break** *Crystal BallroomFoyer*
- Submitted Presentations 2:**  *Haverford/Baccarat Ballroom*
- Trends in Resistance:
Gram-Negative Bacilli**
- Moderator: Stuart H. Cohen, M.D.
University of California Davis Medical Center
Sacramento, CA
- 10:30 a.m. **S5 Increasing Rates of High Level Antibiotic Resistance, Including to Polymyxin, Among *Klebsiella* and Other Gram-negatives in The Bronx**
L. Lemos-Filho, B. P. Currie;
Infectious Diseases, Montefiore Medical Center, Bronx, NY.
- 10:45 a.m. **S6 Perspective on Antimicrobial Susceptibility of *Escherichia coli* Isolates Recovered from Poultry Carcass Rinsates as Part of the Animal Arm of NARMS**
P. J. Fedorka-Cray¹, N. Anandaraman², J. Plumblee¹
¹BEAR, USDA-ARS-RRC, Athens, GA, ²OPHS, USDA-FSIS, Washington, DC.
- 11:00 a.m. **S7 Dissemination of Antimicrobial Resistant *Salmonella* Among Pacific Northwest Dairy Farms**
B. Adhikari¹, D. D. Hancock¹, T. E. Besser², J. M. Gay¹, L. K. Fox¹;
¹Field Disease Investigation Unit, Department of Veterinary Clinical Sciences, Washington State University, Pullman, WA, ²Department of Veterinary Microbiology and Pathology, Washington State University, Pullman, WA.

FINAL PROGRAM

Wednesday, June 27, 2007 (continued)

- 11:15 a.m. **S8 Relationship Between Level of Antibiotic Use and Antibiotic Resistance Among *Escherichia coli* Isolated from Swine in a Multi-site Integrated Farm-to-plate System**
K. L. Christian¹, H. M. Scott¹, W. Q. Alali¹, V. R. Fajt², R. B. Harvey³, D. B. Lawhorn⁴;
¹Veterinary Integrative Biosciences, Texas A&M University, College Station, TX,
²Veterinary Physiology and Pharmacology, Texas A&M University, College Station, TX,
³Food and Feed Safety Research, United States Department of Agriculture, College Station, TX, ⁴Large Animal Clinical Sciences, Texas A&M University, College Station, TX.
- 11:30 a.m. **Adjournment/Participant Evaluation**
- 11:30 a.m. **Meeting of the Interagency Task Force on Antimicrobial Resistance**
Sponsored by the Centers for Disease Control and Prevention, U.S. Food and Drug Administration, and the National Institutes of Health

* Speakers and presentations are subject to change

Poster Session and Reception

Monday, June 25, 2007, 6:00 p.m. – 7:00 p.m.

Waterford/Lalique Ballroom

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

- P1 *In Vitro* Testing of Daptomycin Plus Rifampin against Oxacillin-resistant *Staphylococcus aureus* (MRSA) Resistant to Rifampin**
F. Khasawneh, D. Ashcraft, G. Pankey;
 Infectious Diseases, Ochsner Clinic Foundation, New Orleans, LA.
- P2 Detection of Tetracycline Resistant Bacteria in Human Influenced Environments**
K. Jensen, Jr., K. Bushaw-Newton;
 Biology, American University, Washington, DC.
- P3 Daptomycin Experience in Patients with Coagulase-negative Staphylococcal Bacteremia**
K. Lamp¹, S. Rehm², D. Katz¹, L. Friedrich¹;
¹Cubist Pharmaceuticals, Lexington, MA, ²The Cleveland Clinic, Cleveland, OH.
- P4 A New Rapid Method for the Drug Susceptibility Testing of Mycobacteria**
R. Rieder¹, J. Howatt², E. Rubin³, A. Sloutsky⁴, L. Wu¹, B. Zavizion¹;
¹BioSense Technologies, Inc., Woburn, MA, ²Mentor Engineering, Bedford, MA,
³Department of Immunology and Infectious Diseases, Harvard School of Public Health, Boston, MA, ⁴Mycobacteriology Laboratory, Massachusetts Department of Public Health, Boston, MA.

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- P5 Antibacterial Properties of Soluble, Arginine-functionalized Chitosan**
H. Tang¹, S. Baker², W. P. Wiesmann³, A. Baker¹, S. Shors¹, **S. Rogelj**¹;
¹Biology, New Mexico Tech, Socorro, NM, ²BioSTAR West, Claremont, CA,
³Hawaii Chitopure, Inc., Honolulu, HI.
- P6 CA-MRSA Colonization Rates in Children and SSTI Management in the Ambulatory Setting**
L. H. Cheng-Immergluck¹, S. Jain², R. C. Jerris³, M. A. DeGuzman⁴;
¹Pediatrics, Morehouse School of Medicine, Atlanta, GA, ²Pediatrics, Emory University, Atlanta, GA, ³Clinical Microbiology Laboratories, Children's Healthcare of Atlanta, Atlanta, GA, ⁴Emergency Medicine, Children's Healthcare of Atlanta, Atlanta, GA.
- P7 Development of Oxytetracycline Resistant *Aeromonas salmonicida* in Rainbow Trout During a Laboratory-controlled Efficacy and Pharmacokinetics Study**
R. A. Miller¹, M. Carson¹, A. Kane², R. Reimschuessel¹;
¹Center for Veterinary Medicine, Food and Drug Administration, Laurel, MD,
²School of Medicine, University of Maryland, Baltimore, MD.
- P8 Association of *E. coli* Genotypes and Antimicrobial Resistance**
B. W. Shaheen¹, D. M. Boothe¹, O. A. Oyarzabal², T. Samaha¹;
¹Department of Anatomy, Physiology and Pharmacology, Auburn University, Auburn, AL,
²Department of Poultry Science, Auburn University, Auburn, AL.
- P9 Equine Methicillin-Resistant *Staphylococcus aureus* (MRSA) Typing and Evaluation of Virulence Genes: Preliminary Results from a Veterinary Teaching Hospital**
N. H. Ferguson-Morrison, S. Sanchez;
Infectious Diseases, University of Georgia, Athens, GA.
- P10 Prevalence of Methicillin-Resistant *Staphylococcus aureus* (MRSA) Nasal Colonization in the Adult Intensive Care Unit**
J. L. Murillo¹, C. Migliore², R. DiBrienza³, E. Espina³, P. Harmon⁴, R. Larang⁴;
¹Epidemiology, Newark Beth Israel Medical Center, Newark, NJ, ²Critical Care, Newark Beth Israel Medical Center, Newark, NJ, ³Nursing, Newark Beth Israel Medical Center, Newark, NJ, ⁴Infection Control, Newark Beth Israel Medical Center, Newark, NJ.
- P11 Rapid Multi-drug Resistance Profiling and Characterization of *Mycobacterium tuberculosis***
C. Massire¹, C. Agasino Ivy¹, M. A. Tobar-Mosquera¹, N. E. Kurepina², B. N. Kreiswirth², L. B. Blyn¹, S. A. Hofstadler¹, R. Sampath¹, D. J. Ecker¹;
¹Ibis Biosciences, Inc., Carlsbad, CA, ²Public Health Research Institute Tuberculosis Center, New York, NY.
- P12 Oral Candida Isolates In Radiotherapy/Chemotherapy Patients: Emerging Epidemiological, Virulence and Antifungal Resistance Patterns**
A. Katyayan, S. Batra, P. Bhalla, R. Kaur;
Microbiology, Maulana Azad Medical College, New Delhi, India
- P13 Epidemiology and Risk Factors for Extended-spectrum B-lactamase-producing Organisms: A Case Control Study at a VA Hospital**
S. Kethireddy¹, L. McKinley¹, N. Safdar²;
¹Infection Control/Infectious Disease, Wm. S. Middleton Memorial VA Hospital, Madison, WI, ²Infectious Disease/Hospital Epidemiology, University of Wisconsin-Madison School of Medicine and Public Health, Madison, WI.

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- P14 Enterococci Isolates from the Community Resistant to Antimicrobial Agents Used for Treatment of Enterococcal Infections**
A. M. ThurdeKoos¹, K. D. Joyce², C. Medus³, M. J. Zervos⁴, J. P. Furuno⁵, J. M. Whichard², E. J. Barzilay¹;
¹EDEB, CDC, Atlanta, GA, ²EDLB, CDC, Atlanta, GA, ³Minnesota Department of Health, St. Paul, MN, ⁴Henry Ford Hospital, Detroit, MI, ⁵University of Maryland, Baltimore, MD.
- P15 *Salmonella* Genomic Island 1 (SGI1) is Common Among Human Multi-drug Resistant (ACSSuT) *Salmonella* Isolates Tested in NARMS in the United States, 1996-2005**
J. S. W. Yam, K. Joyce, F. Medalla, E. J. Barzilay, J. M. Whichard;
Centers for Disease Control and Prevention, Atlanta, GA.
- P16 Emerging Resistance to Third-Generation Cephalosporins in *Salmonella* Serotype Heidelberg, NARMS, 1996-2005**
F. Medalla¹, J. M. Whichard¹, A. Stuart², K. Joyce², M. Omondi², R. M. Hoekstra¹, E. J. Barzilay¹;
¹Centers for Disease Control and Prevention, Atlanta, GA, ²Atlanta Research and Education Foundation, and Centers for Disease Control and Prevention, Atlanta, GA.
- P17 Toxin-Gene Variant Strains of *Clostridium difficile* in a Community Hospital**
A. Ramani¹, M. Kearney², M. Lee², R. M. Atkinson³, G. E. Hannett³, M. E. Sweet⁴;
¹Medicine, Columbia Memorial Hospital, Hudson, NY, ²Microbiology, Columbia Memorial Hospital, Hudson, NY, ³Laboratories for Bacterial Diseases, Wadsworth Center, NYSDOH, Albany, NY, ⁴Infection Control, Columbia Memorial Hospital, Hudson, NY.
- P18 Comparison of PCR and EVIGENE™ for Detection of Methicillin Resistance in Staphylococcal Isolates from Nasal Swabs**
K. Gathian¹, D. Lord¹, K. Boye², **A. K. I. Rasmussen**³, J. Bangsberg¹;
¹Herlev Hospital, Herlev, Denmark, ²Hvidovre Hospital, Hvidovre, Denmark, ³AdvanDx, Vedbaek, Denmark.
- P19 A Comparative Study On the Antimicrobial Activity of Meropenem and Other Anti-infective Agents**
R. P. Kaithamanakallam;
Clinical Microbiology, Asian Institute of Medicine, Science and Technology, Sungai Petani, Malaysia.
- P20 Synergy Testing for Highly-resistant *Acinetobacter Baumannii* Isolates**
E. Gonzalez, **L. Lemos-Filho**, C. P. Brian, G. Phillip;
Infectious Siseases, Montefiore Medical Center, Bronx, NY
- P21 Comparative In Vitro Susceptibility of Tigecycline and Polymyxin B for Resistant *Klebsiella* and *Acinetobacter* Isolates**
Bakshi, H. Surya;
Infectious Diseases, Maimonides Medical Center, Brooklyn, NY.

MEET THE EXPERT PRESENTERS

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MEET THE EXPERT PRESENTERS

John S. Bradley, M.D.**Meet the Experts Breakfast Session****Wednesday, June 27, 2007****7:15 am – 7:45 am**

Dr. Bradley is the Director of the Division of Infectious Diseases at Children's Hospital and Health Center, San Diego, California. He holds a teaching faculty appointment with the University of California, San Diego.

He is a member of the American Academy of Pediatrics' Committee in Infectious Diseases, and sits on the Antimicrobial Drug Availability Task Force of the Infectious Diseases Society of America. He has served on the FDA's Anti-Infective Drug Advisory Committee for the past four years. He has participated in the NIH Collaborative Antiviral Study Group for the past 25 years, and has been involved in anti-infective drug development through the NICHD Pediatric Pharmacology Research Unit Network for the past 10 years. He is a member of the SubBoard for Pediatric Infectious Diseases of the American Board of Pediatrics. He has been or is currently involved in creating IDSA National Guidelines for Outpatient Parenteral Therapy of Infectious Diseases, Treatment and Prophylaxis of Influenza Infections, and Treatment of Intra-Abdominal Infections.

Dr. Bradley received his Pediatric Infectious Diseases training at Stanford University and has focused his clinical research on therapeutic agents for infectious diseases, with phase I through IV investigations of antibacterial, antiviral and antifungal agents; he has authored or coauthored more than 120 publications. His focus is the treatment of serious infections caused by antibiotic-resistant pathogens.

J. Peter Cegielski, M.D.**Meet the Experts Breakfast Session****Wednesday, June 27, 2007****7:15 am – 7:45 am**

Dr. Cegielski is Team Leader for Drug-Resistant Tuberculosis at the Centers for Disease Control and Prevention (CDC). He received his Doctor of

Medicine degree from the University of California at San Diego. From there he proceeded to Duke University Medical Center in Durham, North Carolina for residency training in internal medicine, followed by fellowship training in infectious diseases and international health. During his fellowship, he worked as a Lecturer in the Department of Medicine, Muhimbili Medical Center, University of Dar es Salaam in Tanzania.

After returning to the U.S., he joined the faculty at Duke University as an Assistant Professor in the Division of Infectious Diseases and International Health. During that time, he completed a Masters of Public Health degree from the Department of Epidemiology in the School of Public Health at the University of North Carolina at Chapel Hill. Subsequently, he became the head of Tuberculosis Services and Research at the University of Texas Medical Center in Tyler. Dr. Cegielski left Texas to become Field Director of Johns Hopkins University's HIV/AIDS research unit at Chiang Mai University in Chiang Mai, Thailand and joined the international activities unit of the Division of TB Elimination at the CDC. Since his tenure at the CDC, the international TB unit at CDC has tripled in size. Dr. Cegielski was a founding member of the Stop TB Green Light Committee.

Stuart H. Cohen, M.D.**Meet the Experts Breakfast Session****Tuesday, June 26, 2007****7:15 am – 7:45 am**

Dr. Cohen is a Professor in the Division of Infectious and Immunologic Diseases at the University of California Davis Medical Center. He also serves as Clinical Director of Infection Control and Epidemiology and the Medical Microbiology Laboratories. Dr. Cohen is member of numerous professional societies including the American College of Physicians, the Society for Healthcare Epidemiology of America, American Society of Microbiology and is a fellow of the Infectious Diseases Society of America. He has authored over 50 scientific papers and 13 book chapters. He has co-authored over 80 abstracts for presentation at professional scientific meetings.

MEET THE EXPERT PRESENTERS

John P. Quinn, M.D.**Meet the Experts Breakfast Session****Wednesday, June 27, 2007****7:15 am – 7:45 am**

Dr. Quinn is an attending physician in the Infectious Diseases Division at Cook County Hospital, and Professor of Medicine at Rush University. He is scientific director of a nonprofit research institute, the Chicago Infectious Diseases Research Institute.

Dr. Quinn completed his Internal Medicine residency at Loyola University in Maywood, IL, followed by an infectious diseases fellowship at the University of Chicago. His current research interests include molecular epidemiology, mechanisms of antimicrobial resistance in both gram negative and gram positive pathogenic bacteria, and new drug development.

John H. Rex, M.D., F.A.C.P.**Meet the Experts Breakfast Session****Tuesday, June 26, 2007****7:15 am – 7:45 am**

Dr. Rex is Vice President and Medical Director for Infection for AstraZeneca Pharmaceuticals. He is also Adjunct Professor of Medicine for the University of Texas Medical School at Houston. He is a member of several professional societies including the American College of Physicians, Infectious Diseases Society of America, and the American Society for Microbiology. Dr. Rex is on the editorial boards of *Diagnostic Microbiology and Infectious Disease*, *Drug Resistance Updates*, and the *European Journal of Clinical Microbiology and Infectious Diseases*. He is Chairperson of the Antifungal Susceptibility Testing Subcommittee of the National Committee for Clinical Laboratory Standards. Dr. Rex has authored and/or co-authored over 150 peer-reviewed scientific papers and book chapters.

