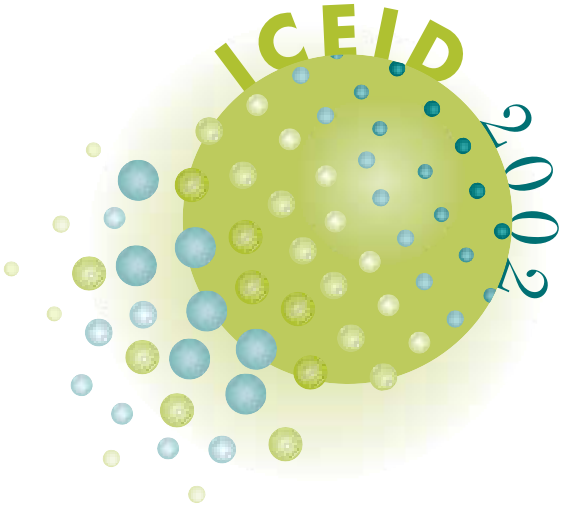
March 24 – 27, 2002

Hyatt Regency

Atlanta, Georgia, USA



International Conference on Emerging Infectious Diseases 2002

- *Which infectious diseases are emerging?*
- *Whom are they affecting?*
- *Why are they emerging now?*
- *What can we do to prevent and control them?*

www.cdc.gov/iceid

Program *and* Abstracts Book

PHL

CDC

AMERICAN SOCIETY FOR MICROBIOLOGY

Council of State and Territorial Epidemiologists

CDC FOUNDATION

FUNDING *Partners*

The organizers and cosponsors of the 2002 International Conference on Emerging Infectious Diseases wish to thank the following Funding Partners for their financial support of the conference:

Corporate and Non-Profit:

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Centers for Disease Control and Prevention
National Institutes of Health
- National Institute of Allergy and Infectious Diseases
- Fogarty International Center

Food and Drug Administration
United States Agency for International Development
United States Department of Defense
- Global Emerging Infections System

Goal:

To bring together colleagues to share the latest information about emerging infectious diseases, to build relationships, and plan the next steps in disease surveillance, response, research and prevention strategies.

Objectives:

1. Exchange scientific information on emerging infectious disease issues in the United States and other countries.
2. Discuss programs and activities that have been implemented to address emerging infectious disease threats.
3. Identify program gaps that need to be addressed.
4. Increase awareness in the public health and scientific communities of issues relating to emerging infectious diseases.
5. Encourage and enhance partnerships to address emerging infectious diseases.

Prerequisite Skills and Knowledge:

Participants should have a medical/science background. Participants may be researchers, clinicians, laboratorians, veterinarians, and other health professionals.

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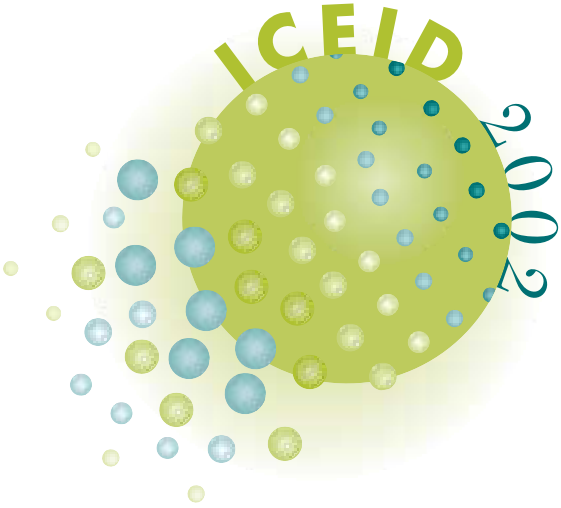

International Conference on Emerging Infectious Diseases 2002

Organized by
the Centers for Disease Control and Prevention (CDC),
the Council of State and Territorial Epidemiologists (CSTE),
the CDC Foundation (CDCF),
the Association for Public Health Laboratories (APHL),
and the World Health Organization (WHO)
The American Society for Microbiology (ASM)

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Emory University School of Medicine, Division of Infectious Diseases
Fogarty International Center
Food and Drug Administration
ILSA N.A. Technical Committee on Food Microbiology
International Society for Infectious Diseases
International Union of Microbiological Societies
National Association of County and City Health Officials
National Foundation for Infectious Diseases
National Institute of Allergy and Infectious Diseases
Pan American Health Organization
The Robert Wood Johnson Foundation
Rollins School of Public Health at Emory University
U.S. Agency for International Development
U.S. Department of Defense, Global Emerging Infections System
The World Bank

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continued on next page

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Regency Ballroom V

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Centennial Ballroom I

34 **Vectorborne Diseases I**
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35 **Molecular Diagnostics and Epidemiology I**
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36 **Latebreakers I**
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37 **Smallpox Response**
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Centennial Ballroom III

GENERAL INFORMATION

Americans with Disabilities Act Compliance

The Hyatt Regency Atlanta is in compliance with the Americans with Disabilities Act to the extent of the law. If special accommodations would enhance your enjoyment of the conference, please visit the Headquarters Office on the Ballroom Level. We will make all reasonable accommodations to ensure your comfort at the meeting.

Audiotapes

Audiotapes of most invited oral sessions will be available for purchase in the Ballroom Level Lobby of the Hyatt. Please consult your Program Addendum for a complete list of sessions available for sale.

Business Center

Executive Express/Business Center is located in the Main Lobby of the Hyatt Regency Atlanta. Hours are posted.

Continuing Education Instructions for Physicians, Nurses, Health Educators, Laboratorians, and Others

All conference participants are eligible for Continuing Education credit. Award is contingent upon completion of an evaluation for every session for which you are requesting Continuing Education and completion of the Overall Conference Evaluation.

Continuing Education credits provided:

Continuing Nursing Education (CNE)

Continuing Medical Education (CME) for physicians and nonphysicians

Continuing Education Units (CEU) available for other professions

Certified Health Education Specialist (CHES) for health educators

Continuing Medical Education (CME)
This activity has been planned and implemented in accordance with the Essential Areas and policies of the Accreditation Council for Continuing Education (ACCME) through the joint sponsorship of Centers for Disease Control and Prevention (CDC) and the Association for Public Health Laboratories (APHL) and the Council for State and Territorial Epidemiologists (CSTE). CDC is accredited by the ACCME to provide continuing medical education for physicians and takes responsibility for the content, quality, and scientific integrity of this CME activity.

CDC designates this educational activity for a maximum of 20 hours in category 1 credit towards the AMA Physician's Recognition Award. Each physician should claim only those hours of credit that he/she actually spent in the educational activity.

Continuing Nursing Education (CNE)
This activity for 24 contact hours is provided by CDC, which is accredited as a provider of continuing education in nursing by the American Nurses Credentialing Center's Commission on Accreditation.

Continuing Education Units (CEU)
CDC awards 2.0 Continuing Education Units (CEUs). CDC is an authorized CEU Sponsor of the International Association for Continuing Education and Training.

Certified Health Education Specialist (CHES)
CDC has been designated as a provider of continuing education contact hours in health education by the National Commission for Health Education Credentialing, Inc. This conference is a designated event and has been approved for 20 Category 1 Continuing Education Contact Hours (CECH) for Certified Health Education Specialist.

Attendance Record and Certificate
Attendees will have two methods for recording ICEID session attendance and generating their CE Attendance Record.

- You may generate your CE Attendance Record on-site by visiting the Cyber Café in the Hanover Room.
- You may generate your CE Attendance Record on-line until June 1, 2002, by visiting www.cdc.gov/iceid .

Exhibits

Exhibits will be held in the Grand Hall East (Exhibit Level) of the Hyatt Regency on Sunday, March 24 through Tuesday, March 26. Don't miss the Opening Reception with food, drink, and camaraderie on Sunday, March 24, following the Opening Session. Additional Exhibit Hall hours are from 12:00 noon to 5:00 p.m. on Sunday, March 24, 10:00 a.m. to 6:00 p.m. on Monday, March 25, and 8:30 a.m. to 1:00 p.m. on Tuesday, March 26.

Headquarters Office

The ICEID Headquarters Office, located on the Ballroom Level, will be open and staffed during registration hours. Feel free to come to us with questions or concerns.

Cyber Café

The CDC is providing internet access for your convenience during registration hours in the Hanover Room.

Presentations Available Online

You will be able to hear the audio and see the slides of selected plenary, invited panel, and slide sessions on the Web (www.cdc.gov/iceid) beginning April 1, 2002. You may receive continuing education credits by watching presentations on line at www.cdc.gov/iceid.

Press Room

Press representatives are welcome at the ICEID. Please check in at the Press Room, located in the Fairlie Room.

Program Addendum

In addition to this program, registrants receive a Program Addendum, which incorporates all Late-Breaker Abstracts, additions to the Program, and changes made after this Program went to press.

Registration

To maintain the quality and size of the conference to ensure meaningful scientific exchange, registration at the ICEID is limited to 2,500 attendees. On-site registration is only available if fewer than 2,500 individuals preregister. Registration will be open during the following times to answer your questions and provide information on the meeting and Atlanta:

Sunday, March 24 . . . . . 12:00 noon – 5:30 p.m.
Monday, March 25 . . . . . 8:00 a.m. – 6:00 p.m.
Tuesday, March 26 . . . . . 8:00 a.m. – 6:00 p.m.
Wednesday, March 27 . . . . . 8:00 a.m. – 12:00 noon

Speaker Ready Room

Speakers may preview materials in the Speaker Ready Room, located in the Greenbriar Room. The room is open during registration hours Sunday, Monday, and Tuesday. Speakers should come by the Speaker Ready Room at their earliest convenience to ensure presentations are in order.

Professional audiovisual consultants will be available for assistance. Both Mac and PC platforms will be available. Presenters will have the opportunity to review, update, or make changes on computers in the Speaker Ready Room. Presenters using PowerPoint must visit the Speaker Ready Room at least 30 minutes prior to their session in order to upload their presentation.

Slide trays and caramates will be available for those presenters not using PowerPoint. Also provided will be blank labels to write name, and session number to identify your slide carousel. Speakers using slides should take their labeled slide carousel to the projectionist stationed in the session room.

Verification of Attendance

Conference attendees requiring a letter verifying their attendance should visit the Headquarters Office during registration hours. We will be happy to provide you with the needed documentation.

SATELLITE PARTNERSHIP **MEETINGS**

Saturday, March 23

8:00 a.m. – 4:30 p.m.

Southern Cone and Amazon Network Surveillance Meeting on Emerging/Reemerging Infectious Diseases
Contact: Eric Mintz
Room:Courtland

Sunday, March 24

8:00 a.m. – 4:30 p.m.

Southern Cone and Amazon Network Surveillance Meeting on Emerging/Reemerging Infectious Diseases
Contact: Eric Mintz
Room:Courtland

9:00 a.m. – 12:00 noon

Pandemic Planning Discussion
Contact: Ann Moen
Room: Baker

12:00 noon – 4:00 p.m.

Asia Pacific Economic Cooperation
Infectious Disease Strategy Discussion
Contact: Melinda Moore
Room: Auburn

12:00 noon – 5:00 p.m.

Biothreat Reduction Meeting
Contact: Chris Robinson
Room: Chicago CD

Monday, March 25

5:30 p.m. – 7:30 p.m.

DTRA Reception
Opportunities for U.S. Scientists with Defense Threat Reduction Agency's Cooperative Biodefense Research Program.
Contact: Caroline Saum
Room: Courtland

6:00 p.m. – 9:00 p.m.

WHO Global Salm-Surv Meeting (open)
Contact: Beth Imhoff
Room: Chicago AB

7:00 p.m. – 9:00 p.m.

IOM Report on Microbial Threats to Health
Contact: Mark Smolinsky
Room: Regency Ballroom V

Tuesday, March 26

6:00 p.m. – 9:00 p.m.

International Food-Net Meeting
Contact: Malinda Kennedy
Room: Chicago AB

Sunday, March 24

Session 1

Poster Session

Bioterrorism

Sunday, March 24, 12:00 noon – 5:00 p.m.; Authors present 3:30 p.m. – 5:00 p.m.

Grand Hall East

For a complete listing of poster titles and abstracts, see pages 31-35.

Session 2

Poster Session

Tuberculosis

Sunday, March 24, 12:00 noon – 5:00 p.m.; Authors present 3:30 p.m. – 5:00 p.m.

Grand Hall East

For a complete listing of poster titles and abstracts, see pages 35-36.

Session 3

Poster Session

Disease Eradication

Sunday, March 24, 12:00 noon – 5:00 p.m.; Authors present 3:30 p.m. – 5:00 p.m.

Grand Hall East

For a complete listing of poster titles and abstracts, see pages 36-37.

Session 4

Poster Session

Emerging Nosocomial Infections

Sunday, March 24, 12:00 noon – 5:00 p.m.; Authors present 3:30 p.m. – 5:00 p.m.

Grand Hall East

For a complete listing of poster titles and abstracts, see pages 37-40.

Session 5

Poster Session

Waterborne Infections I

Sunday, March 24, 12:00 noon – 5:00 p.m.; Authors present 3:30 p.m. – 5:00 p.m.

Grand Hall East

For a complete listing of poster titles and abstracts, see pages 40-42.

Session 6

Poster Session

Emerging Zoonoses I

Sunday, March 24, 12:00 noon – 5:00 p.m.; Authors present 3:30 p.m. – 5:00 p.m.

Grand Hall East

For a complete listing of poster titles and abstracts, see pages 42-47.

Session 7

Poster Session

Evolutionary Potential of Viruses

Sunday, March 24, 12:00 noon – 5:00 p.m.; Authors present 3:30 p.m. – 5:00 p.m.

Grand Hall East

For a complete listing of poster titles and abstracts, see page 48.

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Poster Session

Food Safety I

Sunday, March 24, 12:00 noon – 5:00 p.m.; Authors present 3:30 p.m. – 5:00 p.m.

Grand Hall East

For a complete listing of poster titles and abstracts, see pages 48-57.

Session 9

Poster Session

GIS and Remote Sensing

Sunday, March 24, 12:00 noon – 5:00 p.m.; Authors present 3:30 p.m. – 5:00 p.m.

Grand Hall East

For a complete listing of poster titles and abstracts, see pages 57-58.

Session 10

Poster Session

Health Department Activities

Sunday, March 24, 12:00 noon – 5:00 p.m.; Authors present 3:30 p.m. – 5:00 p.m.

Grand Hall East

For a complete listing of poster titles and abstracts, see pages 58-59.