Peter M. Small, M.D.**Meet the Experts Breakfast Session****Tuesday, June 26, 2007****7:15 am-7:45 am**

Dr. Small is a Senior Program Officer for Tuberculosis at the Bill and Melinda Gates Foundation. He is responsible for developing and implementing the foundation's tuberculosis activities.

Dr. Small trained in internal medicine at UCSF and infectious diseases at Stanford University. Immediately prior to joining the foundation in September of 2002, he was on the faculty of Stanford's Division of Infectious Disease and Geographic Medicine where he was actively involved in research, teaching, and patient care.

His research interests include multiple aspects of tuberculosis, with a focus on the nature and consequences of genetic variability within the species *M. tuberculosis*. Initially this involved collaborative efforts with basic scientists, public health officials and clinicians to use molecular epidemiologic techniques to address pragmatic questions about the control of tuberculosis. This work included population based field research projects in Latin America, Africa, Asia and Europe. He is currently a Professor at the Institute of Systems Biology where his laboratory is focused on the use of genomic approaches such as DNA microarrays and sequence analysis to answer more fundamental questions about mycobacterial ecology and evolution. He served as a member of the Institute of Medicine's committee addressing the elimination of tuberculosis in the United States and currently serves as a member of the WHO Stop TB Coordinating Board. In 2002 he was awarded the Princess Chichibu Global Tuberculosis Award for his contributions to global tuberculosis control.

ABSTRACTS OF INVITED PRESENTATIONS

ABSTRACTS OF INVITED PRESENTATIONS

1 Brave New World: Preventing Emergence and Transmission of Resistant Organisms

T. Perl
Johns Hopkins School of Medicine, Baltimore, MD

Objective: Discuss the current status of antimicrobial resistance in North America, and understand the challenges that persist and must be overcome for their prevention and control in and outside of the healthcare setting.

Summary: Antimicrobial resistance is well described in organisms that cause both community and healthcare acquired infections. The outcry among the public health community because of the emerging and expanding problem with multidrug resistant *M. tuberculosis* and *N. gonorrhoea* are examples of pathogens that contribute to the morbidity and mortality and potentially affect millions of persons worldwide. In the healthcare setting, worldwide, methicillin resistant *S. aureus*, multidrug resistant gram-negative organisms including *Pseudomonas aeruginosa* and *Acinetobacter baumannii* include pathogens of emerging importance. Prevention and control of these pathogens requires an understanding of their pathogenesis—did they emerge as a result of antimicrobial pressure or were they transmitted via contact with people or fomites within in the healthcare setting. Because of the complexities of healthcare, it is not clear that one strategy will be able to decrease resistance. Likely it will require, several strategies that focus on basic infection prevention and control and antimicrobial stewardship to begin to impact resistance in a meaningful way. Success stories are emerging including the role of pneumococcal vaccine in decreasing the burden of disease but resistance. Other unique approaches to behavioral and organizational change coupled with new and novel technologies, healthcare marketing and communication will likely be needed to develop a sustainable change and the will to change the paradigm in healthcare.

References:

1. Goldstein FW. Combating resistance in a challenging, changing environment. *Clin Microbiol Infect.* 2007;13(Suppl):2-6.
2. de Kraker M, van de Sande-Bruinsma N. Trends in antimicrobial resistance in Europe: update of EARSS results. *Euro Surveill.* 2007;12:E070315.3.

2 Epidemiology of Multi-drug Resistant and Extensive Drug Resistant Mycobacterium tuberculosis: Transmission Dynamics and Fitness

P. Small
Bill & Melinda Gates Foundation, Seattle, WA

Objective: Discuss current theories about the evolutionary history of *M. tuberculosis* and the current status of the DR tuberculosis situation and the concept of bacterial fitness.

Summary: Of grave concern, outbreaks of extremely drug resistant tuberculosis (XDR TB) that are resistant to all known antibiotics have been described recently. The premise of this talk is that evolution provides a powerful lens for understanding biology. Using this lens I will describe 1) our use of multilocus sequence typing to understand how we got here, 2) the WHO's drug resistance surveillance data to understand where we are and 3) in vitro competitive fitness assays to predict the future. In the context of a systems approach, integration of divergent data streams such as these hold great promise for transforming epidemiology from a descriptive to a predictive science.

References:

1. Gagneux S, Davis-Long C, Small PM, Van T, Schoolnik GK, Bohannon B. The competitive cost of antibiotic resistance in mycobacterium tuberculosis resistance. *Science* 2006;312(5782):1944-6.
2. Gagneux S, DeRiemer D, Van T, Kato-Maeda M, de Jong BC, Narayanan S, et al. Variable host-pathogen compatibility in Mycobacterium tuberculosis. *PNAS* 2006;103(8): 2869-2873.

3 Diagnostic Tools: Present and Future

M. Perkins

Foundation for Innovative New Diagnostics, Geneva, Switzerland

Objective: Discuss the current technologies and practices used to detect drug resistance in human tuberculosis in industrialized and in disease-endemic countries, and to recognize the challenges and opportunities in improving TB control through more effective drug susceptibility testing.

Summary: There are some 300-500 thousand new cases of multi-drug resistant (MDR) tuberculosis each year, and effectively detecting and treating them is an important and growing challenge in TB control.¹ National strategies to address this problem have been characterized as ranging from denial to obsession. The last decade has seen markedly increased interest in the development and use of new technologies to improve the detection of drug resistance in tuberculosis.

The best way to meet this challenge, and the importance of doing so, are matters of some debate. The private sector is interested in providing tests to meet the need for MDR or XDR TB detection, but needs to understand the character and size of the market, and exactly what kinds of tests are needed. For its part, the public sector, before supporting the development of such tests, needs to understand their potential public health impact.

These questions of market size and health impact are a moving target, and depend upon factors such as whether specific treatment is available at or near the point of testing, whether that treatment significantly effects outcome, when cases need to be detected to effectively decrease morbidity and transmission, what the prevalence of HIV co-infection is, whether standardized or individualized regimens are used, and of what importance is the speed of testing itself. These questions notwithstanding, substantial progress in the development and delivery of new tests targeting drug resistance has recently been made.

Reference:

1. Zignol M, Hosseini MS, Wright A, Weezenbeek CL, Nunn P, Watt CJ, Williams BG, Dye C. Global incidence of multidrug-resistant tuberculosis. *J Infect Dis.* 2006;194(4):479-85.

4 Current Therapy for Tuberculosis: What Do You Do When the Going Gets Tough?

J. Mukherjee

Brigham and Women's Hospital, Boston, MA

Objective: Discuss the current epidemiology of drug resistant forms of tuberculosis (multidrug resistant—MDR and extensively drug resistant—XDR), their relationship to HIV, how current practices have increased the level of drug resistance, and how to detect and treat drug resistant TB.

Summary: Nearly two billion people worldwide have tuberculosis infection. In the last 25 years, the number of those infected with TB who progress to having active disease has increased. This is due in large part to the HIV pandemic because of HIV's effect on 1) an individual's immune system, 2) the TB programs' weakness in case detection among the immune suppressed and 3) weakened health infrastructures. Moreover, resistant tuberculosis is an increasing threat with large proportions of new cases in the countries of the former Soviet Union being identified as MDR-TB and outbreaks of XDR-TB in persons with HIV in South Africa.

Both MDR and XDR-TB can be treated, but an index of suspicion and the ability to detect cases is critical to prompt diagnosis and designing effective treatment. Tuberculosis control programs in resource poor settings have not been designed to address drug resistance as they rely on case detection by smear microscopy only, without culture and drug susceptibility testing. In the last decade the World Health Organization (WHO) has developed a strategy to evaluate and assist tuberculosis programs in resource poor settings so that

ABSTRACTS OF INVITED PRESENTATIONS

treatment for resistant TB can be implemented. However, this group, the Green Light Committee, is under resourced to respond to this increasing global challenge. Increased human resources and improved health infrastructure, including laboratory strengthening and infection control, are needed.

Reference:

- Centers for Disease Control and Prevention. Emergence of *Mycobacterium tuberculosis* with extensive resistance to second-line drugs—worldwide, 2000-2004. *MMWR* 2006;55(11):301-5.

5 TB Drug Pipeline: Are There Meaningful New Drugs on the Event Horizon?

M. Spigelman
Global Alliance for TB Drug Development, New York, NY

Objective: Review the goals of current new TB drug development, the status of the present TB drug pipeline, and discuss the challenges inherent in the process of TB drug research and development.

Summary: With approximately two billion people infected, almost nine million new cases of active disease each year, an increasing incidence of resistant disease, and over 1.5 million deaths a year, tuberculosis remains one of the major global infectious disease threats. Although no truly novel drugs to treat TB have been approved over the past 40 years, there has been, especially in the last five years, a resurgence of interest in developing improved TB therapies. There are presently seven compounds in clinical development for TB along with a larger number of drug discovery projects. The major thrust of these efforts is to shorten the treatment time for active disease. With most compounds exhibiting novel mechanisms of action, these drugs should also be active against resistant TB.

However, formidable challenges exist. In addition to the lack of adequate clinical trial capacity worldwide, clinical development times, under the best of circumstances, remain unacceptably long. In addition, there are no clear roadmaps for how to develop a new drug for resistant disease. Animal models to guide discovery work remain suspect and, because of the prolonged inactivity in this area, regulatory guidance is remarkably absent. Despite these hurdles, new compounds are proceeding through the development cycle.

Reference:

- Ginsberg AM & Spigelman M. Challenges in tuberculosis drug research and development. *Nature Medicine*, 2007;13(3):290-294.

6 Role of Rapid Diagnostics

N. Shrestha
The Cleveland Clinic Foundation, Cleveland, OH

Objective: Discuss some current uses, the potential, and the limitations of rapid diagnostic technology in the diagnosis of infectious diseases.

Summary: Rapid diagnostic technology has revolutionized the diagnosis of infectious diseases. Rapid tests have a definite role in the early detection of pathogens, early specific identification of pathogens and early detection of resistance. Rapid detection of *Staphylococcus aureus* carriers facilitates targeted decolonization programs, thus reducing unnecessary antibiotic use. Rapid detection of pathogens such as MRSA, VRE and *Mycobacterium tuberculosis* allows early infection control decisions to be made. Earlier identification of *S. aureus*, *Enterococcus faecalis* and *Candida albicans* in clinical specimens allows more targeted patient work-up and earlier specific treatment. Molecular technologies can now easily detect genetic markers of antimicrobial resistance. Although these cannot completely replace conventional susceptibility testing methods, we can expect the information provided by such tests to be increasingly used for antibiotic selection or restriction in the future. Rapid diagnostic

technology also provides the ability to rapidly detect pathogens of potential pandemic or bioterrorist threat.

The cost of molecular tests is a major limiting factor. Although these are very powerful tools, the question really is whether the added information they provide is worth their cost. Newer rapid tests will only be relevant if the added cost of testing is offset by the benefits obtained by having an early answer.

Reference:

- Baron EJ. Implications for new technology for Infectious Diseases Practice. *Clin Infect Dis*. 2006;43:1318-23.

7 Rapid Diagnostics in Veterinary Medicine

R. Oberst
Kansas State University, Manhattan, KS

Objective: Review current initiatives to advance rapid diagnostics for routine animal disease detection and early diagnosis of exotic and emerging diseases of economic and animal/public health concerns.

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.

This presentation will define progress to implement the NAHLN mission and progress in 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.

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>

8 Current and Emerging Technologies

L. Peterson
Evanston Northwestern Healthcare, Evanston, IL

Objective: Describe the rapidly changing field of rapid detection of infectious diseases, novel technologies for disease surveillance, and the current status of electronic systems for use in infection control.

Summary: A critical element in the optimal treatment of infectious diseases as well as for better use of antimicrobial agents is the development of rapid and accurate diagnostic testing. For the past decade there has been great progress in this area for the field of viral pathogens, but rapid testing for bacterial infections has lagged behind. Also, while rapid testing can often detect a single pathogen, it has not been able provide a diagnosis for multiple potential agents in a given clinical disease syndrome. This is now starting to change. Current and future technologies include PCR, Real-time PCR, Arrays, Nanoparticles,

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Quantum Dots, and Broad Range Amplification followed by Sequencing for detection and identification of infecting pathogens. Rapid techniques (<2 hour) are available for accurate detection of colonization with multidrug-resistant bacteria like vancomycin-resistant enterococci and methicillin-resistant *Staphylococcus aureus*. Soon diagnostic testing for disease will be available for these plus *Clostridium difficile*-associated diarrhea. Furthermore, novel applications of artificial intelligence and informatics is improving recognition of disease outbreaks and providing real-time detection of nosocomial infection. These technologies have the potential to meaningfully alter the practice of infectious disease, and if properly utilized add to improved patient outcomes and even reduce healthcare cost.

References:

1. Peterson LR, Dalhoff A. Towards targeted prescribing: Will the cure for antimicrobial resistance be specific, directed therapy through improved diagnostic testing? *J Antimicrob Chemother* 2004;53:902-905.
2. Brossette SE, Hacek DM, Gavin PJ, Kamdar MA, Gadbois KD, Fisher AG, Peterson LR. A laboratory-based, hospital-wide, electronic marker for nosocomial infection: The future of infection control surveillance? *Am J Clin Pathol* 2006;125:34-39.

9 Impact of Rapid Testing for Antimicrobial Resistance

F. Nolte

Emory University School of Medicine, Atlanta, GA

Objective: Evaluate how rapid testing for antimicrobial resistance can impact antibiotic use, patient management, and the laboratory environment.

Summary: Antimicrobial susceptibility test (AST) results have important therapeutic implications for individual patients and provide a basis for infection control measures. A variety of phenotypic and genotypic methods are available to clinical microbiology laboratories for the rapid detection resistance to antimicrobials in bacteria. Rapid phenotypic methods include rapid instrument-assisted ASTs, PBP2a latex agglutination tests for *mecA*, and beta-lactamase tests. Over the past two decades, a wide variety of DNA probes and nucleic acid amplification tests for detection of resistance genes have been described. Genetic tests for antimicrobial resistance can be used for direct detection of the resistant pathogen in clinical specimens with analysis times of only two to six hours. An important milestone was reached in April, 2007 with FDA clearance of the first diagnostic for molecular detection of a resistant bacterium (MRSA) directly in a clinical sample. Although providing rapid AST results more rapidly seems a logical advance in patient care, well-controlled studies documenting the clinical impact are scarce and often have contradictory results. In this presentation, two examples will be cited; the clinical impact of rapid, instrument-assisted AST systems, and the use of *mecA* PCR for rapid screening of patients for MRSA to reduce cross-infections.

Reference:

1. Harbarth S, Masuet-Aumatell C, Schrenzel J, Francois P, et. al. Evaluation of rapid screening and pre-emptive contact isolation for detecting and controlling methicillin-resistant *Staphylococcus aureus* in critical care: an interventional cohort study. *Critical Care* 2006;10:R25.

10 Fundamental Economic Tradeoffs in Addressing the Problem of Resistance

A. Malani

University of Chicago Law School, Chicago, IL

Objective: Review the basic economic incentives that drive excessive antibiotic use and resistance and limit efforts to battle resistance either by limiting antibiotic use or developing new antibiotics.

Summary: Excessive antibiotic use is driven by a disconnect between the private benefits of empiric use and the social costs of speeding up bacterial resistance to antibiotics. Efforts to combat antibiotic resistance fall in four categories: efforts to reduce antibiotic use, efforts to make antibiotics more "efficient" (in terms of health benefits per unit of resistance), efforts to better allocate antibiotics to patients, and efforts to generate new antibiotics. A challenge facing efforts to limit antibiotic use is that it creates a direct clash between private incentives to use antibiotics and social benefits from reducing resistance. This makes it difficult to ensure compliance with this strategy. The other strategies for combating resistance do not face this problem. A challenge facing efforts to either curb antibiotic use or to make antibiotics more efficient is that this reduction in demand for new antibiotics discourages the development of new antibiotics. Of course the opposite is also true: efforts to encourage the supply of new antibiotics discourages efforts to reduce antibiotic demand or make antibiotics more efficient. Choosing the appropriate strategy for combating resistance requires consideration not just of technological hurdles to making antibiotics efficient or developing new antibiotics, but also economic hurdles.