Session 11

Poster Session

Infectious Causes of Chronic Diseases

Sunday, March 24, 12:00 noon – 5:00 p.m.; Authors present 3:30 p.m. – 5:00 p.m.

Grand Hall East

For a complete listing of poster titles and abstracts, see pages 60-61.

Session 12

Poster Session

Prevention and Control Programs

Sunday, March 24, 12:00 noon – 5:00 p.m.; Authors present 3:30 p.m. – 5:00 p.m.

Grand Hall East

For a complete listing of poster titles and abstracts, see pages 61-63.

Session 13

Poster Session

Surveillance and Information Systems Technology

Sunday, March 24, 12:00 noon – 5:00 p.m.; Authors present 3:30 p.m. – 5:00 p.m.

Grand Hall East

For a complete listing of poster titles and abstracts, see pages 63-68.

Session 14

ICEID 2002 Keynote Session

Sunday, March 24, 5:00 p.m. – 7:00 p.m.

Centennial Ballroom

PATTY STONESIFER, Co-chair and President, Bill and Melinda Gates Foundation, Seattle, WA

TOMMY THOMPSON, Secretary, U.S. Department of Health and Human Services, Washington, DC

JOHN H. MARBURGER, Director, White House Office of Science and Technology Policy, Washington, DC

Monday, March 25

Session 15

Meet-the-Experts

Monday, March 25, 7:30 a.m. – 8:15 a.m.

Regency Ballroom VI/VII

Emerging Vectorborne Infections

DUANE GUBLER, CDC, Fort Collins, Co

BARRY BEATY, Colorado State University, Fort Collins, CO

Laboratory Capacity

RAY ARTHUR, World Health Organization, Geneva, Switzerland

Session 16

Plenary Session I

Monday, March 25, 8:30 a.m. – 10:00 a.m.

Centennial Ballroom I/II

Moderators:

CLAIRE BROOME, CDC, Atlanta, GA

RICHARD GUERRANT, University of Virginia Hospital, Charlottesville, VA

Bioterrorism Preparedness: Lessons, Challenges, and Opportunities

JAMES HUGHES, CDC, Atlanta, GA

Emerging and Reemerging STDs

GAIL A. BOLAN, California Department of Health Services, Berkeley, CA

Session 17

Plenary Session II

Monday, March 25, 8:30 a.m. – 10:00 a.m.

Centennial Ballroom III/IV

Moderators:

BRIAN MAHY, CDC, Atlanta, GA

MORRIS POTTER, Food and Drug Administration, Atlanta, GA

The Impact of Infectious Agents on Farming and Human Health

PETER J. WALKER, CSIRO Livestock Industries, Indooroopilly, Australia

The Interface of Animal and Human Health

CORRIE BROWN, College of Veterinary Medicine, University of Georgia, Athens, GA

Session 20

Poster Session

Antimicrobial Resistance I

Monday, March 25, 10:00 a.m. – 6:00 p.m.; Authors present 4:30 p.m. – 6:00 p.m.

Grand Hall East

For a complete listing of poster titles and abstracts, see pages 69-77.

Session 21

Poster Session

Syndromes and Diagnosis I

Monday, March 25, 10:00 a.m. – 6:00 p.m.; Authors present 4:30 p.m. – 6:00 p.m.

Grand Hall East

For a complete listing of poster titles and abstracts, see page 77.

Session 22

Poster Session

Bioterrorism II

Monday, March 25, 10:00 a.m. – 6:00 p.m.; Authors present 4:30 p.m. – 6:00 p.m.

Grand Hall East

For a complete listing of poster titles and abstracts, see pages 77-81.

Session 23

Poster Session

Vectorborne Diseases I

Monday, March 25, 10:00 a.m. – 6:00 p.m.; Authors present 4:30 p.m. – 6:00 p.m.

Grand Hall East

For a complete listing of poster titles and abstracts, see pages 81-83.

Session 24

Poster Session

Waterborne Infections II

Monday, March 25, 10:00 a.m. – 6:00 p.m.; Authors present 4:30 p.m. – 6:00 p.m.

Grand Hall East

For a complete listing of poster titles and abstracts, see page 84.

Session 25

Poster Session

Emerging Opportunistic Infections

Monday, March 25, 10:00 a.m. – 6:00 p.m.; Authors present 4:30 p.m. – 6:00 p.m.

Grand Hall East

For a complete listing of poster titles and abstracts, see pages 84-86.

Session 26

Poster Session

Emerging Aspects of HIV and STDs

Monday, March 25, 10:00 a.m. – 6:00 p.m.; Authors present 4:30 p.m. – 6:00 p.m.

Grand Hall East

For a complete listing of poster titles and abstracts, see pages 86-88.

Session 27

Poster Session

Emerging Zoonoses II

Monday, March 25, 10:00 a.m. – 6:00 p.m.; Authors present 4:30 p.m. – 6:00 p.m.

Grand Hall East

For a complete listing of poster titles and abstracts, see pages 88-93.

Session 28

Poster Session

Food Safety II

Monday, March 25, 10:00 a.m. – 6:00 p.m.; Authors present 4:30 p.m. – 6:00 p.m.

Grand Hall East

For a complete listing of poster titles and abstracts, see pages 93-103.

Session 29

Poster Session

Malaria

Monday, March 25, 10:00 a.m. – 6:00 p.m.; Authors present 4:30 p.m. – 6:00 p.m.

Grand Hall East

For a complete listing of poster titles and abstracts, see pages 103-105.

Session 30

Poster Session

Molecular Epidemiology I

Monday, March 25, 10:00 a.m. – 6:00 p.m.; Authors present 4:30 p.m. – 6:00 p.m.

Grand Hall East

For a complete listing of poster titles and abstracts, see pages 105-108.

Session 31

Poster Session

New or Rapid Diagnostics I

Monday, March 25, 10:00 a.m. – 6:00 p.m.; Authors present 4:30 p.m. – 6:00 p.m.

Grand Hall East

For a complete listing of poster titles and abstracts, see pages 108-109.

Session 32

Poster Session

Environmental Changes

Monday, March 25, 10:00 a.m. – 6:00 p.m.; Authors present 4:30 p.m. – 6:00 p.m.

Grand Hall East

For a complete listing of poster titles and abstracts, see pages 109-110.

Session 33

Slide Session

Foodborne Illness and Antibiotic Resistance

Monday, March 25, 10:30 a.m. – 11:30 a.m.

Centennial Ballroom I

Moderators:
JANET NICHOLSON, CDC, Atlanta, GA
DEBORAH LEVY, CDC, Atlanta, GA

Campylobacter coli – What's the Big Deal?

S. J. O'Brien, G. K. Adak, S. M. Long, I. A. Gillespie, J. A. Frost

Public Health Laboratory Service, London, UNITED KINGDOM

Is Drinking Water a Risk Factor for Endemic Cryptosporidiosis in the Immunocompetent General Population of the San Francisco Bay Area?

A. Khalakdina[1,2,3], D. J. Vugia[2,4], J. Nadle[2], J. M. Colford, Jr.[1,2]

[1]Division of Public Health Biology and Epidemiology, Centers for Family & Community Health and Occupational & Environmental Health, School of Public Health, University of California at Berkeley, Berkeley, CA, [2]California Emerging Infections Program, Oakland, CA, [3]Community Health Epidemiology and Disease Control, San Francisco Department of Public Health, San Francisco, CA, [4]Division of Communicable Disease Control, California Department of Health Services, Berkeley, CA

Washington Clinical Laboratory Initiative – Assessment of Laboratory Practice

J. M. Counts

University of Washington, Seattle, WA

Session 33 continued

Real-Time International Surveillance of Antimicrobial Resistance by the Enter-net Surveillance Network

I. S. Fisher[1], N. Gill[1], B. Reilly[2], H. Smith[3], J. Threlfall[3], on behalf of the Enter-net participants[4]

[1]PHLS Communicable Disease Surveillance Centre, London, UNITED KINGDOM, [2]Scottish Centre for Infection and Environmental Health, Glasgow, UNITED KINGDOM, [3]PHLS Central Public Health Laboratory, London, UNITED KINGDOM, [4]Enter-net Surveillance Hub, London, UNITED KINGDOM

Session 34

Slide Session

Vectorborne Diseases I

Monday, March 25, 10:30 a.m. – 11:30 a.m.

Regency Ballroom V

Moderators:

BARRY BEATY, Colorado State University, Ft. Collins, CO

LYLE PETERSEN, CDC, Ft. Collins, CO

The Emergence of Rift Valley Fever in the Arabian Peninsula, 2000

H. El Sakka[1], R. Graham[1], E. Mohareb[1], D. Salma1, S. Lewis[1], A. El Kholy[2], M. Ibrahim[2], F. Mahoney[1,3]

[1]U.S. Naval Medical Research Unit No. 3, Cairo, EGYPT, [2]Field Epidemiology Training Program, Egyptian Ministry of Health and Population, Cairo, EGYPT, [3]CDC, Atlanta, GA

Microheterogenicity of the Volgograd Clone of West Nile Virus

A. E. Platonov[1], L. S. Karan[1], S. B. Yazyshina1, K. O. Mironov[1], E. M. Krasnova[2], V. V. Lazorenko[2], N. V. Rusakova[2], A. N. Zhukov[2], V. A. Antonov[3], I. L. Obukhov[4], G. A. Shipulin[1]

[1]Central Research Institute of Epidemiology, Moscow, RUSSIAN FEDERATION, [2]State Center for Sanitary and Epidemic Control, Volgograd, RUSSIAN FEDERATION, [3]Anti-Plague Institute, Volgograd, RUSSIAN FEDERATION, [4]State Institute for Control of Veterinary Products, Moscow, RUSSIAN FEDERATION

Rapid Screening and Identification of West Nile Virus in Captive and Wild Birds Using Non-Invasive Environmental Samples and a Portable TaqMan RT-PCR

J. D. Callahan[1], T. S. McNamara[2], A. L. Glaser[3], M. Turell[4], K. Gaffney[1], S. Ellis[1], W. M. Nelson[1]

[1]Tetracore, Inc, Gaithersburg, MD, [2]Wildlife Conservation Society, New York, NY, [3]Cornell University, Ithaca, NY, [4]US Army Medical Research Institute of Infectious Diseases, Fort Detrick, MD

West Nile Virus First Transmission Season in Florida, 2001 – More than 400 Horse Cases and 170 Chicken Seroconversions but Only Sporadic Human Disease

C. Blackmore[1], L. M. Stark[2], R. L. Oliveri[3], L. A. Conti[3], S. T. Wiersma[3]

[1]Florida Department of Health, Jacksonville, FL, [2]Florida Department of Health, Tampa, FL, [3]Florida Department of Health, Tallahassee, FL

Session 35

Slide Session

Molecular Diagnostics and Epidemiology I

Monday, March 25, 10:30 a.m. – 11:30 a.m.

Centennial Ballroom III

Moderators:

JAMIE MAGUIRE, CDC, Atlanta, GA

STEVE MORSE, CDC, Atlanta, GA

A Molecular Approach to the Epidemiology of *Giardia duodenalis* in a Peruvian Shantytown

P. J. Hoover[1], C. Reed1, G. D. Sturbaum[1], R. H. Gilman[2], C. R. Sterling[1]

[1]University of Arizona, Tucson, AZ, [2]Johns Hopkins University, Baltimore, MD

Increasing Detection of Malaria in U.S. Hospitals Using the OptiMAL Rapid Diagnostic Test

C. J. Palmer[1], J. A. Bonilla1, D. A. Bruckner[2], E. Barnett[3], N. S. Miller[4], J. Masci[5], M. A. Haseeb[6]

[1]University of Florida, Gainesville, FL, [2]UCLA Medical Center, Los Angeles, CA, [3]Boston Medical Center, Boston, MA, [4]Washington Hospital Center, Washington, DC, [5]Elmhurst Hospital Center, Elmhurst, NY, [6]Kings County Hospital, Brooklyn, NY

Incidence and Type Distribution of Astrovirus Among Spanish Children

R. M. Dalton[1], E. Roman[2], N. Negredo[1], I. Wilhelmi[3], **A. Sánchez Fauquier**[1]

[1]Centro Nacional de Microbiología, Madrid, SPAIN, [2]Servicio de Pediatría, Hospital Severo Ochoa, Leganés, Madrid, SPAIN, [3]Servicio de Microbiología, Hospital Severo Ochoa, Leganés, Madrid, SPAIN

Detection and Typing of Enterovirus in Cerebrospinal Fluid

B. I. Rosen, B. Slater, M. Dupuis, R. Hull, R. Ferrera, C. Huang

New York State Department of Health, Slingerlands, NY

Session 36

Slide Session

Latebreakers I

Monday, March 25, 10:30 a.m. – 11:30 a.m.

Centennial Ballroom IV

Moderators:

STEVE OSTROFF, CDC, Atlanta, GA

JAMIE MAGUIRE, CDC, Atlanta, GA

Session 37

Slide Session

Smallpox Response

Monday, March 25, 10:30 a.m. – 11:30 a.m.

Centennial Ballroom II

Moderators:

D. A. HENDERSON, U.S. Department of Health and Human Services

HAROLD MARGOLIS, CDC, Atlanta, GA

Session 38

Bring-Your-Lunch

First Encounters with New Diseases: The Clinician's Perspective

Monday, March 25, 11:30 a.m. – 1:00 p.m.

Regency Ballroom VI/VII

Moderator:
MERLE A. SANDE, University of Utah, Salt Lake City, UT

AIDS in Rural Tennessee: The Search for Meaning in a Medical Life

ABRAHAM VERGHESE, Texas Tech University Health Sciences Center, El Paso, TX

Session 39

Invited Panel

Zoonotic Diseases

Monday, March 25, 1:00 p.m. – 2:30 p.m.

Centennial Ballroom I

Conveners/Moderators:
JAMIE CHILDS, CDC, Atlanta, GA

CHERIE DRENZEK, National Association of Public Health Veterinarians, Atlanta, GA

Surveillance of Livestock for Zoonotic Diseases and Veterinary Bio-threat Agents

WILLIAM D. HUESTON, College of Veterinary Medicine, University of Minnesota, St. Paul, MN

The Emergence of Infectious Diseases Among Wildlife and the Origin of Human Zoonoses

PETER DASZAK, Consortium for Conservation Medicine, Palisades, NY

Shared Animal and Human Influenza Viruses: A Role in the Next Pandemic?