Reference:

1. Laxminaaayan R, Malani A, Howard D, Smith D. Extending the cure: policy responses to the growing threat of antibiotic resistance. *Resources for the Future*, 2007.

11 Case Presentation: The Challenges of Life-Threatening CA-MRSA Infection

J. Bradley

Children's Hospital, San Diego

Objective: Discuss the life-threatening nature of lower respiratory tract infections caused by community-acquired MRSA.

Summary: Community-acquired MRSA was first noted to cause deaths in children in 1997 in the Midwest US and has since spread to virtually all sections of the country, causing serious, debilitating and frequently recurrent disease in healthy children and adults of all ages.

We present a case of a healthy one year old, taken to his pediatrician for symptoms consistent with a cold that subsequently developed into life-threatening, necrotizing pneumonia; his infection responded poorly to combination therapy with types of antibiotics used out of necessity when methicillin-class antibiotics, considered "best therapy" for *Staphylococcus aureus*, cannot be used.

Of the three antibiotics approved by the FDA during the past seven years with activity against MRSA (linezolid, tigecycline, daptomycin), only linezolid, a bacteriostatic agent, has FDA approval for children. Of four antibiotics in clinical trials (dalbavancin, oritavancin, telavancin, ceftobiprole), none are currently being assessed in children.

There is a critical need for more effective antibiotics for serious infections caused by antibiotic-resistant pathogens, particularly for children. Regulatory, political, and economic reasons for the current situation will be discussed.

Reference:

1. Creech CB Jr, Johnson BG, Bartilson RE, Yang E, Barr FE. Increasing use of extracorporeal life support in methicillin-resistant *Staphylococcus aureus* sepsis in children. *Pediatr Crit Care Med*. 2007; [Epub ahead of print]

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12 Why Do Consumers Pursue Antibiotics? Cultural Influences on Antibiotic Seeking Behavior

K. Corbett

Simon Fraser University, British Columbia, Canada

Objective: Describe cultural and personal influences on inappropriate community-based antibiotic use in terms of patients' expectations, attitudes, knowledge, and practices, and recognize the importance for interventions of contextual influences, cross-cultural, and intra-ethnic diversity in these factors.

Summary: Antibiotic use is strongly influenced by non-pharmacological determinants. These include system and organizational factors, factors relating to prescribers and dispensers, and factors relating to patients/consumers. In assessing community-based antibiotic use, much research has examined the role of healthcare providers; few studies have explored in depth the contribution of patients to problematic use. This presentation employs the construct of patients' explanatory models to highlight socio-cultural, informational, interactional, experiential, and individual-level aspects of why patients or parents seek antibiotics. First, data are presented from cross-national and US studies that show culturally patterned diversity in knowledge, attitudes, and practices. Second, findings from qualitative, anthropologically informed studies of US Latinos and Mexicans are presented to illustrate the salience of socio-cultural, symbolic, and political economic factors in expectations for antibiotics, strategies to acquire them, and self-medication practices. When the perspective of consumers is examined, the "irrationality" of inappropriate antibiotic use is better framed as culturally, contextually, and personally rational responses to illness and the larger healthcare system, in which access to and acceptability of care influences decisions about treatment-seeking, and antibiotics are commodities considered essential to health. Finally, implications for approaches to improve antibiotic use, as well as research needs, are discussed.

Reference:

1. Avorn J, Solomon DH. Cultural and economic factors that misshape antibiotic use: the nonpharmacologic basis of therapeutics. *Annals of Internal Medicine* 133:128-135.

13 Physicians and Inappropriate Prescribing: What Can Be Done to Change Their Behavior?

J. Linder

Brigham and Women's Hospital, Boston, MA

Objective: Evaluate the effectiveness of interventions for improving the appropriateness of antibiotic prescribing for acute respiratory infections.

Summary: Acute respiratory infections account for about 50% of antibiotic prescribing to adults and 80% of antibiotic prescribing to children. National initiatives have resulted in some improvement in antibiotic prescribing for acute respiratory infections over the past 20 years. However, much antibiotic prescribing for acute respiratory infections is inappropriate – physicians in the US prescribe antibiotics to 45% of adults with the common cold and 60% of adults with acute bronchitis – and physicians are increasingly selecting unnecessarily broad-spectrum antibiotics. Inappropriate antibiotic prescribing exposes patients to adverse drug events, increases the prevalence of antibiotic-resistant bacteria, and increases costs.

Potential interventions to decrease inappropriate antibiotic prescribing include physician education, physician audit and feedback, patient education, multidimensional interventions, delayed antibiotic prescriptions, health information technology solutions, and financial or regulatory incentives. Unfortunately, most interventions result in only modest reductions in inappropriate antibiotic prescribing, on the order of 10%. A recent systematic review found that multidimensional interventions involving physicians and patients appear more effective than clinician educational interventions, which, in

turn, were more effective than interventions that used audit and feedback. Despite the gains of the last 20 years, there continues to be a need for interventions that are low-cost, effective, scalable, and sustainable.

Reference:

1. Steinman MA, Ranji SR, Shojania KG, Gonzales R. Improving antibiotic selection: a systematic review and quantitative analysis of quality improvement strategies. *Medical Care* 2006;4(7):617-628.

14 Interventions to Improve Antibiotic Use in Acute Care Treatment: Results of the IMPAACT

R. Gonzales

University of California, San Francisco, San Francisco, CA

Objective: Discuss the impact of different types of education-based interventions on antibiotic prescribing in emergency departments for URIs and acute bronchitis in adults.

Summary: The overarching goals of the IMPAACT Project, jointly sponsored by AHRQ and the VA HSR&D, are to develop and evaluate strategies to improve antibiotic treatment of adults with acute respiratory tract infections (ARIs) using a network of eight VA and eight non-VA emergency departments located throughout the US; and to identify organizational factors that serve as barriers and facilitators to successful interventions. Key findings from IMPAACT studies include:

Overuse of antibiotics for acute cough illness varies widely, and is especially frequent for patients diagnosed with acute bronchitis. Overuse is less common for housestaff-associated ARI visits.

Using a cluster-randomized design, a combined patient and physician educational intervention led to an average decrease in antibiotic use for ARIs of about 10-12 percent.

At a single ED, implementation of a point-of-care management algorithm for adults with acute cough illness led to a decrease in antibiotic use of about 25 percent, and there was no additional benefit to patients randomized to a rapid c-reactive protein test.

Organizational factors that appear to contribute to improvements in antibiotic prescribing include support from a strong opinion leader, and an ED practice culture that endorses judicious antibiotic use.

References:

1. Gonzales R, Camargo CA Jr, MacKenzie TD, Kersey AS, et. al. Antibiotic treatment of acute respiratory tract infections in acute care settings. *Academic Emergency Medicine*, 2006;13:288-294.
2. Metlay JP, Camargo CA Jr, MacKenzie TD, Kersey AS, Maselli JH, et. al. Randomized trial of a multidimensional educational intervention to improve antibiotic use for adults with acute respiratory infections managed in the emergency department. *Annals of Emergency Medicine*, in press.

15 Is There a Relationship Between Health Care Quality and Appropriate Antibiotic Use?

J. Metlay

University of Pennsylvania School of Medicine, Philadelphia, PA

Objective: Review the current status of evidence linking appropriate antibiotic prescribing patterns to improved health care outcomes and understand the intended and unintended consequences.

Summary: Outcomes for patients with selected infectious diseases are improved by the timely administration of appropriate antimicrobial drugs. Non-experimental studies over the last several years have helped establish guidelines for

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the treatment of patients with serious infectious diseases, including community-acquired pneumonia. These guidelines have established standards of care that have become of increasing importance to physicians and health care system leaders in response to efforts to publicly report and tie reimbursement to these antibiotic prescribing measures. However, implementation of antibiotic prescribing measures as quality performance indicators may induce both intended and unintended results. Overuse of antibiotics for non-antibiotic responsive conditions is one example of an unintended negative consequence that threatens the overall drive towards health care quality underlying these measures. Balancing the intended and unintended consequences of these antibiotic prescribing measures is a challenge that reflects tensions in balancing individual and public health interests.

Reference:

1. Werner RM, Bradlow ET. Relationship between medicare's hospital compare performance measures and mortality rates. *JAMA* 2006;296(22):2694-702.

16 Severe Infections Due to Hospital-Associated MRSA

A. Karchmer
Beth Israel Deaconess Medical Center, Boston, MA

Objective: Examine the variables associated with the poor response to therapy of severe HA-MRSA infections and the alternative therapies that may improve outcome of severe HA-MRSA infection.

Summary: The epidemiology of MRSA has been exceptionally dynamic over the past 15 years. Studies have documented the progressive increase in the frequency of multidrug resistant HA-MRSA among *S. aureus* isolates in United States hospitals of all sizes. Additionally, the isolates are recognized in the community. A new genotype of MRSA, called community acquired MRSA (CA-MRSA), has been recognized, become increasingly established in patients without links to health care, and is now spreading into hospitals. HA-MRSA has become a notable cause of infections in intensive care units, of blood stream infection, nosocomial pneumonia, and multiple other severe infections. When examined in detail, HA-MRSA infections are associated with increased morbidity and often mortality in with similar infections caused by MSSA.

HA-MRSA does not appear to be a static genotype. Studies have demonstrated the emergence of infrequent isolates resistant to vancomycin (by *vanA* mediated mechanisms) and stable vancomycin intermediate isolates (MICs 8-16). Most vexing, however, is the recognition of heteroresistance to vancomycin among HA-MRSA. Called hVISA, these are isolates with subpopulations recoverable in media containing vancomycin concentrations from 3-10 mg/ml yet on standard MIC determination appear susceptible. Infection with hVISA responded less readily to treatment with vancomycin. Similarly, infections caused by HA-MRSA isolates with vancomycin MICs > 1.0 mg/ml (susceptible) appear to respond less well to vancomycin treatment.

In addition to organism-based reasons for difficulties in treating HA-MRSA infection, pharmacokinetic-pharmacodynamic considerations limiting therapy options have been recognized. These are particularly relevant in defining optimal treatment for pneumonia.

New agents have been developed for the treatment of HA-MRSA infections and have been shown to be at least comparable to vancomycin, the established standard therapy. Daptomycin and linezolid are two such agents. Other agents for treatment of MRSA infections are under development, e.g. televancin, ceftibiprole, ceftaroline. Data are not available to make definitive recommendations for optimal therapy of severe HA-MRSA infections. Nevertheless, therapeutic decisions must be made. Thus, the options and rationale treatment of selected HA-MRSA will be discussed.

Reference:

1. Moellering RC Jr. Predicting and defining vancomycin efficacy. *Clinical Infectious Diseases* 2006;42:S1-57.

17 Severe Infections Caused by Hospital Associated Gram-negative Bacteria

J. Quinn

Rush Medical School, Chicago, IL

Objective: Review the most recent trends in emerging gram negative resistance.

Summary: Gram negative rods remain the major bacterial agents to cause lethal infections in most critical care units. Although the pharmaceutical pipeline of novel anti-gram positive agents is promising at present, the same cannot be said for therapy directed against gram negative pathogens.

In-vitro surveillance systems reveal that the major emerging resistance problems among gram negative bacilli in the United States in recent years have been multiresistant *Pseudomonas aeruginosa* and *Acinetobacter*. Fluoroquinolone resistance rates in *P. aeruginosa* tripled during the decade of the 1990's. Multiresistance among *Acinetobacter* is also rapidly emerging. Molecular typing reveals that this species is more likely to be clonal, reflecting hospital hygiene breakdown, than is *P. aeruginosa*. Although the carbapenems remain the most active class against *Acinetobacter*, resistance to these compounds is increasing over time, usually due either to carbapenemase production or a combination of beta-lactamases and porin mutations. Our lab has recently described the first nosocomial outbreaks of infections due to carbapenemase producing *Acinetobacter* and *P. aeruginosa* in the US.

An expanding number of plasmid-mediated carbapenemases are also being reported with increasing frequency in many countries. The KPC enzymes pose a particular threat and are now in many species.

Reference:

1. Lolans K, Rice T, Munoz-Price S and Quinn JP. Multicity outbreak of carbapenem resistant *A. baumannii* isolates producing the OXA-40 carbapenemase. *Antimicrob Agents Chemother* 2006; 50:2941-2945.

18 CA-MRSA: Birth Through Adolescence

C. Baker

Baylor College of Medicine, Houston, TX

Objective: Discuss the contemporary clinical features and molecular epidemiology of CA MRSA infections in infants and children, virulence factors that dictate disease expression, and the challenges of treating and preventing recurrences of these infections.

Summary: During the past decade, the emergence of CA-MRSA from most communities in the United States has led to a surge in incidence of skin and soft tissue infections that often require surgical drainage in addition to appropriate antimicrobial agents. Factors increasing risk for these infections are black race, chronic skin conditions, obesity, contact sports, and infected family members, among others. Molecular typing has identified two predominant CA MRSA clones, USA 300 and USA 400; their genomes now have been sequenced. Panton-Valentine leukocidin (PVL), a bicomponent cytotoxin, appears to be a virulence factor for USA 300 since its presence is associated with necrotizing pneumonia, more severe osteomyelitis and a high mortality rate in young healthy persons. Appropriate therapy of these infections require collection of culture specimen (s) early in illness as they cannot be distinguished from infection caused by MSSA. While methicillin-resistant, CA MRSA are susceptible to several other antibiotic classes, including vancomycin, trimethoprim-sulfamethoxazole, doxycycline/minocycline, gentamicin, linezolid and other clindamycin. However, many infections require aggressive surgical management for cure. Recurrence is frequent as colonization often persists even after typical protocols for eradication of MSSA.

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References:

1. Kaplan SL. Community-acquired methicillin-resistant *Staphylococcus aureus* infections in children. *Semin Pediatr Infect Dis* 2006;17:113-119.
2. Klevens RM, Edwards JR, Tenover FC et al. Changes in the epidemiology of methicillin-resistant *Staphylococcus aureus* in intensive care units in US hospitals. *Clin Infect Dis* 2006;42:389-391.

19**Drug Resistance in Fungal Infections****J. Rex**

AstraZeneca Pharmaceuticals, Cheshire, United Kingdom

Objective: Discuss the current debates about the reliability of antifungal susceptibility testing and understand current trends in antifungal resistance for azoles, polyenes, echinocandins.

Summary: Antifungal susceptibility testing began to be standardized in the late 1980s and emerged as a potentially reliable tool for *Candida* and fluconazole in the mid 1990s. Within the limits of the biological boundaries defined by the 90-60 rule, accumulated data since that time have proven the reliability of MICs for this bug-drug combination. Data for *Candida* & other azoles, *Cryptococcus* & fluconazole, and *Candida* & the echinocandins have also emerged. Sufficient data now exist to suggest interpretive breakpoints for *Candida* & the echinocandins: a Susceptible-only breakpoint of ≤ 2 micrograms/ml seems plausible for all three echinocandins. Consistently meaningful testing methods for amphotericin B remain elusive despite significant efforts, although statistical correlations are seen in some circumstances. Similarly, consistently meaningful methods for the moulds remain elusive, but recent standardization of testing methods may permit consensus data to emerge.

For the clinician, certain patterns of susceptibility are now apparent and therapeutic choices can be guided based on knowledge of species. Choice of therapy is further guided by in vitro susceptibility data for *Candida* vs. azoles and echinocandins.

References:

1. Pfaller MA, Diekema DJ, Sheehan DJ. Interpretive breakpoints for fluconazole and *Candida* revisited: a blueprint for the future of antifungal susceptibility testing. *Clin Microbiol Rev* 2006; 19:435-447,CP3,CP4.
2. Pfaller MA, Diekema DJ. Epidemiology of invasive candidiasis: A persistent public health problem. *Clin Microbiol Rev* 2007; 20:133-163.
3. Verweij PE, Mellado E, Melchers WJG. Multiple-triazole-resistant aspergillosis. *N Engl J Med* 2007; 356:1481-1483.
4. Kahn JN, Garcia-Effron G, Hsu MJ, Park S, Marr KA, Perlin DS. Acquired echinocandin resistance in a *Candida krusei* isolate due to modification of glucan synthase. *Antimicrob Agents Chemother.* 2007; 51:1876-8.