KENNEDY F. SHORTRIDGE, University of Hong Kong, Queen Mary Hospital, HONG KONG

Preventing Human Disease by Controlling Pathogen Transmission in the Animal Reservoir

CHARLES E. RUPPRECHT, CDC, Atlanta, GA

Session 40

Invited Panel

Innovative Surveillance Systems

Monday, March 25, 1:00 p.m. – 2:30 p.m.

Centennial Ballroom II

Conveners/Moderators:
ROBERT PINNER, CDC, Atlanta, GA

DALE MORSE, New York State Department of Health, Albany, NY

Syndromic Surveillance in a Managed Care Setting

RICHARD PLATT, Harvard Medical School, Boston, MA

Bioterrorism Surveillance in New York City

FARZAD MOSTASHARI, New York City Department of Health, New York, NY

CD Electronic Surveillance in the United Kingdom and European Union

MICHAEL CATCHPOLE, PHLS Communicable Disease Surveillance Centre, London, UNITED KINGDOM

PULSENET and Beyond

BALASUBRA SWAMINATHAN, CDC, Atlanta, GA

Session 41

Invited Panel

Foodborne/Waterborne Disease

Monday, March 25, 1:00 p.m. – 2:30 p.m.

Centennial Ballroom III

Conveners:
PAUL BERGER, Environmental Protection Agency, Washington, DC

DEBORAH LEVY, CDC, Atlanta, GA

ART LIANG, CDC, Atlanta, GA

Moderators:
PAUL BERGER, ART LIANG

Public Health and Policy Implications of the Recent Large Drinking Water Outbreaks in Canada

ANDREA ELLIS, Center for Infectious Diseases Prevention and Control, Guelph, Ontario, CANADA

The Risk of Food and Water Contamination from Animal Manure

CHRISTINE MOE, Rollins School of Public Health, Emory University, Atlanta, GA

Food Safety: Perceived Risk and Public Trust

CAROL TUCKER FOREMAN, Consumer Federation of America, Washington, DC

Session 42

Invited Panel

Public Health Policy/Law

Monday, March 25, 1:00 p.m. – 2:30 p.m.

Centennial Ballroom IV

Conveners/Moderators:
RICK GOODMAN, CDC, Atlanta, GA

JOEL GAYDOS, U.S. Department of Defense, Washington, DC

Foodborne Disease

LESLIE KUX, U.S. Food and Drug Administration, Rockville, MD

Bioterrorism

RICHARD HOFFMAN, Colorado Department of Public Health and Environment, Denver, CO

West Nile Virus Outbreak in New York City

WILFREDO LOPEZ, New York City Department of Health, New York, NY

Global Health and International Regulations

DAVID FIDLER, School of Law, Indiana University, Bloomington, IN

Session 43

Invited Panel

Disease Eradication

Monday, March 25, 1:00 p.m. – 2:30 p.m.

Regency Ballroom V

Conveners:

CAROLYN BLACK, CDC, Atlanta, GA

WALTER DOWDLE, Task Force for Child Survival and Development, Atlanta, GA

FRANK RICHARDS, CDC, Atlanta, GA

Moderators:

FRANK RICHARDS, CAROLYN BLACK

Overview

WALTER DOWDLE, Task Force for Child Survival and Development, Atlanta, GA

Eradication of Dracunculiasis

ERNESTO RUIZ-TIBEN, CDC, Atlanta, GA

Eradication of Lymphatic Filariasis and Onchocerciasis

ERIC OTTESEN, Rollins School of Public Health, Emory University, Atlanta, GA

Eradication of Chagas Disease

GABRIEL SCHMUNIS, Pan American Health Organization, Washington, DC

Eradication of T. solium Cysticercosis

PETER SCHANTZ, CDC, Atlanta, GA

Session 44

Slide Session

Emerging Zoonoses I

Monday, March 25, 3:00 p.m. – 4:30 p.m.

Regency Ballroom V

Moderators:

FREDERICK A. MURPHY, School of Veterinary Medicine, University of California, Davis, CA

SHERIF ZAKI, CDC, Atlanta, GA

Emergence of Canine Visceral Leishmaniasis in Dogs in North America

Z. Duprey[1], P. M. Schantz[1], F. Steurer[1], J. Jackson[2], J. Rooney[3], E. Rowton[4], M. Gramiccia[5], E. Breitschwerdt[6]

[1]Division of Parasitic Diseases, NCID, CDC, Atlanta, GA, [2]Walter Reed Army Institute of Research, Silver Spring, MD, [3]Virginia State Department of Health, Richmond, VA, [4]Walter Reed Army Institute of Research, Washington, D.C., DC, [5]Institute of Public Health, Rome, ITALY, [6]College of Veterinary Medicine, North Carolina State University, Raleigh, NC

Detection and Genetic Analysis of Swine Hepatitis E Virus in Farm Waste

T. L. Cromeans[1,2], A. S. Foust[1,2], A. E. Fiore1, M. D. Sobsey[2], B. P. Bell1, H. S. Margolis[1], B. H. Robertson[1]

[1]CDC, Atlanta, GA, [2]University of North Carolina, Chapel Hill, NC

Enhanced Laboratory-based Surveillance of Shiga Toxin-Producing *Escherichia coli* O157, the Netherlands

Y. T. Van Duynhoven, Sr.[1], C. M. De Jager[1], A. E. Heuvelink, Sr.[2], W. K. Van der Zwaluw[1], H. M. Maas1, W. Van Pelt, Sr.[1], W. J. Wannet, Sr.[1]

[1]National Institute of Public Health and the Environment, Bilthoven, NETHERLANDS, [2]Inspectorate for Health Protection and Veterinary Public Health, Zutphen, NETHERLANDS

Outbreaks of Multidrug-Resistant *Salmonella* Serotype Typhimurium Infections Associated with Small Animal Veterinary Facilities in Idaho, Minnesota and Washington, 1999

J. G. Wright[1], K. E. Smith[2], L. Tengelsen[3], J. Grendon[4], D. Boxrud[2], B. Holland[1], A. D. Anderson[1]

[1]CDC, Atlanta, GA, [2]Minnesota Department of Health, Minneapolis, MN, [3]Idaho Department of Health and Welfare, Boise, ID, [4]Washington State Department of Health, Olympia, WA

An Outbreak of *Salmonella* Javiana Associated with Amphibian Contact – Mississippi, 2001

P. Srikantiah[1], J. C. Lay[1], J. A. Crump[1], S. Hand[2], J. Campbell[2], V. Janakiraman[1], H. Fletemier[1], R. Middendorf[1], S. Van Duyne1, M. Currier[2], P. S. Mead[1], K. Molbak[1]

[1]CDC, Atlanta, GA, [2]Mississippi State Department of Health, Jackson, MS

Outbreaks of Salmonellosis at Elementary Schools Associated with Dissection of Owl Pellets

F. Anderson[1], C. Medus[2], F. Leano[2], J. Adams[2], K. Smith[2]

[1]Washington County Department of Public Health and Environment, Stillwater, MN, [2]Minnesota Department of Health, Minneapolis, MN

Session 45

Slide Session

Bioterrorism

Monday, March 25, 3:00 p.m. – 4:30 p.m.

Centennial Ballroom II

Moderators:

RONALD ATLAS, University of Louisville, Louisville, KY

EDWARD EITZEN, U. S. Army Medical Research Institute of Infectious Diseases, Fort Detrick, MD

Public Health Laboratory Response to an Anthrax Incident in Connecticut

D. Barden, T. Brennan, G. Budnick, E. Gaynor, A. Kinney, **D. R. Mayo**, M. Ridley, K. Kelley

Connecticut State Health Department, Hartford, CT

Rapid Molecular Identification of *B. anthracis* in New York State in Response to Recent Bioterrorism Incidents

K. Musser, M. Kelly, S. Davis, C. Egan, N. Dumas, A. Waring, T. Halse, P. Maupin, K. Hechemy, J. Hibbs, D. Morse, R. Limberger

New York State Department of Health, Albany, NY

Laboratory Response in the Commonwealth of Virginia to the Intentional Release of *Bacillus anthracis*

D. A. Pettit, J. V. Carroll, E. M. Basinger, M. R. Ettinger, S. S. Walker, T. L. York, J. L. Pearson

Division of Consolidated Laboratory Services, Richmond, VA

Monitoring of Human Exposure to *Bacillus thuringiensis* after Aerial Applications for Insect Control

D. B. Levin, G. V. de Amorim

University of Victoria, Victoria, BC, CANADA

Threat Letter Menace: The Fiji Experience

K. Kishore[1], E. Buadromo[2], S. Singh[2]

[1]Fiji School of Medicine, Suva, FIJI, [2]Colonial War Memorial Hospital, Suva, FIJI

Enhanced Emergency Department Surveillance System Following the World Trade Disaster – New York City, September 14 to October 10, 2001

D. Das[1], D. Weiss[1], S. Balter[1], T. Treadwell[2], J. McQuiston[2], L. Hutwagner[2], A. Karpati[2],[1], F. Mostashari[1], K. Bornschlegel[1], B. Cherry1, S. Mathew[2], A. Fine1, M. Layton[1]

[1]New York City Department of Health, New York, NY, [2]CDC, Atlanta, GA

Session 46

Slide Session

Chronic Diseases

Monday, March 25, 3:00 p.m. – 4:30 p.m.

Centennial Ballroom III

Moderators:

SIOBHAN O'CONNOR, CDC, Atlanta, GA

CLADD STEVENS, New York Blood Center, New York, NY

Failure to Detect *C. pneumoniae* in Atherosclerotic Specimens from Major Arteries of 93 Patients

J. Bishara[1], **S. Pitlik**[1], A. Vojdani[2], A. Kazakov[1], G. Sahar[1], M. Haddad[1], S. Rosenberg[3], Z. Samra[3]

[1]Rabin Medical Center; Beilinson Campus, Petach-Tikva, ISRAEL, [2]Immunosciences Lab, Inc., Drew University School of Medicine and Science, Los Angeles, CA, [3]Chlamydia and Mycoplasma National Center, Department of Microbiology. Rabin Medical Center, Beilinson Campus, Petach-Tikva, ISRAEL

Prevalence of Hepatitis C and Other Chronic Liver Disease Etiologies in Primary Care Practices

T. St. Louis[1], V. Navarro[1], A. Sofair[1], B. Bell[2]

[1]Connecticut Emerging Infections Program, New Haven, CT, [2]CDC, Atlanta, GA

Intestinal Anaerobic Bacteria in Early Rheumatoid Arthritis

R. Manninen1, S. Vartiainen[1], J. Jalava1, R. Luukkainen[2], T. Möttönen[3], E. Eerola[1], **P. Toivanen**[1]

[1]Department of Medical Microbiology, Turku University, Turku, FINLAND, [2]Satalinna Hospital, Harjavalta, FINLAND, [3]Division of Rheumatology, Department of Medicine, Turku University Central Hospital, Turku, FINLAND

Postdiarrheal Hemolytic Uremic Syndrome in New York State

B. Tserenpuntsag, **H. H. Chang**, M. Kacica, P. F. Smith, D. L. Morse

New York State Department of Health, Albany, NY

Outbreak of *Cryptococcus neoformans* var. gattii in a Restricted Zone in British Columbia

M. Starr[1], M. Fyfe[1], W. Black[1], P. Kibsey[2], L. MacDougall[1], S. Mak[1], M. Pearce[3], J. Isaac-Renton[1], M. Romney[1], L. Stein[1], C. Stephen[4], D. Patrick[1]

[1]University of British Columbia Centre for Disease Control, Vancouver, BC, CANADA, [2]Victoria General Hospital, Victoria, BC, CANADA, [3]Capital Health Region, Victoria, BC, CANADA, [4]Centre for Coastal Health, Nanaimo, BC, CANADA

Tuberculosis Gene Deletion Typing, Not YATM ("Yet Another Typing Method")

Y. Goguet

Stanford University, Stanford, CA

Session 47

Slide Session

Foodborne and Waterborne Illness I

Monday, March 25, 3:00 p.m. – 4:30 p.m.

Centennial Ballroom IV

Moderators:

ROGER GLASS, CDC, Atlanta, GA

MARGUERITE NEILL, Memorial Hospital of Rhode Island, Providence, RI

Outbreak of Viral Gastroenteritis and an Ill Baker Who Should Have Known Better: Novel Application of Email for Rapid Investigation

M. Widdowson[1], M. A. de Wit[2], H. Vennema[2], M. Koopmans[2]

[1]CDC, Atlanta, GA, [2]National Institute of Public Health and the Environment, Bilthoven, NETHERLANDS

Challenges in the Interpretation of Classical and Molecular Epidemiology Results; Two *Calicivirus* Outbreaks Due to Oysters: Denmark at New Year 2000

F. X. Hanon[1], S. Corbet[1], B. Böttiger[1], A. C. Schultz[2], P. Saadbye[2], A. Perge[2], K. Mølbak[1]

[1]Statens Serum Institut, Copenhagen, DENMARK, [2]National Food Agency, Søborg, DENMARK

Coordinating Environmental Public Health Practice with Epidemiology and Laboratory Analysis: A Waterborne Outbreak of "Norwalk-like Virus" in the Big Horn Mountains of Wyoming

S. A. Seys[1], H. M. Mainzer[2], A. G. Heryford[1], A. D. Anderson[3],[4], S. S. Monroe[4], G. S. Fout[5], J. P. Sarisky[2], K. J. Musgrave[1]

[1]Wyoming Department of Health, Cheyenne, WY, [2]National Center for Environmental Health, CDC, Atlanta, GA, [3]Epidemiology Program Office, CDC, Atlanta, GA, [4]National Center for Infectious Diseases, CDC, Atlanta, GA, [5]National Exposure Research Laboratory, U.S. Environmental Protection Agency, Cincinnati, OH

Session 47 continued

Sesame-Seed Paste Caused an International Outbreak Due to *Salmonella* Typhimurium DT104 – The Investigation in Norway

O. Alvseike[1], P. J. Guerin[1,2], T. Stavnes[1], P. Aavitsland[1]

[1]Norwegian Institute of Public Health, Oslo, NORWAY, [2]EPIET (European Programme for Intervention Epidemiology Training), Oslo, NORWAY

Changing Epidemiological Patterns of *Salmonella* Serotype Enteritidis in Barbados: Implications for Tourism and Trade

L. Indar[1], P. N. Levett[2], R. Knight[3], M. Ingram[3], E. Commissiong[1], G. Baccus-Taylor[1], P. Prabhakar[4], J. Hospedales[4]

[1]University of the West Indies, St.Augustine, TRINIDAD AND TOBAGO, [2]University of the West Indies, Bridgetown, BARBADOS, [3]Ministry of Health, Bridgetown, BARBADOS, [4]CAREC, Port of Spain, TRINIDAD AND TOBAGO

Health Impact of the *Salmonella enterica* Serotype Enteritidis Phage Type 4 Epidemic

G. K. Adak, S. M. Long, S. J. O'Brien, L. R. Ward

Public Health Laboratory Service, London, UNITED KINGDOM

Session 48

Slide Session

Antimicrobial Resistance I

Monday, March 25, 3:00 p.m. – 4:30 p.m.