20**The Convergence of Animal and Human Health****L. King**

Centers for Disease Control and Prevention, Atlanta, GA

Objective: Examine the driving forces that are creating the emergence of a new group of infectious disease threats and a new appreciation of the role of animals and their products in the biological phenomenon.

Summary: Infectious diseases have helped shape the course of human history and there is every indication that these diseases will continue to be significant global events. A number of driving forces and societal changes are now creating an unprecedented environment that favors the expansion and perhaps even acceleration of a group of these diseases termed emerging or re-emerging zoonoses.

In a recent publication by the United States Institute of Medicine entitled *Microbial Threats to Health, Emergence, Detection, and Response*, the authors

suggested that these forces are swirling and converging to create a perfect microbial storm. This metaphor helps describe the conditions and dynamics that have produced the new era of emerging diseases that began approximately 25 years ago. The convergence of animal and human health are central to this phenomenon. This convergence is also changing the dynamics among agriculture, food systems and human health; thus, new public health and infectious diseases strategies and policies will need to be reconsidered in the future along with a new partnership to address these threats.

Reference:

1. Smolinski M, Hamburg M, Lederberg J: Eds. Microbial Threats to Health: Emergence, Detection and Response. *National Academies Press*, 2003.

21**Molecular Mechanisms in the Emergence of Resistance****D. White**

U.S. Food and Drug Administration, Laurel, MD

Objective: Analyze certain mechanisms that bacteria have elaborated to avoid the toxic action of antimicrobials and the continued challenges that remain in deciphering the complex interactions between antimicrobials, microorganisms, and the surrounding environments.

Summary: Antimicrobial resistance mechanisms to circumvent the toxic action of antimicrobials have been identified and described for all known antimicrobials currently available for clinical use in veterinary and human medicine. Acquired bacterial antibiotic resistance can result from the mutation of normal cellular genes, the acquisition of foreign resistance genes, or a combination of these two mechanisms. The most common resistance mechanisms employed by bacteria include enzymatic degradation or alteration of the antimicrobial, mutation in the antimicrobial target site, decreased cell wall permeability to antimicrobials, and active efflux of the antimicrobial across the cell membrane. Additionally, the spread of mobile genetic elements such as plasmids, transposons, and integrons has greatly contributed to the rapid dissemination of antimicrobial resistance among numerous bacterial genera. Antimicrobial resistance genes have also been shown to accumulate on DNA mobile elements, leading to a situation where multidrug resistance (MDR) phenotypes can be transferred to a susceptible recipient via a single genetic event. The versatility with which bacteria adapt to their environment and exchange DNA between different bacterial genera highlights the need to implement effective antimicrobial stewardship and infection control programs in both veterinary and human medicine.

Reference:

1. Alekshun MN, Levy SB. Molecular mechanisms of antibacterial multidrug resistance. *Cell* 2007;128:037-1050.

22**The Role of NARMS in Detecting and Tracking Antimicrobial Resistance****P. McDermott**

U.S. Food and Drug Administration, Laurel, MD

Objective: Review the design and operation of the National Antimicrobial Resistance Monitoring system for enteric bacteria, and discuss how this data is used to assess potential human health risks associated with the use of antimicrobials in food animals.

Summary: The National Antimicrobial Resistance Monitoring System – Enteric Bacteria (NARMS) was established in 1996 as a collaborative effort between the FDA Center for Veterinary Medicine, U.S. Department of Agriculture, and the Centers for Disease Control and Prevention. The NARMS program monitors

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changes in antimicrobial drug susceptibilities of select enteric bacterial organisms in humans, animals, and retail meats to a panel of antimicrobial drugs important in human and veterinary medicine. The primary objectives of NARMS are to provide descriptive data on the extent and temporal trends of antimicrobial drug susceptibility in *Salmonella* and other enteric bacterial organisms; to facilitate the identification of antimicrobial drug resistance in humans, animals, and retail meats as it arises; and, to provide timely information to veterinarians and physicians on antimicrobial drug resistance patterns. Additionally, NARMS provides a national source of enteric bacterial isolates for research purposes, such as diagnostic test development; and for investigations of and molecular mechanisms associated with resistance, virulence and colonization. The ultimate goal of these activities is to prolong the lifespan of approved drugs by promoting prudent and judicious use of antimicrobial drugs and to identify areas for more detailed investigation.

Reference:

1. Food and Drug Administration, C. F. V. M. 2004. National Antimicrobial Resistance Monitoring System for Enteric Bacteria (NARMS): NARMS Retail Meat Annual Report, 2002. Rockville MD. U.S. Department of Health and Human Services, FDA. Available at: http://www.fda.gov/cvm/narms_pg.html

23 Review the History of Antibiotic Duration Studies for Various Bacterial Infections

J. Powers

Scientific Applications International Corporation, Bethesda, MD

Objective: Discuss the historical evidence regarding duration of therapy for various bacterial infections, and the lack of evidence upon which to base current recommendations; and review the public health issues related to defining appropriate duration of therapy, including increases incidence of adverse events due to unnecessary therapy, potential increase in the spread of antimicrobial resistance, and increased costs of health care.

Summary: The first use of “ten days” of therapy dates back to Biblical times, as documented in the first chapter of the Book of Daniel. The selection of ten days of therapy at that time seemed an arbitrary choice, and the data to support the duration of therapy of many infections today seems based on a similarly deficient database.

The choice of appropriate duration of therapy has several important public health implications. An adequate duration of treatment can result in a greater proportion of patients who are cured compared to no therapy. However, extending the duration of therapy beyond that needed to cure patients can increase the incidence of adverse events experienced by patients.

The earliest treatment of serious infections in the dawn of the antimicrobial era decreased the mortality associated with meningitis and pneumonia. Early reports also note “rapid” responses to antimicrobial therapy, implying an informal comparison in the duration of illness with and without therapy. Few reports, however, quantified the time course of illness in a systematic way. The lack of availability of drug limited the duration of therapy such that clinicians treated patients only until they began to “improve” clinically. Given the lack of drug, clinicians often decreased the dosage of the drug as the patient improved. Since data on exposure-response relationships did not exist, it is unclear how beneficial prolonging the course of therapy was to patients. Most patients resolved their illness in a few days, but in some cases, patients had a prolonged course. It appears that once drug substance became more widely available, that durations of therapy became based on a desire to decrease “relapse rates” with little evidence that increasing the duration of therapy actually affected rate of relapse compared to placebo. As the use of antimicrobials expanded to less serious disease, clinicians based the durations of treatment for self-resolving infections on the durations of therapy for serious illnesses, again with a focus on “decreasing relapse rates.” Recent data on decreasing the duration of therapy in self-resolving infections does not answer the question of whether any therapy is needed at all in some patients. In addition, recent data in some more serious

diseases like pneumonia indicate that prolonged courses many not be necessary for many patients.

This talk will discuss the data on duration of therapy in various common infectious diseases, outline areas where more research is needed, and discuss the public health implications of better data on optimizing therapy based on time to patient response.

References:

1. Finland M. Empiric therapy for bacterial infections: this historical perspective. *Rev Infect Dis* 1983;5 Suppl:1:S2-8.
2. Round table: optimal duration of antibiotic therapy in severe bacterial infections. *Antimicrob Agents Chemother*. 1967;183-202.

24 Pharmacokinetic/Pharmacodynamic Modeling of Appropriate Duration of Antibiotic Treatment

G. Drusano

Ordway Research, Albany, NY

Objective: Demonstrate the dual influences of therapy intensity and therapy duration on the amplification of resistant bacterial subpopulations.

Summary: We are in a crisis of resistance. *Pseudomonas aeruginosa*, *Acinetobacter* sp and other Gram-negatives are frequently multi-resistant, leaving the clinician with few or, in some instances, no choice of therapeutic intervention. Community-acquired MRSA has exploded across the United States, extending issues of resistance to the community. It is critical, therefore, to identify ways of combating resistance to safeguard the therapeutic choices still within the physician’s armamentarium.

While prudent use of antimicrobials and appropriate infection control techniques are absolutely necessary interventions, the choice of drug dose and schedule as well as the choice of therapy duration are weapons that have been overlooked for use in this war.

Our laboratory has demonstrated for *Pseudomonas aeruginosa*, both in an *in vitro* model system as well as in a mouse thigh infection model that a proper choice of dose (drug exposure, indexed to Area Under the concentration-time Curve – AUC) will kill the susceptible population optimally and, more importantly, will suppress amplification of a resistant mutant subpopulation, if one was present *a priori*.

Therapy duration is critical. Somewhat counter-intuitively, the longer therapy continues, the larger the exposure necessary to suppress resistance, a proposition demonstrated in an *in vitro* model system. Proper choice of therapy intensity and schedule as well as limiting duration can help suppress emergence of resistance.

Reference:

1. Mouton J, Dudley M, Cars O, Derendorf H, Drusano G. Standardization of pharmacokinetic/pharmacodynamic (PK/PD) terminology for anti-infective drugs: an update. *J Antimicrob Chemother* 2005;55(5):601-607.

25 Influence and Interrelationship of Duration of Treatment, Choice of Agent, and Adherence on Resistance in HIV Therapy

S. Mannheimer

Columbia University, New York, NY

Objective: Discuss the influence and interrelationship of treatment duration, choice of agent and adherence level on resistance and other outcomes of treatment with HIV antiretroviral therapy.

Summary: Adherence to antiretroviral medications is critical for achieving successful outcomes in the treatment of HIV. Suboptimal antiretroviral adherence has been associated with worse virologic (HIV RNA) and immunologic

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(CD4 lymphocyte) outcomes, higher hospitalization rates, progression to AIDS, increased mortality, and resistance to therapy.

Unfortunately, suboptimal adherence is common in HIV therapy. Many factors can contribute to medication nonadherence, including patient-related factors such as depression and substance use, and treatment-related factors such as treatment side effects. Adherence to antiretroviral therapy also has been shown to decrease over time, possibly related to "pill fatigue." Poor adherence to antiretroviral therapy can result in incomplete HIV viral suppression. Ongoing HIV replication in the presence of the antiretroviral medications can allow for the selection of genetic mutations that are resistant to the current antiretroviral therapy.

The relationship between adherence, virologic suppression, and the development of HIV resistance to antiretroviral therapy is complex and related to a drug's potency, pharmacokinetics, and the number of mutations associated with resistance. Specific adherence levels can lead to different rates of viral suppression as well as different risks of resistance, depending on the agent and class of antiretroviral therapy used.

References:

1. Mannheimer S, Friedland G, Matts J, Child C, and Chesney M, for the Terry Beinr Community Programs for Clinical Research on AIDS. The consistency of adherence to antiretroviral therapy predicts biologic outcomes for human immunodeficiency virus-infected persons in clinical trials. *Clin Infect Dis* 2002;34:1115-1121.
2. Bangsberg DR, Acosta EP, Gupta R, et al. Adherence-resistance relationships for protease and non-nucleoside reverse transcriptase inhibitors explained by virological fitness. *AIDS* 2006;20:223-231.

26 Relationship Between Duration of Therapy and Resistance for Tuberculosis

P. Cegielski

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Objective: Examine four lines of evidence about the relationship between the duration of treatment and the development of acquired drug resistance in tuberculosis.

Summary: Drug-resistant tuberculosis (TB) emerged during the first human trial of the first anti-TB drug, streptomycin. In the past 20 years, however, highly drug-resistant TB has become a major public health problem worldwide.

How rapidly does drug resistance develop during treatment? Four lines of evidence, directly or indirectly, bear on this question: (1) the prevalence of drug resistance in new vs. previously treated patients, (2) the prevalence of drug resistance in patients according to the duration of treatment, (3) experimental data describing the development of drug resistance mutations and drug-resistant phenotypes after exposure to an anti-TB drug, and (4) theoretical evidence based on mathematical models of the frequency of mutations, the growth kinetics of *M. tuberculosis*, and the pathogenesis of TB disease.

These lines of evidence reinforce each other but also raise important questions about current approaches to the diagnosis, treatment, and control of drug-resistant TB.

Reference:

1. Espinal MA, et al. *Internat J Tuberc Lung Dis* 2001; 5:887-893.

**ABSTRACTS OF
SUBMITTED ORAL
PRESENTATIONS**

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S1 Changes in *Staphylococcus aureus* Nasal Colonization in the United States, 2001-2004

R. J. Gorwitz, D. Kruszon-Moran, S. K. McAllister, G. McQuillan, L. K. McDougal, G. E. Fosheim, B. E. Jensen, G. Killgore, F. C. Tenover, M. J. Kuehnert;
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Objective:

Discuss changes in *S. aureus* nasal colonization in the United States between 2001-2002 and 2003-2004.

Summary:

Background: *Staphylococcus aureus* is a common cause of infection, particularly in colonized individuals. Virulent strains of methicillin-resistant *S. aureus* (MRSA) have emerged in the general community. **Methods:** A nationally representative *S. aureus* nasal colonization survey was conducted annually from 2001 through 2004 as part of the National Health and Nutrition Examination Survey. MRSA and a subset of methicillin-susceptible *S. aureus* isolates were characterized by pulsed-field gel electrophoresis type (PFT). A statistic from a linear contrast procedure was used to test for differences in prevalence between NHANES 2001-2002 and 2003-2004. A backward stepwise logistic modeling procedure was used to determine cofactors independently associated with colonization. **Results:** The prevalence of *S. aureus* colonization decreased from 32.4% (95% confidence interval [CI], 30.8%-34.0%) in 2001-2002 to 28.6% (95% CI, 27.2%-30.0%) in 2003-2004 ($P<0.01$). The prevalence of MRSA colonization increased from 0.8% (95% CI, 0.5%-1.4%) to 1.5% (95% CI, 1.2%-1.8%) ($P<0.05$). In males, MRSA colonization was independently associated with healthcare exposure ($P<0.05$). In females, MRSA colonization was associated with US (versus foreign) birth ($P<0.001$), age ≥ 60 years ($P<0.01$), diabetes ($P<0.05$), and poverty ($P<0.05$). In 2003-2004, 19.7% (95% CI, 12.4%-28.8%) of MRSA-colonized individuals carried a PFT associated with MRSA transmission in the community (USA300 or 400), compared with 8.1% (95% CI, 1.1%-25.3%) in 2001-2002; this difference was not statistically significant. **Conclusions:** Nasal colonization with MRSA has increased in the United States, despite a decrease in *S. aureus* colonization overall. The majority of MRSA-colonized individuals did not carry a strain associated with community transmission.

References:

1. Lowy FD. *Staphylococcus aureus* infections. *N Engl J Med* 1998;339:520-532
2. Fridkin SK, Hageman JC, Morrison M, et al. Methicillin-resistant *Staphylococcus aureus* disease in three communities. *N Engl J Med* 2005;352:1436-1444

S2 Risk Factors for Community-Associated Methicillin-Resistant *Staphylococcus aureus* Skin Infection in New York City

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Objective:

Discuss the epidemiology, risk factors and prevention of community-associated methicillin-resistant *staphylococcus aureus* infections.

Summary:

Background: Risk factors for community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) are not known outside of outbreaks. We evaluated skin-to-skin contact and use of recreational facilities as risk factors for CA-MRSA in adult male NYC residents diagnosed in outpatient clinics. **Methods:** In 2005, a large commercial laboratory began reporting CA-MRSA to DOHMH. We restricted this analysis to adult men. Cases were patients diagnosed with CA-

MRSA skin and soft tissue infections. Controls were patients reported by the same lab and diagnosed with amebiasis or giardiasis. We administered structured questionnaires by phone, and compared risk behaviors of cases and controls by using chi-square or Fisher's exact tests. **Results:** Cases (n=245) and controls (n=118) had similar age, income level, education and borough of residence. Sex with men (MSM) was reported by 148 (60%) of cases and 76 (64%) of controls. Cases were more likely than controls to have had physical contact with someone with skin infection (16% vs. 5%, $p<0.01$). Cases were less likely than controls to have used a recreational facility (55% vs. 70%, $p<0.01$) or used towel provided at the facilities (28% vs. 43%, $p<0.01$). Similar proportion of cases and controls reported sharing towels (43% vs. 45%, $p=0.80$).

Conclusions: This preliminary analysis supports the widely-held notion that physical contact with infected individuals is associated with CA-MRSA. Recreational facilities or the use of towels did not appear to be risk factors for these adult men who accessed outpatient care. Guidance around covering and avoiding contact with wounds should be targeted to this group. Future analyses should examine types of physical contact that are associated with CA-MRSA.

References:

1. Lee NE, Taylor MM, Bancroft E, 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;40:1529-34.
2. Moran, GJ, Krishnadasan A, Gorwitz RJ et al. Methicillin-resistant *Staphylococcus aureus* infections among patients in the emergency department. *N Engl J Med* 2006; 355: 666-674.

S3 Prevention of Nosocomial Transmission of Methicillin-Resistant *Staphylococcus aureus* (MRSA) Infections in the Neonatal Intensive Care Unit using Admission Screening

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Newark Beth Israel Medical Center, Newark, NJ.

Objective:

Describe the effectiveness of admission screening for methicillin-resistant *Staphylococcus aureus* in the neonatal intensive care unit.

Summary:

Background: The control of MRSA infections in the neonatal intensive care unit (NICU) remains a challenging problem for neonatologists and infection control professionals. **Methods:** Prospective screening for MRSA nasal colonization of all admissions to the NICU was performed from August 2005 to January 2007. Nasal swabs were obtained and tested for MRSA using conventional culture and polymerase chain reaction (PCR)-based technology. Positive patients were decolonized with intranasal mupirocin and retested before discontinuing contact isolation. **Results:** 19 out of 1239 babies (1.5%) screened were colonized with MRSA on admission to the NICU. 11 babies were colonized at birth, six were positive at one day of age and two transferred babies were positive at two and four days of age. The median birth weight was 2660 grams (range 660-5300), the median gestational age was 38 weeks (range 24-40 weeks). 14 of 19 babies (73.7%) were delivered vaginally and seven of 19 babies (36.8%) were transferred from referral institutions. 11 babies were culture-positive and eight babies were PCR-positive. Three months after initiation of admission screening, no MRSA infection occurred for 14 consecutive months. **Conclusions:** MRSA screening for nasal colonization at the time of admission prevented the nosocomial transmission of MRSA infection in the NICU during 14 months of surveillance.

References:

1. Healy CM, Hulten KG, Palazzi DL et al. Emergence of new strains of methicillin-resistant *Staphylococcus aureus* in a neonatal intensive care unit. *Clin Infect Dis*. 2004;39:1460-1466.
2. Centers for Disease Control and Prevention. Community-associated methicillin-resistant *Staphylococcus aureus* infection among healthy newborns-Chicago and Los Angeles county, 2004. *MMWR* 2006;55:229-32.

ABSTRACTS OF SUBMITTED ORAL PRESENTATIONS

S4 Update on National Outpatient Utilization of Oral Antimicrobial Drugs, 1995-2006

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¹Office of Surveillance and Epidemiology, Food and Drug Administration Center for Drug Evaluation and Research, Silver Spring, MD, ²Scientific Applications International Corporation, in support of Collaborative Clinical Research Branch, NIAID, Bethesda, MD.

Objective:

Discuss recent trends in the utilization of oral antimicrobial drugs by the US outpatient population with a focus on indications of use.

Summary:

Annual survey data from the 1991-2000 National Ambulatory Medical Care Survey reported that while overall antimicrobial prescribing declined, changing patterns of selection occurred. The change in use from targeted to broader-spectrum agents had consequences to antibiotic resistance. We examined antimicrobial utilization from 1/1995 - 6/2006 using a different database (Verispan, LLC, Vector One®: National which integrates retail pharmacy prescription [Rx] activity and Physician Drug and Diagnosis Audit, a monthly survey of office-based prescribers that monitors diseases states and prescribing habits) to obtain updated and confirmatory information. Cochran-Mantel-Haenszel Chi-square testing was used for comparisons. Among the top 90% of dispensed retail Rx, total Rx = 3,079,441,000 with Rx = 286,587,000 for 1995 and Rx = 263,307,000 for 2005, an overall decrease of 8.1%. By drug class, Rx decreased 13.8% (p<.0001) for beta-lactams from 1995 to 2005, whereas macrolides increased by 6.5% and fluoroquinolones by 7.5% (p<.0001). Azithromycin alone increased from 2.2% of total Rx share in 1995 to 16.3% in 2005 (p<.0001). The top 5 indications of use accounting for half of total use were otitis media (13% total share), sinusitis (11%), bronchitis (10%), urinary tract disorders (7%), and acute pharyngitis (6%). There has been a modest decrease in the overall oral antimicrobial Rx. However, shifts in drug classes show increasing use of macrolides and fluoroquinolones consistent with previous observations. Large fraction of use is attributed to few indications. These data point to directed education on limited numbers of molecules and indications. Research targeted to specific indications including rapid diagnostics and quantification of benefit to risk will provide tools needed for public health effort on judicious antimicrobial use.

References:

- Steinman MA, Gonzales R, Linder JA, Landesfeld CS. Changing use of antibiotics in community-based outpatient practice, 1991-1999. *Ann Intern Med.* 2003;138:525-33.
- McCaig LF, Besser RE, Hughes JM. Trends in antimicrobial prescribing rates for children and adolescents. *JAMA* 2002;287:3096-3102.

S5 Increasing Rates of High Level Antibiotic Resistance, Including to Polymyxin, Among *Klebsiella* and Other Gram-negatives in The Bronx

L. Lemos-Filho, B. P. Currie;
Infectious Diseases, Montefiore Medical Center, Bronx, NY.

Objective:

Describe the emergence of polymyxin resistance among gram-negative bacteria.

Summary:

Increasingly, resistant nosocomial gram-negative bacilli (GNB) are a serious challenge. Carbapenem resistance has forced physicians to resort to polymyxins, despite toxicity concerns, for such pathogens. However polymyxin resistance (PR) has been reported from several groups spanning the globe. We describe the emergence of PR at our institution. The clinical database of all isolates collected

from 1/1/2004-12/31/2005 was mined for unique patient isolates of GNB resistant to polymyxin B, imipenem, and amikacin. Intermediate susceptibility was coded as resistance. Polymyxin B MIC of >2mg/ml was considered resistant. STATA 9.2 was used for analysis. PR was identified only among highly resistant isolates of: *Acinetobacter baumannii*, *Klebsiella pneumoniae* (KP), and *Pseudomonas aeruginosa*. There were increases of resistance rates in all three species (Table 1), with statistical significance in KP. Alarmingly, 11 of 29 of the 2005 PRKP (Table 2) were present at hospital admission, and 22 were also imipenem-resistant. We have shown increases in PR in resistant GNB especially KP, with PR present prior to hospitalization.

Table 1. Resistance rates by organism and calendar year.

	2004	2005	P-value*
<i>Klebsiella pneumoniae</i> unique patient isolates			
Total	1317	1437	
Resistant to imipenem and/or amikacin	204 (15.4)	276 (19.2)	<0.01
Resistant to polymyxin B	2 (0.1)	29 (2.0)	<0.001
Resistant to polymyxin B and imipenem	0	22 (1.5)	<0.001
<i>Acinetobacter baumannii</i> unique patient isolates			
Total	356	323	
Resistant to imipenem and/or amikacin	103 (28.9)	115 (35.6)	0.063
Resistant to polymyxin B	3 (0.8)	9 (2.7)	0.055
Resistant to polymyxin B and imipenem	3 (0.8)	7 (2.1)	0.152
<i>Pseudomonas aeruginosa</i> unique patient isolates			
Total	691	810	
Resistant to imipenem and/or amikacin	139 (20.1)	166 (20.4)	0.854
Resistant to polymyxin B	0 (0)	5 (0.6)	0.066
Resistant to polymyxin B and imipenem	0 (0)	3 (0.4)	0.254

Values given as n (% of total). *By chi-squared or Fisher's exact test.

Table 2. Non-hospital related polymyxin B-resistant

<i>K. pneumoniae</i> isolates by year and nursing home status.	2004	2005
Polymyxin-resistant <i>K. pneumoniae</i> unique patient isolates		
Total	2	29
Emergency room culture from nursing home patient	0	4 (13.8)
Emergency room culture, non-nursing home related	0	1 (3.5)
Inpatient culture collected within 2 days from nursing home patient	0	2 (6.9)
Inpatient culture collected within 2 days of admission, non-nursing home related	0	4 (13.8)

Values given as n (% of total).

Reference:

- Bratu S, Toloney P, Karumudi U, et al. Carbapenemase-producing *Klebsiella pneumoniae* in Brooklyn, NY: molecular epidemiology and in vitro activity of polymyxin B and other agents. *J Antimicrob Chemother* 2005;56:128-132.

S5 Increasing Rates of High Level Antibiotic Resistance, Including to Polymyxin, Among *Klebsiella* and Other Gram-negatives in The Bronx

L. Lemos-Filho, B. P. Currie;
Infectious Diseases, Montefiore Medical Center, Bronx, NY.

Objective:

Describe the emergence of polymyxin resistance among gram-negative bacteria.

Summary:

Increasingly, resistant nosocomial gram-negative bacilli (GNB) are a serious challenge. Carbapenem resistance has forced physicians to resort to polymyxins, despite toxicity concerns, for such pathogens. However polymyxin resistance (PR) has been reported from several groups spanning the globe. We describe the emergence of PR at our institution. The clinical database of all isolates collected

S6 Perspective on Antimicrobial Susceptibility of *Escherichia coli* Isolates Recovered from Poultry Carcass Rinsates as Part of the Animal Arm of NARMS

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Objective:

Review information regarding susceptibility trends in generic *E. coli* originating from poultry carcass rinsates.

Summary:

Escherichia coli are considered commensal intestinal flora in both animals and humans and are known to transfer antimicrobial resistance genes to other bacteria. Consequently, they may play a role in the dissemination of these genes

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to other food borne bacteria. From 2000 through 2004, *E. coli* isolates were recovered from chicken carcass rinsates collected at federally inspected slaughter and processing establishments in the U.S. as part of the animal arm of the National Antimicrobial Resistance Monitoring System – Enteric Bacteria (NARMS). Antimicrobial susceptibility profiles were determined using broth microdilution (Sensititre™) against a custom made panel of antimicrobials which are important in both human and veterinary medicine. From 2004 to 2006, resistance to ampicillin increased from 17.6% to 25.6% while resistance to amoxicillin/clavulanic acid increased from 8.8% to 16.0%, respectively. Resistance to the cephalosporin, ceftiofur also increased; however, < 1% of isolates exhibited resistance to ceftriaxone. Ceftiofur is only used in veterinary medicine while ceftriaxone is only used in human medicine. In 2006, total percent resistance to kanamycin (9.1%), streptomycin (49.5%), nalidixic acid (5.4%), and trimethoprim-sulfamethoxazole (8.3%) was below levels observed in 2004. The potential for gene transfer associated with these bacteria continues to demonstrate the need for continued susceptibility monitoring of *E. coli*.

Reference:

1. Feder I, Wallace F, Gray J, Fratamico P, et. al. Isolation of *Escherichia coli* O157:H7 from Intact Colon Fecal Samples of Swine. *Emerg Infect Dis* 2003; 9(3):380-383

S7 Dissemination of Antimicrobial Resistant *Salmonella* Among Pacific Northwest Dairy Farms

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Objective:

Discuss the antimicrobial resistance of new strains of *Salmonella* on Washington dairy farms and the factors associated with their introduction.

Summary:

Background: The emergence of antimicrobial resistant *Salmonella* in food animals is potentially a risk for human health. This study was designed to quantitatively evaluate the rate of introduction of new strains of multidrug resistant *Salmonella* on dairy farms. **Methods:** Pooled fecal (n =2490) and feed (n =1864) samples collected at four months intervals over a two-year period on 60 Washington dairy farms were cultured for *Salmonella*. All isolates were serogrouped and *in vitro* susceptibility to 11 antimicrobials was evaluated. **Results:** The rate of new *Salmonella* strain introduction was 206 per 1000 herd-months (95% CI 182-231). Of the new strains introduced, 35% were multidrug resistant. Of 2490 fecal pools, 78 (3%) contained new *Salmonella* strains. Serogroup C1 was the most frequent (24%) followed by B (15%), E1 (13%), D1 (12%), C2 (8%), and others (28%). New *Salmonella* strains were resistant to ampicillin, chloramphenicol, streptomycin, triple-sulfa (a combination of sulfadiazine, sulfamethazine and sulfamerazine), gentamycin, kanamycin, tetracycline and ceftazidime. 105 (5%) feed specimens were positive for *Salmonella*. Serogroup C1 was the most frequent (38%) followed by C2 (27%), B (11%), E1 (9%), and others (15%). In general, feed isolates different in serogroup and resistance pattern from fecal isolates on the same farm. **Conclusions:** New multidrug resistance *Salmonella enterica* strains are commonly introduced into Northwest dairy farms. This is the first known report of rate of new strain introduction.

Reference:

1. Besser TE, Goldoft M, Pritchett LC, et. al. Multiresistant *Salmonella* Typhimurium DT104 infections of humans and domestic animals in the Pacific Northwest of the United States. *Epidemiol. Infect* 2000;124:193-200.

2. Evans S, Davies R. Case control study of multiple-resistant *Salmonella* typhimurium DT104 infection of cattle in Great Britain. *Vet Rec* 1996;139:557-558.

S8 Relationship Between Level of Antibiotic Use and Antibiotic Resistance among *Escherichia coli* Isolated from Swine in a Multi-site Integrated Farm-to-Plate System

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¹Veterinary Integrative Biosciences, Texas A&M University, College Station, TX, ²Veterinary Physiology and Pharmacology, Texas A&M University, College Station, TX, ³Food and Feed Safety Research, United States Department of Agriculture, College Station, TX, ⁴Large Animal Clinical Sciences, Texas A&M University, College Station, TX.

Objective:

Discuss the effects of varying levels of prescribed antibiotics on changes in antibiotic-resistant *E. coli* among swine, while controlling for temporal variability of production risk factors in a vertically integrated agri-food system.

Summary:

Background: The objective was to study the relationship between changes in prevalence of resistant enteric bacteria and defined doses of antibiotics used in the host species. **Methods:** From 02/04-01/07, monthly swine aggregated fecal samples were drawn from 15 units in a multi-site study population. Antibiotic records were collected from 10/03-01/07, and defined monthly dosages (DMDs) were calculated (mg per pig-kg-month). Isolates cultivated from CHROMagar were tested for antimicrobial susceptibility. The relationship between resistant bacteria, sampling period, and antibiotic use was assessed in a generalized linear model adjusted for dependence of responses within location using a binomial distribution and logit link function in STATA. **Results:** The relationship between tetracycline resistance and DMD illustrated a dose-response association, with adjusted odds ratios (OR) of 1.14 and 1.66 (P < 0.05) for third and fourth quantiles of chlorotetracycline (CTC) use in feed. Odds ratios were adjusted for confounding effects of swine production group and season. While much of the variability in tetracycline resistance was explained by the variable levels of CTC use in feed, there were unexplained factors associated with temporal factors. The baseline level of resistance among untreated animals was 81.7%. In contrast, the tetracycline resistance of *E. coli* isolated from an associated human population of swine/non-swine workers was 20.4%. **Conclusions:** Our study shows that risk of tetracycline resistance in swine is dependent on CTC use, and swine production cycle and temporal/seasonal effects on the risk of tetracycline resistance are important. A concurrent study of agricultural workers and pork consumers in the integrated agri-food system is ongoing.

References:

1. Teshager T, Herrero I, Porrero M, Garde J, Moreno M, Dominguez L. Surveillance of antimicrobial resistance in *Escherichia coli* strains isolated from pigs at Spanish slaughterhouses. *Int J Antimicrob Agents* 2000;15:137-142.
2. Anderson A, Nelson J, Rossiter S, Angulo F. Public health consequences of use of antimicrobial agents in food animals in the United States. *Microb Drug Resist* 2003;9:373-379.