Centennial Ballroom I

Moderators:

JULIE GERBERDING, CDC, Atlanta, GA

ROBERT WEINSTEIN, Cook County Hospital, Chicago, IL

Antibiotic Susceptibility and the Mechanisms of Macrolide Resistance in Invasive Group B *Streptococcus*, Minnesota, 1998 and 2000

J. Bartkus, C. Morin, S. Vetter, E. Thompson, A. Glennen, R. Lynfield

Minnesota Department of Health, Minneapolis, MN

Multi-Drug Resistant *Neisseria gonorrhoeae* with Decreased Susceptibility to Cefixime, Hawaii, 2001

S. A. WANG1, M. V. Lee[2], C. J. Iverson[1], N. O'Connor[3], R. G. Ohye[2], J. A. Hale[4], J. S. Knapp[1], P. V. Effler[2], H. S. Weinstock[1]

[1]CDC, Atlanta, GA, [2]Hawaii Dept of Health, Honolulu, HI, [3]Hawaii Dept of Health State Laboratory, Pearl City, HI, [4]Seattle GISP Laboratory, Seattle, WA

Shigella dysenteriae Serotype 1 in West Africa: Intervention Strategy for an Outbreak in Sierra Leone, 1999-2000

P. J. Guerin[1,2,3], C. Brasher[4], E. Baron4, D. Mic[4], F. Grimont[5], M. Ryan[6], P. Aavitsland[3], D. Legros[1]

[1]Epicentre, Paris, FRANCE, [2]EPIET (European Programme for Intervention Epidemiology Training), Oslo, NORWAY, [3]Norwegian Institute of Public Health, Oslo, NORWAY, [4]Médecins Sans Frontières, Paris, FRANCE, [5]Centre National de Référence de Typage Moléculaire Entérique. Unité Biodiversité des Bactéries Pathogènes Emergentes. Institut Pasteur, Paris, FRANCE, [6]Department of Communicable Disease Surveillance and Response, World Health Organisation, Geneva, SWITZERLAND

The Acquisition of Ciprofloxacin Resistance in Travel-Associated and Home-Acquired *Campylobacter jejuni* Infection: A Case-Case Comparison

I. A. Gillespie[1], S. J. O'Brien[2], J. A. Frost[2]

[1]Public Health Laboratory Service, London, UNITED KINGDOM, [2]Public Health laboratory Service, London, UNITED KINGDOM

Prevalence and Consequences of Fluoroquinolone-Resistant *Campylobacter* Infections: NARMS 1997-2000

J. McClellan, S. Rossiter, K. Joyce, K. Stamey, A. D. Anderson, and the NARMS Working Group

CDC, Atlanta, GA

High Prevalence of Antibiotic Resistance in Enterotoxigenic *E. coli* (ETEC); Minnesota 2000 - 2001

J. M. Besser, K. Smith, C. Taylor, P. Gahr, C. Medus

Minnesota Department of Health, Minneapolis, MN

Tuesday, March 26

Session 49

International Health Panel

Tuesday, March 26, 7:30 a.m. – 8:30 a.m.

Regency Ballroom VI/VII

Moderators:

RAY ARTHUR, World Health Organization, Geneva, SWITZERLAND

JAMES LEDUC, CDC, Atlanta, GA

CDC-PAHO Collaboration: Surveillance of Emerging/Reemerging Diseases in the Amazon and the Southern Cone Region

GABRIEL SCHMUNIS, Pan American Health Organization, Washington, DC

Eradication of Chagas' Disease

GABRIEL SCHMUNIS, Pan American Health Organization, Washington, DC

Emerging Infectious Diseases – India

N.K. GANGULY, Indian Council of Medical Research, New Delhi, INDIA

Protecting the Nation's Health in an Era of Globalization: CDC's Global Infectious Disease Strategy

SCOTT DOWELL, CDC , Atlanta, GA

Session 50

Poster Session

Antimicrobial Resistance II

Tuesday, March 26, 8:30 a.m. – 1:00 p.m.; Authors present 8:30 a.m. – 10:00 a.m.

Grand Hall East

For a complete listing of poster titles and abstracts, see pages 127-136.

Session 51

Poster Session

Syndromes and Diagnosis II

Tuesday, March 26, 8:30 a.m. – 1:00 p.m.; Authors present 8:30 a.m. – 10:00 a.m.

Grand Hall East

For a complete listing of poster titles and abstracts, see page 137.

Session 52

Poster Session

Travelers' Health

Tuesday, March 26, 8:30 a.m. – 1:00 p.m.; Authors present 8:30 a.m. – 10:00 a.m.

Grand Hall East

For a complete listing of poster titles and abstracts, see page 137.

Session 53

Poster Session

Blood Safety

Tuesday, March 26, 8:30 a.m. – 1:00 p.m.; Authors present 8:30 a.m. – 10:00 a.m.

Grand Hall East

For a complete listing of poster titles and abstracts, see pages 137-138.

Session 54

Poster Session

Detection of Novel Agents

Tuesday, March 26, 8:30 a.m. – 1:00 p.m.; Authors present 8:30 a.m. – 10:00 a.m.

Grand Hall East

For a complete listing of poster titles and abstracts, see pages 138-140.

Session 55

Poster Session

Vaccines

Tuesday, March 26, 8:30 a.m. – 1:00 p.m.; Authors present 8:30 a.m. – 10:00 a.m.

Grand Hall East

For a complete listing of poster titles and abstracts, see pages 140-142.

Session 56

Poster Session

Vectorborne Diseases II

Tuesday, March 26, 8:30 a.m. – 1:00 p.m.; Authors present 8:30 a.m. – 10:00 a.m.

Grand Hall East

For a complete listing of poster titles and abstracts, see pages 143-149.

Session 57

Poster Session

Global Climate Change

Tuesday, March 26, 8:30 a.m. – 1:00 p.m.; Authors present 8:30 a.m. – 10:00 a.m.

Grand Hall East

For a complete listing of poster titles and abstracts, see page 149.

Session 58

Poster Session

Health Communication

Tuesday, March 26, 8:30 a.m. – 1:00 p.m.; Authors present 8:30 a.m. – 10:00 a.m.

Grand Hall East

For a complete listing of poster titles and abstracts, see pages 150-151.

Session 59

Poster Session

Influenza

Tuesday, March 26, 8:30 a.m. – 1:00 p.m.; Authors present 8:30 a.m. – 10:00 a.m.

Grand Hall East

For a complete listing of poster titles and abstracts, see pages 151-154.

Session 60

Poster Session

International Cooperation

Tuesday, March 26, 8:30 a.m. – 1:00 p.m.; Authors present 8:30 a.m. – 10:00 a.m.

Grand Hall East

For a complete listing of poster titles and abstracts, see pages 154-156.