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P1 **In Vitro Testing of Daptomycin plus Rifampin against Oxacillin-resistant *Staphylococcus aureus* (MRSA) resistant to Rifampin**
F. Khasawneh, D. Ashcraft, G. Pankey;
 Infectious Diseases, Ochsner Clinic Foundation, New Orleans, LA.

Summary:

Objective: Determine if rifampin plus daptomycin were synergistic or antagonistic *in vitro* against rifampin-resistant MRSA. **Background:** The combination of a cell wall active antimicrobial, such as a beta-lactam or vancomycin plus rifampin is used in the empiric treatment of some MRSA infections such as of implanted devices or bone. There is no information on the combination of daptomycin and rifampin when used to treat MRSA infections before susceptibilities are reported (i.e. rifampin resistance). **Methods:** Seven clinically unique rifampin-resistant MRSA isolates were identified out of 490 (1.4%) collected during 4/2003-8/2006 from patients at the Ochsner Medical Center in New Orleans, LA. Synergy testing was performed by an Etest® method and time-kill assay. Etest MIC's (µg/ml) were > 32 (resistant) for rifampin and 0.5 - 1.5 (susceptible) for daptomycin. Etest synergy (performed in triplicate) was defined as ΣFIC ≤ 0.5, indifference as >0.5- 4 and antagonism as > 4. Time-kill assay were performed in triplicate for discordant results. **Results:** The daptomycin plus rifampin combination was indifferent by Etest for all isolates. Time-kill assay results were in agreement with the exception of one isolate that was antagonistic. Concordance between the two methods was 86%.

Conclusions: This *in vitro* study failed to demonstrate synergy of rifampin + daptomycin against our rifampin-resistant MRSA isolates (both methods). Daptomycin plus rifampin was antagonistic by time-kill assay but not by Etest for one isolate. More rifampin-resistant MRSA isolates should be tested to determine if other isolates demonstrate *in vitro* daptomycin + rifampin antagonism.

Reference:

1. Pankey G, Ashcraft D, and Patel, N. In Vitro Synergy of Daptomycin plus Rifampin against Enterococcus faecium Resistant to both Linezolid and Vancomycin. *Antimicrob Agents Chemother* 2005;12:5166-5168.

P2 **Detection of Tetracycline Resistant Bacteria in Human Influenced Environments**

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 Biology, American University, Washington, DC.

Summary:

The purpose of this experiment was to examine the presence of bacterial resistance to tetracycline in two sub-watersheds of the Chesapeake Bay and examine what resistant genes are present throughout each watershed. The persistence and prevalence of bacteria resistant to antibiotics in natural aquatic systems is of growing concern. Tetracycline is used to treat infections and promote growth in livestock. Through a variety of potential mechanisms including sewage discharge and runoff, tetracycline resistant bacteria are gaining access to natural systems. Through direct isolation and molecular techniques, we examined the presence of bacterial resistance to tetracycline in two sub-watersheds of the Chesapeake Bay. Water samples were taken from several locations within the Anacostia and Chester River systems. The Anacostia River system is highly urbanized while the Chester River system is less urbanized and has more agriculture. Water samples were diluted and plated onto nutrient agar infused with tetracycline (10µg/1mL). Isolates resistant to tetracycline were found at all Anacostia and Chester River sites and were all Gram negative. Samples were analyzed for the presence of plasmids and eight tetracycline resistant genes, coding for ribosomal protection proteins and efflux pumps. DNA analyses revealed no isolates containing plasmids and isolates from all sites of the Anacostia River contained the *tet(B)* gene; however no tet genes were found in Chester River isolates. Using filter-sterilized water from the Anacostia River and nutrient broth, one isolate positive for the *tet(B)* gene was

grown in the presence and absence of tetracycline (10µg/1mL). This isolate demonstrated similar growth patterns with or without the presence of tetracycline in both mediums. These current results demonstrate not only the presence of unique tetracycline resistant bacteria in two natural ecosystems but also the potential for these organisms to play an ecological role via the ability to grow in their natural waters.

References:

1. Aminov RI, Chee-Sanford JC, Garrigues N, et al. Development, validation, and application of PCR primers for detection of tetracycline efflux genes of gram-negative bacteria. *Appl Environ Microbiol* 2002;68:1786-1793
2. Chee-Sanford JC, Aminov RI, Krapac IJ, et al. Occurrence and diversity of tetracycline resistance genes in lagoons and groundwater underlying two swine production facilities. *Appl Environ Microbiol* 2001;67:1494-1502

P3 **Daptomycin Experience in Patients with Coagulase-negative Staphylococcal Bacteremia**

K. Lamp¹, S. Rehm², D. Katz¹, L. Friedrich¹;
¹Cubist Pharmaceuticals, Lexington, MA, ²The Cleveland Clinic, Cleveland, OH.

Summary:

Objective: The participant will describe the treatment of coagulase-negative staphylococcal (CoNS) bacteremia with daptomycin. **Background:** Daptomycin was recently approved for the treatment of methicillin-susceptible and -resistant *Staphylococcus aureus* bloodstream infections. There are limited outcomes data for bacteremia due to other pathogens such as coagulase-negative staphylococci (CoNS). **Methods:** The Cubicin® Outcomes Registry & Experience collected data on daptomycin treatment in 2005. Surgical interventions were not collected. Clinically evaluable patients with blood cultures positive for CoNS were included. Clinical success (cure + improvement) and failure were determined at the end of therapy using standard definitions. **Results:** Seventy patients were identified; 51% were males and 33% were ≥66 years of age. Common comorbidities included hypertension (39%), cancer (37%) and diabetes (20%). Fifty-two (74%) patients were in an institutional setting 2 days before daptomycin therapy was initiated, 15 (21%) received daptomycin in an ICU and 11 (16%) were on dialysis. Fifty-seven (81%) patients received prior antibiotic therapy, most commonly with vancomycin (54%; of which 39% clinically failed). Forty-three (61%) patients had infections related to intravascular catheters or intravascular/intracardiac foreign devices. The median daptomycin dose was 5.5 mg/kg (range 0.01 to 8 mg/kg). 48% of patients received a dose of 6 mg/kg and 34% received 4 mg/kg; 1 patient received 0.01 mg/kg daptomycin via antibiotic lock. The median duration of daptomycin therapy was 11 days (1-370 days). Clinical success was achieved in 97%. Nine (13%) patients had an adverse event reported; adverse events were assessed as possibly related to daptomycin in five cases; one of these events was characterized as serious. **Conclusions:** Daptomycin appeared to provide effective and well-tolerated therapy for the treatment of CoNS bacteremia. Daptomycin is frequently given in doses lower than that labeled for use in bacteremia (6 mg/kg), indicating additional educational efforts are needed. Further studies are needed to confirm these findings.

References:

1. Fowler VG Jr., Boucher H, Corey G, et al. Daptomycin versus standard therapy for bacteremia and endocarditis caused by *Staphylococcus aureus*. *N Engl J Med*. 2006;355:653-665.
2. Segreti JA, Crank CW, Finney MS. Daptomycin for the treatment of Gram-positive bacteremia and infective endocarditis: a retrospective case series of 31 patients. *Pharmacotherapy* 2006;26:347-352.

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P4 A New Rapid Method for the Drug Susceptibility Testing of Mycobacteria

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¹BioSense Technologies, Inc., Woburn, MA, ²Mentor Engineering, Bedford, MA, ³Department of Immunology and Infectious Diseases, Harvard School of Public Health, Boston, MA, ⁴Mycobacteriology Laboratory, Massachusetts Department of Public Health, Boston, MA.

Summary:

Objective: At the conclusion of this presentation, the participant will have learned about a novel approach to drug susceptibility testing of mycobacteria capable of providing results in a few hours time. **Background:** A novel method for drug susceptibility testing (DST) of mycobacteria is presented that provides results in only a few hours time. Currently used culture-based DST methods require many weeks to obtain results for slow-growing mycobacteria because of their reliance on bacterial population growth to reach detectable changes in the total biomass. The long time required to acquire test results can result in the prescription of inappropriate therapies and the consequential spread of antimicrobial resistance. **Methods:** The susceptibility of mycobacteria to antimicrobial compounds was measured using a new approach that relies on quantitative measurements of the bacterial stress response during exposure to antimicrobials. Measurements of the stress response are optimally implemented by monitoring subtle changes in the dielectric properties of the suspension using impedance sensing. The stress response is both immediate and more intense than the response from normal growth enabling test results to be obtained rapidly.

Results: Data were obtained using slow-growing *Mycobacterium bovis* BCG as a model. Stress responses were measured for strains of BCG known to be both resistant and susceptible to isoniazid and rifampicin in only a few hours and were readily correlated with known susceptibilities. **Conclusions:** Monitoring the stress response of mycobacteria in contrast to monitoring increases in biomass is an effective way to obtain drug susceptibility results rapidly. The ability to measure susceptibility and identify drug resistance in a few hours for slow-growing organisms has been successfully demonstrated for several first-line antibiotics commonly prescribed for tuberculosis treatment. A related approach is applicable for the rapid detection of low levels of mycobacteria in blood and sputum specimens.

References:

1. Pai M, Kalantri S, Dheda K. New tools and emerging technologies for the diagnosis of tuberculosis: part II. Active tuberculosis and drug resistance. *Expert Rev Mol Diagn* 2006;(3):423-32.
2. Perkins, MD, Small, PM. Partnering for better microbial diagnostics. *Nat Biotechnol* 2006;24(8):919-21.

P5 Antibacterial Properties of Soluble, Arginine-Functionalized Chitosan

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Summary:

Objective: The proprietary arginine-functionalized chitosan is superior to chitosan in its solubility in neutral pH environment, possesses higher antibacterial effectiveness, and displays a broader spectrum of antibacterial activity. **Background:** Chitosan is a biopolymer derived from chitin, the main component of shrimp and crab exoskeletons. Chitosan's biological properties, such as antimicrobial activity, haemostatic activity, and acceleration of wound healing, make it medically important. Though the mechanism of its action remains unknown, chitosan's antimicrobial activity is established to be fairly broad spectrum. Since chitosan use is limited by its insolubility at neutral pH, we

have analyzed proprietary, arginine-functionalized chitosan derivatives that are soluble in physiological environments. **Objective:** The purpose of our study was to evaluate these proprietary arginine-functionalized chitosan derivatives in terms of their antibacterial activity on gram-positive and gram-negative, non-pathogenic and pathogenic bacteria, either on planktonic growth or biofilm formation. **Methods:** We tested a variety of gram-negative and gram-positive bacteria for growth inhibition by 6% or 30% substituted arginine-chitosan. Planktonic growth was tracked by OD measurements and viability counts, while biofilm accumulation was assessed by crystal violet staining. MTT assays were used to determine mammalian cytotoxicity. **Results:** Anti-bacterial properties and solubility of chitosan are greatly enhanced by functionalization with arginine. A low concentration of arginine-chitosan dramatically (viability decrease >> 90%) interferes with the planktonic growth of *B. subtilis*, *S. epidermidis*, *P. fluorescens* and pathogens *A. baumannii*, *S. pyogenes*, *K. pneumoniae*, *S. flexneri* and *S. enteritidis*. Functionalized chitosan also totally prevents *S. epidermidis* biofilm accumulation. Poly-arginine alone is not responsible for the anti-bacterial properties of this material. This material is non-toxic to HeLa cells in culture below 30 microgram per milliliter of tissue culture media. **Summary:** Arginine-functionalized chitosan is superior to chitosan in its solubility in neutral pH, possesses higher antibacterial effectiveness, and has broader spectrum antibacterial activity.

References:

1. Rabea EI, Badawy MET, Stevens CV, Smaghe G, Steurbaut W. Chitosan as antimicrobial agent: applications and mode of action. *Biomacromolecules* 2003;4:1457-1465.
2. Burkatovskaya M, Tegos GP, Swietlik E, Demidova TN, Castano A, Hamblin MR. Use of chitosan bandage to prevent fatal infections developing from highly contaminated wounds in mice. *Biomaterials* 2006;27:4157-4164.

P6 CA-MRSA Colonization Rates in Children and SSTI Management in the Ambulatory Setting

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Summary:

Objective: The participant will understand the epidemiology of CA-MRSA as it pertains to colonization and skin and soft tissue infections (SSTI's) in otherwise healthy children who present in the ambulatory setting. **Background:** There are few studies evaluating CA-MRSA colonization rates in outpatient pediatric populations or in those with SSTI's. We studied: 1) The CA-MRSA colonization rates in the pediatric population receiving care in our ambulatory setting, 2) colonization rates in children with SSTI's, 3) Management strategies and treatment outcomes of children with SSTI's. **Methods:** Prospective, cross-sectional surveillance for MRSA colonization was performed in a random sample of children presenting to a pediatric emergency center and in a sample of children diagnosed with SSTI's, using nasal and axillary swabs. For those with SSTI, medical record review and follow-up was performed. **Results:** During the first 14 weeks of an ongoing study, 280 children were enrolled for MRSA colonization. Mean age was 68 months; 46% were female. 16 (5.7%) were colonized with MRSA. During this same period, 49 children SSTI were enrolled. Mean age was 60 months; 55% were female. 5/49 (10.2%) were MRSA colonized. 41/49 (84%) SSTI's were diagnosed as abscesses. Of the 30 who had cultures done 17 (57%) grew MRSA and seven (23%) grew MSSA. 24/49 SSTI's received an incision and drainage. All showed improvement at follow at two weeks; of these, antibiotics were used in 20 (83.3%). **Conclusions:** MRSA colonization rate among children seen in our ED is 5.7%, compared to 10.2% in those with

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SSTIs. Abscesses were the majority of SSTIs; about half of these had an I and D. 57% of cultured SSTI's were due to MRSA. In this preliminary dataset, all children who received I&D were clinically improved.

References:

1. Moran G, Krishnadasan A, Gorwitz R, et al. Methicillin-resistant *S. aureus* infections among patient in the emergency department. *New Engl J Med* 2006;355(7):666-74.
2. Hussain F, Boyle-Vavra S, Daum R. Community acquired methicillin resistant *Staphylococcus aureus* colonization in healthy children attending an outpatient pediatric clinic. *Pediatr Infect Dis J* 2001;20:763-767

P7 Development of Oxytetracycline Resistant *Aeromonas salmonicida* in Rainbow Trout During a Laboratory-controlled Efficacy and Pharmacokinetics Study

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Summary:

Objective: To learn how clinical efficacy and pharmacokinetic data can be applied in fish to help set PK/PD cutoffs. **Background:** Clinical breakpoints are not available for any drugs used in aquaculture. In order to develop such breakpoints we determined: 1) oxytetracycline (OTC) efficacy against *Aeromonas salmonicida* (MIC=0.25µg/mL) in rainbow trout, 2) drug concentrations associated with clinical efficacy, and 3) the percent OTC-resistant *A. salmonicida* isolates in the spleen over time. **Methods:** Seventy-two trout were challenged by immersion in 10⁸ CFU/mL after light abrasion of a 2cm area of skin over the epaxial muscles. Two days after bacterial challenge, OTC feed (75mg OTC/kg) or non-medicated feed was administered by gavage to 36 fish each for 10 consecutive days. Serum OTC concentrations were determined for all moribund and surviving fish and CFU/g of spleen were determined for all fish. We determined the MIC of one *A. salmonicida* isolate per fish (spleen). **Results:** Mortality was 100% in non-medicated fish versus 42% in medicated fish with serum OTC concentrations ranging from 0.16-1.94µg/mL in the medicated fish. *A. salmonicida* isolates were recovered from 36 spleens from non-medicated fish and 14 of the medicated fish. Of the 14 isolates from medicated fish, 10 were resistant (≥8µg/mL) to OTC. **Conclusions:** OTC is highly effective against infection caused by this OTC-susceptible isolate. Serum OTC concentrations in two moribund fish were above the current micro-epi cutoff of 1.0µg/mL for *A. salmonicida*, suggesting the micro-epi cutoff may be too high. Additional studies are needed to investigate therapeutic serum OTC concentrations during the course of treatment.

References:

1. Miller RA, Reimschuessel R. Epidemiologic cut-off values for antimicrobial agents against *Aeromonas salmonicida* isolates determined by frequency distributions. *Am J Vet Res* 2006;67:1837-1843.
2. Miller RA, Reimschuessel R, Carson MC. Determination of oxytetracycline levels in rainbow trout serum on a biphenyl column using high-performance liquid chromatography. *J Chromatogr B Analyt Technol Biomed Life Sci* 2007 Feb 3; [Epub ahead of print]

P8

Association of *E. coli* Genotypes and Antimicrobial Resistance.

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Summary:

This study is to investigate possible shared patterns of resistance within regions; the genetic relatedness of MDR isolates was determined. Pathogenic *E coli* isolates associated with spontaneous disease in dogs or cats (n=450) were collected from four different regions in the US from May-September 2005. Isolates were collected from four geographical areas: West, South, Central and Northeast, and were not collected from any patient more than once. Isolates were subjected to E-test® susceptibility testing to seven drugs (four drug classes). Percent of isolates expressing multi-drug resistance (MDR) was greater (61%) in the South compared to the other three regions. To investigate possible shared patterns of resistance within regions, the genetic relatedness of MDR isolates (n=90, representing 21 antimicrobial phenotypes, 18 tissues, nine states and all four regions) was determined. Isolates were subjected to pulsed-field gel electrophoresis (PFGE), and dendrograms were generated using the Dice correlation coefficient and the unweighted pair group mathematical average clustering algorithm of Bionumerics™. A total of 82 genotypes were identified. Five profiles were identified based on ≥ 90% similarity; these represented 14 isolates, six tissues and two states. For Alabama, four profiles represented six phenotypes. Three of these consisted of two isolates and two phenotypes each, while one consisted of six isolates and three phenotypes. For Indiana, one profile had two phenotypes. The proportion of isolates in any profile collected from any one tissue (most were urine) was not significantly different from the proportion of total isolates collected from the same tissue. There was no geographical relatedness based on PFGE profiles or antimicrobial resistance. Furthermore, the genetic relatedness of isolates cannot be predicted phenotypically. Molecular mechanisms of resistance for these isolates will be determined next.

References:

1. Guardabassi L, Schwarz S, Lloyd DH. Pet animals as reservoirs of antimicrobial resistant bacteria. *J Antimicrob Chemother* 2004;54:321-332.
2. Cooke CL, Singer RS, Jang SS, et. al. Enrofloxacin resistance in *Escherichia coli* isolated from dogs with urinary tract infections. *J Am Vet Med Assoc* 2002;220:190-192.

P9

Equine Methicillin-Resistant *Staphylococcus aureus* (MRSA) Typing and Evaluation of Virulence Genes: Preliminary Results from a Veterinary Teaching Hospital

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Summary:

Equine MRSA isolates from the University of Georgia VTH were characterized by SCCmec allotyping and superantigens (Sags) and virulence genes determined via PCR-based assays. MRSA is a major human and veterinary public health concern due to the emergence of highly pathogenic CA-MRSA. Numerous publications have described MRSA in animals. In other countries, clusters of equine MRSA have similarities to human isolates. This is the first study in the United States to determine typing and clonality of equine isolates. Clinical isolates of eleven cases of equine MRSA from 2002-2006 were obtained. Antibiotic use varied prior to culture. Stock isolates were cultured, subcultured, incubated, and DNA extracted. Single reaction PCR was used for *mecA* confirmation and to identify Sags *sea*, *seb*, *sec*, *sed*, *see*, *seg*, *sei*, *sej*, *eta*, *etb* and *tsst-1*. Single reaction and multiplex PCRs were used for SCCmec allotyping. Based on the time of infection acquisition, 27.3% were considered CA-MRSA and 72.7% HA-MRSA. The majority of isolates (93.75%) were multiple Sag carriers; one isolate was negative for all Sags. Seventy-five percent were positive for *sea*, 81.25% for *seb*, 18.75% for *sed*, *seg*, *sei* and *tsst-1*, and 12.5% for *sei*. None were

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positive for *sec*, *see*, *eta* and *etb*. Ten isolates were identified as SCCmec type IV. Three isolates were negative for all loci and three isolates contained loci B and D. In accordance with other equine studies, SCCmec type IV is the predominant allotype in horses admitted to the VTH. The majority of isolates were carriers of multiple Sags, with *seb* predominating. Prior studies in Georgia revealed *seb* was the most common Sag, followed by *tsst-1*. Equine MRSA is a potential reverse zoonosis with owners and veterinary personnel most at risk.

References:

1. Shukla SK. Community-associated methicillin-Resistant *Staphylococcus aureus* and its emerging virulence. *Clin Med & Res* 2005;3:57-60.
2. Cuny C, Kuemmerle J, Stanek C et al. Emergence of MRSA infections in horses in a veterinary hospital: strain characterisation and comparison with MRSA from humans. *Eurosurveill* 2006;11:44-47.

P10 Prevalence of Methicillin-Resistant *Staphylococcus aureus* (MRSA) Nasal Colonization in the Adult Intensive Care Unit

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Summary:

Objective: Describe the control measures used to reduce MRSA infections in the adult intensive care unit. **Background:** MRSA infections remain a significant and escalating problem in the adult intensive care unit (ICU). **Methods:** All admissions to the adult ICU were prospectively screened for nasal colonization with MRSA from September 2006 to February 2007 using qualitative assay based on amplification of MRSA DNA by real-time polymerase chain reaction (PCR) followed by fluorogenic target-specific hybridization probes for the detection of the amplified DNA. Positive patients were placed on contact isolation and decolonized with intranasal topical mupirocin. Patients were retested post-mupirocin therapy and contact isolation was discontinued after successful decolonization. **Results:** 95 out of 445 patients (21.3%) were positive for nasal colonization with MRSA. 306 patients (68.8%) were admitted from the emergency department while 139 patients were transferred from non-critical care units. 94.7% of patients were successfully decolonized with intranasal topical mupirocin. Five patients who failed decolonization progressed to infection. 11 of 504 patients were infected with MRSA during the six month study period compared to 21 of 474 patients from September 2005 to February 2006 ($p < 0.05$). **Conclusions:** MRSA screening for nasal colonization at the time of admission to the adult ICU using PCR-based technology is an effective tool in identifying colonized patients at risk for MRSA infections and in preventing transmission to other patients.

References:

1. Harbarth S, Masuet C, Schrenzel J, et al. Evaluation of rapid screening and preemptive contact isolation for detecting and controlling MRSA in critical care: an interventional cohort study. *Critical Care* 2006;10:1-8.
2. Davis KA, Stewart JJ, Crouch HK et al. MRSA nares colonization at hospital admission and its effect on subsequent MRSA infection. *Clin Infect Dis* 2004;39:776-782.

P11 Rapid Multidrug-Resistance Profiling and Characterization of *Mycobacterium tuberculosis*

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Summary:

Recent outbreaks of multidrug-resistant tuberculosis underline the urgent need for new resistance-profiling methods that would allow for timely determination of proper treatment. To rapidly analyze large numbers of samples and obtain resolving power approximating sequence-based methods, we have developed the Ibis T5000 technology, where PCR amplicons are analyzed by electrospray ionization mass spectrometry (ESI-MS) and base composition determination. Using the T5000 platform, we developed an *M. tuberculosis* assay that scrutinizes mutations associated with resistance to rifampin, isoniazid, ethambutol, pyrazinamide, streptomycin and fluoroquinolone. In addition, several silent mutations disseminated throughout the *M. tuberculosis* genome are simultaneously queried in order to discriminate the different species of the *M. tuberculosis* complex, down to the nine *M. tuberculosis* SNP-based clusters. The assay was tested using 36 diverse strains from the Public Health Research Institute. We found that a 24-primer pair scheme, which can be multiplexed into eight PCR reactions, can characterize an isolate into the appropriate subtype and provide the essential drug resistance profiling needed for prescribing the correct drugs and understanding the epidemiology of an outbreak.

References:

1. Ecker DJ et al. The Ibis T5000 universal biosensor: an automated platform for pathogen identification and strain typing. *J Assoc Lab Autom* 2006; 11:341-351
2. Mathema B, Kurepina NE, Bifani PJ & Kreiswirth BN. Molecular epidemiology of tuberculosis: current insights. *Clin Microbiol Rev* 2006; 19:658-685

P12 Oral *Candida* Isolates In Radiotherapy/Chemotherapy Patients: Emerging Epidemiological, Virulence and Antifungal Resistance Patterns

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Summary:

Objectives: To study the oropharyngeal carriage of *Candida* species in 50 cancer patients undergoing radiotherapy/chemotherapy, to determine the in vitro susceptibility of yeast isolates to the commonly used antifungal agents by disc diffusion method and to study the pathogenicity by testing for virulence mechanisms. **Methods:** 50 random patients with cancers undergoing radio/chemotherapy at Lok Nayak Hospital, New Delhi, were selected for the study. After identifying *Candida* species, antifungal susceptibility testing was done by the disc diffusion method on Mueller Hinton agar with 2% glucose and 0.5 ug Methylene Blue. Virulence mechanisms were tested for using the microtiter plate method for testing biofilms. **Results:** *Candida* species were isolated in 68% of the patients, out of which 32% were *C.tropicalis*, 29% were *C.albicans*, 21% were *C.intermedia*, 8% were *C.guilliermondi*, 6% were *C.pseudotropicalis* and 1% were *C.parapsilosis*. Tests for susceptibility against 3 anti fungal drugs - fluconazole, itraconazole and clotrimazole revealed that 30% of *C.tropicalis* strains were resistant to fluconazole while 50% were resistant to itraconazole and 60% to clotrimazole. *C.albicans* strains showed a relatively lower resistance, with 23%, 33% and 65% strains resistant to fluconazole, itraconazole and clotrimazole respectively. Adherence assay revealed that increased adherence

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was shown by 55% of the test strains with *C. tropicalis* showing the highest (72%) amount of adherence. **Conclusions:** Non albicans *Candida species* predominated which showed a higher degree of resistance to anti fungal agents and increased virulence as well. This calls for appropriate mycological surveillance and susceptibility testing in such patients and appropriate guidelines for starting antifungal drugs to reduce morbidity should be initiated

References:

1. Bagg J, Sweeney MP, Lewis MA, Jackson MS, et al. High prevalence of non albicans yeasts and detection of anti fungal resistance in oral flora of patients with advanced cancer. *Palliat Med* 2003;17(6):477-41
2. Matar MJ, Zeichner L, Paetznick VL et al. Correlation between E-test, disk diffusion and microdilution methods for antifungal susceptibility testing of fluconazole and voriconazole. *Antimicrob Agents Chemother* 2003;1647-1651.

P13 Epidemiology and Risk Factors for Extended-Spectrum β -lactamase-Producing Organisms: A Case Control Study at a VA Hospital

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Summary:

Objective: Discuss the epidemiology, prevention, and treatment of extended-spectrum B-lactamase-producing *Escherichia coli* and *Klebsiella sp.* infections. **Background:** Antimicrobial resistance is a grave issue in healthcare. We investigated an increase of extended-spectrum B-lactamase-producing (ESBL) producing *Escherichia coli* (EC) and *Klebsiella sp.* (KS) infections at our VA hospital. **Methods:** A case-control study was conducted to identify risk factors. All patients (inpatient or outpatient) who had a clinical culture result positive for EC or KS during September 1, 2005 through October 30, 2006 were eligible for inclusion. All patients with ESBL-EC or KS were designated as case patients. A random sample of patients with EC isolates that did not meet criteria for ESBL were designated as control patients. Univariate analysis was undertaken using Chi-square and Fishers exact tests. **Results:** 21 patients were cases and 138 were selected as controls. Most isolates were from the urinary tract. Only 46 were inpatients at the time of the positive culture, among these nine were transfers from an outside institution. In univariate analysis, transfer from an outside facility was associated with an eight fold greater risk of an ESBL positive culture (OR 8.2, 95% CI 1.4-46.3), as was antibiotic use in the last 30 days (OR 3.1, 95% CI 3.1-9.3). Fluoroquinolone resistance was five fold more likely in ESBL isolates than in susceptible *E coli* or *K. pneumoniae*. Aminoglycoside resistance and trimethoprim-sulfamethoxazole was also five-fold more likely in ESBL producing isolates. Of the 99 patients who were empirically treated, the majority received fluoroquinolones. **Conclusions:** Inter-institutional transfer is a major risk factor for ESBL producing EC or KS. Prompt institution of isolation precautions for inter-institutional transfers may reduce the risk of horizontal spread.

References:

1. Hyle EP, Lipworth AD, Zaoutis TE, et al. Risk factors for increasing multi-drug resistance among extended-spectrum B-lactamase-producing *escherichia coli* and *klebsiella species*. *Clin Infect Dis* 2005;40:1317-1324.
2. Paterson DL, Ko WC, Von Gottberg A, et al. International prospective study of *klebsiella pneumoniae* bacteremia: implications of extended-spectrum beta-lactamase-production in nosocomial infections. *Ann Intern Med* 2004;140:26-32.

P14 Enterococci Isolates from the Community Resistant to Antimicrobial Agents Used for Treatment of Enterococcal Infections

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Summary:

Objective: Discuss the epidemiology of antimicrobial resistant enterococci from the community. **Background:** Antimicrobial agents used for treatment of enterococci infections include vancomycin, gentamicin, and quinupristin-dalfopristin (Q/D). We report the susceptibility profiles to these agents of community enterococci. **Methods:** Stool samples were collected from outpatients with diarrhea who reported no overnight hospitalization in the two weeks before collection. Three sites (MD, MI, and MN) collected 10-20 stool specimens per month from 2004-2005. Samples were cultured on non-selective Enterococcosel media. From each stool sample, one enterococcus isolate was sent to CDC and tested for antimicrobial susceptibility by broth microdilution. Participants were asked questions concerning antimicrobial use, healthcare exposure (hospitalization, or residence in a nursing home, or assisted living facility), and international travel in the six months before stool collection. **Results:** From 2004-2005, 723 stools were collected, and 570 (78.8%) yielded enterococci. Of the 570 patients, 352 (49.2%) reported no healthcare exposure in the six months before stool collection. One (0.3%) enterococcus isolate was vancomycin resistant *E. faecium* (VRE). Five (1.4%) enterococci isolates were high-level gentamicin resistant *E. faecalis* (HLGRE). No *E. faecium* isolates were resistant to Q/D. **Conclusion:** Enterococci isolated from community stool samples were resistant to antimicrobial agents used for treatment of enterococcal infections of persons with no history of healthcare exposure. This may indicate acquisition of these bacteria from community sources. It will be important to understand and identify these sources especially as they relate to the acquisition and transfer of resistance of newly approved and critical antimicrobial agents among commensal bacteria.

References:

1. Centers for Disease Control and Prevention. Nosocomial enterococci resistant to vancomycin: United States, 1989-1993. *MMWR* 1993;42:597-599.
2. McDonald LC, Rossiter S., Mackinson C. Quinupristin-dalfopristin-resistant Enterococcus Faecium on chicken and in human stool specimens. *NEJM* 2001;345:1155-1160.
3. Schaberg DR, Culver DH, Gaynes RP. Major trends in the microbial etiology of nosocomial infection. *Am J Med* 1991;91(Suppl 3B):72-75.

P15 Salmonella Genomic Island 1 (SGI1) is Common Among Human Multidrug-Resistant (ACSSuT) Salmonella Isolates tested in NARMS in the United States, 1996-2005

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Summary:

Objective: Evaluate the presence of Salmonella Genomic Island 1 among multidrug-resistant Salmonella isolated from humans in the United States. **Background:** The National Antimicrobial Resistance Monitoring System (NARMS) monitors antimicrobial susceptibility among *Salmonella* collected from humans in the US. Resistance to ampicillin, chloramphenicol, streptomycin, sulfamethoxazole, and tetracycline (ACSSuT) is commonly found in serotype Typhimurium, particularly Definitive Type 104 (DT104), and is associated with higher hospitalization rates than non-ACSSuT Typhimurium infections; ACSSuT has also been found in at least 30 other serotypes. In Typhimurium DT104, *Salmonella* Genomic Island 1 (SGI1) is a 43-kb

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chromosomal region that harbors the genes conferring ACSSuT resistance. Since its discovery, SGII, or some variation, has been detected in other *Salmonella* serotypes, which raises public health concern about resistance gene mobilization. **Methods:** Minimum inhibitory concentrations were determined for antimicrobial agents, including ACSSuT, using broth microdilution (Sensititre®). At least one ACSSuT isolate from all serotypes with ACSSuT was selected for SGII screening, using polymerase chain to amplify the characteristic left and right junctions (+/- retron) of SGII and associated resistance genes. **Results:** Fifty-eight isolates representing 30 serotypes were selected; 18 (31%) were positive for SGII. These 18 isolates included 10 serotypes, or variants thereof: Agona, Derby, Dublin, Hadar, Heidelberg, Paratyphi B, Paratyphi B var. L(+) tartrate-positive, Saintpaul, Subspecies I 4,[5],12:-I-, and Subspecies I 4,[5],12:-:1,2. Thirteen (72%) of these 18 isolates with SGII possessed some portion of the retron sequence. **Conclusion:** SGII is common among human multidrug-resistant *Salmonella* isolates of different serotypes, supporting frequent horizontal transfer of SGII and its associated resistant genes among salmonellae. Further studies are needed to understand the public health implications of this frequent horizontal transfer.

References:

1. Levings RS, Lightfoot D, Partridge SR, et al. The genomic island SGII, containing the multiple antibiotic resistance region of *Salmonella enterica* serovar Typhimurium DT104 or variants of it, is widely distributed in other *S. enterica* serovars. *J Bacteriol* 2005;187:4401-4409.
2. Martin LJ, Fyfe M, Dore K, et al. Increased burden of illness associated with antimicrobial-resistant *Salmonella enterica* serotype Typhimurium infections. *J Infect Dis* 2004;189:377-384.

P16 Emerging Resistance to Third-Generation Cephalosporins in *Salmonella* Serotype Heidelberg, NARMS, 1996-2005

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Summary:

Objective: Discuss emerging resistance to third-generation cephalosporins in *Salmonella* serotype Heidelberg isolates submitted to NARMS from 1996-2005. **Background:** Non-Typhi *Salmonella* (NTS) is a leading cause of bacterial foodborne illness in the United States. Antimicrobial agents, such as third-generation cephalosporins, are essential to treat invasive human infections. Use of antimicrobial agents in food animals contributes to resistance in NTS. *Salmonella* Heidelberg is a leading NTS serotype among human isolates in the National Antimicrobial Resistance Monitoring System (NARMS). Resistance to ceftriaxone, amoxicillin-clavulanate and ceftiofur, a third-generation cephalosporin used in food animals, has been linked to a plasmid-encoded AmpC-like β -lactamase, CMY-2, in the United States. **Methods:** Since 1996, participating sites submitted NTS isolates to NARMS for susceptibility testing. Participation increased from 14 sites in 1996 to nationwide in 2003. Minimum inhibitory concentrations (MICs) were determined by broth microdilution and interpreted using CLSI criteria when available. Ceftiofur resistance was defined as MIC \geq 8 μ g/mL. **Results:** From 1996-2005, 931 (6%) of 16,065 NTS isolates were serotype Heidelberg. Of 931 Heidelberg isolates, 40 were ceftiofur-resistant and 47 were amoxicillin-clavulanate-resistant. Ceftiofur resistance increased from 1% in 1996 to 9% in 2005. Amoxicillin-clavulanate resistance increased from 3% in 1996 to 9% in 2005. Ceftiofur-resistant isolates were more likely than susceptible isolates to be resistant to amoxicillin-clavulanate: all 40 ceftiofur-resistant but only seven (1%) among susceptible isolates showed amoxicillin-clavulanate resistance. **Conclusions:** Since 1996, ceftiofur resistance has increased among *Salmonella* Heidelberg in NARMS. Ceftiofur-resistant Heidelberg isolates are likely to also be resistant to amoxicillin-

clavulanate. Further work is needed to determine whether dissemination of plasmids among NTS or pressure from antibiotic use in food animals could be contributing to this emergence. Detection of emerging resistance is important for guiding public health interventions.

References:

1. Carattoli A, Tosini F, Giles WP, et al. Characterization of plasmids carrying CMY-2 from expanded-spectrum cephalosporin-resistant *Salmonella* strains isolated in the United States between 1996 and 1998. *Antimicrob Agents Chemother* 2002;46(5):1269-1272.
2. Alcaine SD, Sukhnanand SS, Warnick LD, et al. Ceftiofur-resistant *Salmonella* strains isolated from dairy farms represent multiple widely distributed subtypes that evolved by independent horizontal gene transfer. *Antimicrob Agents Chemother* 2005;49(10):4061-7.

P17 Toxin-Gene Variant Strains Of *Clostridium difficile* In a Community Hospital

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Summary:

Objective: Review severe fatal *Clostridium difficile* colitis due to toxin-gene variant strain is reported from a community hospital. **Background:** *Clostridium difficile* (*C. diff*) is emerging as a major threat worldwide as the leading cause of infectious diarrhea. The increasing rate and severity of *C. diff* colitis may be associated with the emergence of a new epidemic strain with increased virulence and resistance. In this study an outbreak of *C. diff* colitis with variations in toxin-gene is reported from a community hospital. **Methods:** Five hundred and twenty eight stool samples were tested for *C. diff* toxin from patients admitted to the Columbia Memorial Hospital, a 192-bed community hospital in Upstate New York, from January 1 to December 31, 2006. *C. diff* toxin A and/or B was detected using enzyme immunoassays according to the manufacturer's instructions. Seventy-eight patients had positive results. Elderly patients (>60 years) accounted for 87% of all infections. Seventy-nine percent of all patients had received one or more antibiotics prior to their illness. Ten patients (12.82%) had severe disease and succumbed to their illness. Three isolates from these patients were tested for partial deletions of the *tcdC* gene according to the methods of Gonçalves et al. **Results:** The three isolates associated with severe disease and fatal outcome were positive for a deletion in the pathogenicity locus gene *tcdC*. This might result in increased production of toxins A & B and explain severity of the disease and fatal outcome. **Conclusions:** Severe fatal colitis has emerged as a cause of geographically dispersed *C. diff* associated disease affecting even a community hospital.

References:

1. McDonald LC, Killgore GE, Thompson A, et al. An epidemic, toxin gene-variant strain of *Clostridium difficile*. *N Engl J Med* 2005;353: 2433-2441.
2. Gonçalves C, Decre D, Barbut F, Burghoffer B, Petit JC. Prevalence and characterization of a binary toxin (actin-specific ADPribosyltransferase) from *Clostridium difficile*. *J Clin Microbiol* 2004;42:1933-1939.

ABSTRACTS OF SUBMITTED POSTER PRESENTATIONS

P18 Comparison of PCR and EVIGENE™ for Detection of Methicillin Resistance in Staphylococcal Isolates from Nasal Swabs

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Summary:

Objective: Discuss EVIGENE as an alternative to PCR to obtain a genotypic detection of MRSA. **Background:** Methicillin-resistant (MR) *Staphylococcus aureus* (SA) strains have increased steadily, and nosocomial and community acquired infections have become a serious problem worldwide. Many strains are heterogeneous in their phenotypic expression of methicillin resistance, which makes detection of MRSA by conventional susceptibility testing methods difficult. Tests based on the detection of the *mecA* gene is therefore considered the "gold standard" for methicillin resistance and will correctly identify heterogeneous and borderline resistant *S. aureus* (BORSA) strains as MRSA and methicillin-susceptible (MSSA), respectively. **Methods:** In this study we compared EVIGENE™ (AdvanDx) and an in-house PCR method by analyzing 197 SA and coagulase-negative staphylococci (CNS) isolates from nasal swabs for the *mecA* gene as well as the SA-specific nuclease (*nuc*) gene. The isolates were previously characterized by conventional methods and comprised 68 MRSA, 56 MSSA, 31 MR-CNS, 34 MS-CNS and 8 BORSA. **Results:** Both EVIGENE™ and PCR correctly identified 100% (68/68) MRSA, 98% (55/56) MSSA, 100% (34/34) MS-CNS and 100% (8/8) BORSA, whereas EVIGENE™ and PCR correctly identified 81% (25/31) and 77% (24/31), respectively, as MR-CNS. **Conclusion:** Genotypic detection of drug resistance is becoming an important component of the diagnostic inventory of routine diagnostic laboratories. The EVIGENE™ procedure was developed to fit into the daily work pattern of a routine clinical laboratory because it does not require specialized instruments other than an incubator and a plate shaker. In conclusion, this study has shown that the EVIGENE™ correctly identified all MRSA strains and the method is therefore a good alternative to PCR in a routine clinical laboratory to obtain a genotypic detection of MRSA.

Reference:

1. Poulsen AB, Skov R, Pallesen LV. Detection of methicillin resistance in coagulase-negative staphylococci and in staphylococci directly from simulated blood cultures using the EVIGENE MRSA Detection Kit. *J Antimicrob Chemother.* 2003;51:419-421.

P19 A Comparative Study On The Antimicrobial Activity of Meropenem and Other Anti-infective Agents

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Summary:

Increasing and sometimes inappropriate antibiotic therapy has resulted in a greater incidence of resistant bacteria and thus the need to develop newer antibiotics. Any new antibiotic should have a distinct advantage in the spectrum of efficacy and the tolerability profile. The antibacterial efficacy of Meropenem was compared with amikacin, ceftazidime, cefpirome, cefoperazone/sulbactam, imipenem, ofloxacin and piperacilin/tazobactam. Two-hundred bacterial isolates comprising up to 100 aerobic gram positive bacteria and up to 100 aerobic gram negative bacteria, were speciated and tested for their susceptibility pattern. The isolates were all resistant to commonly used first line drugs and not more than 10% of the total isolates were from the same species. Bacteria known to be resistant to meropenem like methicillin resistant staphylococci, *Enterococcus faecium*, *Stenotrophomonas maltophilia* were excluded. Quality control strain replicates were included. Every clinical sample tested was compiled in a case record form that included patient particulars, diagnosis, the type of sample and

the site of collection. Samples included pus, wound swabs, bronchoalveolar lavage fluid, blood cultures and urine specimen. Kirby-Bauer method as active recommended by NCCLS was followed. Meropenem was the only drug 12% of the isolates. Eight percent of the strains, mostly *Pseudomonas* species, were resistant to Meropenem. Imipenem and Piperazillin/Tazobactam was sensitive in 2% and 6% of cases where Meropenem was resistant. Piperazillin/Tazobactam was found to be better for Pseudomonas infections. The spectrum of activity of Amikacin was found to be better than the cephalosporins. The major advantage of Meropenem is its wide spectrum activity in polymicrobial infections encompassing both gram positive and gram negative organisms.

Reference:

1. Wiseman LR, Wagstaff AJ, Brogden RN, Bryson HM. Meropenem: A review of its antibacterial activity. *Pharmacokinetic Properties and Clinical Efficacy Drugs* 1995;50(1):73-101.

P20 Synergy Testing for Highly-resistant Acinetobacter Baumannii Isolates

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Summary:

Treatment options for *Acinetobacter baumannii*(AB) infections are limited. For carbapenem-resistant isolates, most use polymyxin B (PB) or combinations based on limited data. We tested a panel of 33 AB [27 multi-resistant (Table2) + 6 pan-susceptible] isolates against IP, AK, and non-traditional drugs, [PB, rifampin(RF), azithromycin(AZ), doxycycline(DX), and tigecycline(TG)], and screened for synergistic combinations. MICs were measured by E-test. CLSI MICs were used except for RF, AZ, and TG (manufacturer's MICs). Crossed E-test methodology was used to test for synergy (13 two-drug combinations per isolate). FIC and FIC Indices were calculated. An index of ≤ 0.5 was considered synergy and reconciled for clinical significance (change in MIC from resistant to sensitive). For single drug tests [% Sensitive isolates]: PB[100% MIC 0.75-1.5]; AZ[9% MIC<2.0]; RF[3%]; DX[57%]; TG[83%, MIC<8, 23% MIC ≤ 2].

Table 1 shows synergy data. Our data supports that: 1)PB TG and DX are useful MAR AB drugs 2)No synergy between PB and other drugs 3)Synergy between drugs infrequent 4)Clinically significant synergy suggested for four combinations IP+TG, IP+AZ, IP+DX and TG+AZ 5)No antagonism observed

Antibiotic Combination Exhibiting Synergy for 10% or More Isolates	
Antibiotic Combination	FIC Index ≤ 0.5 (% of isolates)
Imipenem + Azithromycin	18%
Imipenem + Doxycycline	18%
Imipenem + Tigecycline	20%
Tigecycline + Azithromycin	10%

MAR Acinetobacter baumannii Isolates	
Antibiotic Susceptibilities	Number of Isolates
Imipenem (R)	
Amikacin (R)	5
Imipenem (R)	
Amikacin (I)	4
Imipenem (R)	
Amikacin (S)	17
Imipenem (S)	
Amikacin (S)	
Ampicillin/Sulbactam (S)	1

ABSTRACTS OF SUBMITTED POSTER PRESENTATIONS

References:

1. White RL, Burgess DS, Manduru M, Bosso JA. Comparison of three different in vitro methods of detecting synergy: time-kill, checkerboard, and E test. *Antimicrob Agents Chemother.* 1996;40:1914-1918.
2. Timurkaynak F, et al. *In vitro* activities of non-traditional antimicrobials alone or in combination against multidrug-resistant strains of *Pseudomonas aeruginosa* and *Acinetobacter baumannii*. *Int J Antimicrob Agents* 2006;27

P21 Comparative In Vitro Susceptibility of Tigecycline and Polymyxin B for Resistant *Klebsiella* and *Acinetobacter* Isolates

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Summary:

Objective: We compared the MIC's of tigecycline and polymyxin B for resistant *Klebsiella* and *Acinetobacter*, sensitive to less than or equal to three classes of antibiotics. **Background:** The emergence of multi-drug resistant gram negative organisms and the lack of novel antibiotics led to the revival of polymyxin B. Then, tigecycline was approved in 2005. We decided to compare them to see if we could use tigecycline for our resistant *Klebsiella* and *Acinetobacter* isolates. **Methods:** Minimum inhibitory concentration's (MIC's) for tigecycline and polymyxin B were recorded using E-test (AB Biodisk, Solna, Sweden) for resistant *Klebsiella* and *Acinetobacter*. MIC's of less than or equal to two mg/l was considered susceptible. Only one isolate per patient was included. Isolates were obtained from blood, urine, respiratory, catheter tip and tissue specimens. **Results:** We identified 96 isolates of *Klebsiella* and 50 isolates of *Acinetobacter* for analysis. The average MIC of *Klebsiella* isolates for polymyxin B was 1.19 mg/l and for tigecycline was 1.12 mg/l. The average MIC of *Acinetobacter* isolates was 0.68 mg/l for polymyxin B and 2.19 mg/l for tigecycline. Greatest difference was found in pan-resistant isolates of *Acinetobacter*, average MIC's for polymyxin B was 0.6 mg/l and for tigecycline was 5.15 mg/l. **Conclusions:** The *in vitro* activity of tigecycline against *Klebsiella*, particularly pan-resistant isolates, is comparable with polymyxin B and can be used in situations where polymyxin B is relatively contraindicated. We will be cautious in using tigecycline for multidrug resistant *Acinetobacter*, as average MIC's are higher for tigecycline than for polymyxin B.

Reference:

1. Souli M, Kontopidou FV, et al. In vitro activity of tigecycline against multiple-drug-resistant, including pan-resistant, gram-negative and gram-positive clinical isolates from Greek hospitals. *Antimicrob Agents Chemother* 2006;50:3166-3169.

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