Session 61

Poster Session

Molecular Epidemiology II

Tuesday, March 26, 8:30 a.m. – 1:00 p.m.; Authors present 8:30 a.m. – 10:00 a.m.

Grand Hall East

For a complete listing of poster titles and abstracts, see pages 157-160.

Session 62

Poster Session

New or Rapid Diagnostics II

Tuesday, March 26, 8:30 a.m. – 1:00 p.m.; Authors present 8:30 a.m. – 10:00 a.m.

Grand Hall East

For a complete listing of poster titles and abstracts, see pages 160-164.

Session 63

Poster Session

Prions and Public Health

Tuesday, March 26, 8:30 a.m. – 1:00 p.m.; Authors present 8:30 a.m. – 10:00 a.m.

Grand Hall East

For a complete listing of poster titles and abstracts, see page 164.

Session 64

Plenary Session III

Tuesday, March 26, 10:00 a.m. – 11:30 a.m.

Centennial Ballroom I/II

Moderators:

BRIAN MAHY, CDC, Atlanta, GA

ROBERT TAUXE, CDC, Atlanta, GA

Foot and Mouth Disease

CHRISTOPHER BOSTOCK, Institute of Animal Health, Compton, UNITED KINGDOM

Integrated Surveillance and Control of Emerging Foodborne Diseases—The Successful Danish Experience

HENRIK C. WEGENER, Danish Zoonosis Institute, DENMARK

Session 65

Plenary Session IV

Tuesday, March 26, 10:00 a.m. – 11:30 a.m.

Centennial Ballroom III/IV

Moderators:

ENRIQUETA C. BOND, The Burroughs Wellcome Fund, Research Triangle Park, NC

DUANE GUBLER, CDC, Fort Collins, CO

Trypanosomiasis as a Reemerging Infection

ANNE MOORE, CDC, Atlanta, GA

New Strategies on the Old Ideas: Malaria Control Without Insecticides and Community Participation in *Aedes aegypti* Control, Mexico Experiences

JORGE F. MÉNDEZ GALVÁÁN, Ministry of Health, Mexico City, MEXICO

Session 68

Bring-Your-Lunch

First Encounters with New Diseases: The Clinician's Perspective

Tuesday, March 26, 11:30 a.m. – 1:00 p.m.

Regency Ballroom VI/VII

Moderator:

RIMA KHABBAZ, CDC, Atlanta, GA

HAROLD JAFFE, CDC, Atlanta, GA

AIDS

MICHAEL S. GOTTLIEB, Los Angeles, CA

West Nile Virus Infection

DEBORAH ASNIS, Brooklyn, NY

Hantavirus Pulmonary Syndrome

BRUCE TEMPEST, Gallup, NM

Session 69

Invited Panel

Pathogen Discovery

Tuesday, March 26, 1:00 p.m. – 2:30 a.m.

Centennial Ballroom I

Conveners:

LARRY ANDERSON, CDC, Atlanta, GA

CHRISTOPHER HUSTON, American Society of Tropical Medicine and Hygiene

Moderators:

CHRISTOPHER HUSTON

IAN LIPKIN, Mailman School of Public Health, Columbia University, New York, NY

Multiple Array Technology To Look for mRNA Patterns Associated with Disease and Pathogens

DAVID A. RELMAN, Stanford University, Stanford, CA

Clusters of Clinical Syndromes in Patients with Unexplained Encephalitis

CAROL A. GLASER, California Department of Health Services, Berkeley, CA

Proteomics and Pathogen Discovery

DONALD HUNT, University of Virginia, Charlottesville, VA

The New Human Metapneumovirus

ALBERT OSTERHAUS, University of Rotterdam, Rotterdam, NETHERLANDS

Session 70

Invited Panel

Emerging Issues in Healthcare Settings

Tuesday, March 26, 1:00 p.m. – 2:30 p.m.

Centennial Ballroom II

Conveners/Moderators:

WILLIAM JARVIS, CDC, Atlanta GA

GEORGIA DASH, Association for Professionals in Infection Control and Epidemiology, Washington, DC

Controlling Antimicrobial Resistance

BARRY FARR, University of Virginia Hospital, Charlottesville, VA

Prevention of Device-Associated Infections

LEONARD MERMEL, Rhode Island Hospital, Providence, RI

Patient Safety: Applying Industrial Quality Models in Healthcare Settings To Improve Outcomes

JULIE GERBERDING, CDC, Atlanta, GA

The Role of Healthcare Systems in Bioterrorism Preparedness

TRISH PERL, Johns Hopkins Hospital, Baltimore, MD

Session 71

Invited Panel

Anthrax 2001: Lessons That Stunned Us

Tuesday, March 26, 1:00 p.m. – 2:30 p.m.

Centennial Ballroom III

Conveners:

RIMA KHABBAZ, CDC, Atlanta, GA

BRADLEY PERKINS, CDC, Atlanta, GA

Moderators:
ANDREA MEYERHOFF, Food and Drug Administration, Washington, DC

BRADLEY PERKINS

Inhalation Anthrax in Florida
STEVE WIERSMA, Florida Department of Health, Tallahassee, FL

Cutaneous Anthrax in New York City
MARCELLE LAYTON, New York City Department of Health, New York, NY

Inhalation Anthrax of Unknown Source
JAMES L. HADLER, Connecticut Department of Public Health, Hartford, CT

Anthrax in the U.S. Postal System
MICHELE L. PEARSON, CDC, Atlanta, GA

Session 72

Invited Panel

Preventing Infectious Disease through Behavior Change
Tuesday, March 26, 1:00 p.m. – 2:30 p.m.

Centennial Ballroom IV

Conveners:
STEPHEN CORBER, Pan American Health Organization, Washington, DC

MEREDITH HICKSON, CDC, Atlanta, GA

BOBBIE PERSON, CDC, Atlanta, GA

Moderators:
MITCH COHEN, CDC, Atlanta, GA

MEREDITH HICKSON

The Essential Role of Behavioral and Social Sciences in the Prevention of Emerging Infectious Diseases
EMILY ZIELINSKI-GUTIERREZ, CDC, Fort Collins, CO

Bringing Dengue Prevention Down to Earth: Evaluation of a Head Start Project in Puerto Rico
CARMEN L. PEREZ-GUERRA, CDC, San Juan, PR

Increasing Water Vessel Use in Kenya
PHILIP S. MAKUTSA, CARE International in Kenya, Homa Bay, KENYA

Sex Workers as Targets of and Agents for HIV/STI Prevention
RAFAEL MAZIN, Pan American Health Organization, Washington, DC

Session 73

Invited Panel

The World and Its Moving Parts: Implications for Emerging Infectious Diseases
Tuesday, March 26, 1:00 p.m. – 2:30 p.m.

Regency Ballroom V

Conveners:
SUSAN MALONEY, CDC, Atlanta, GA

MICHAEL OSTERHOLM, University of Minnesota Academic Health Center, Minneapolis, MN

Moderators:
MICHELE BARRY, Yale University School of Medicine, New Haven, CT

SUSAN MALONEY

The World and Its Moving Parts: An Overview
MARTIN CETRON, CDC, Atlanta, GA

Global Migration and Emerging Infectious Diseases
DANIELE GRONDIN, International Organization of Migration, Geneva, SWITZERLAND

The Gobalization of Our Food Supply: Implications for Emerging Infectious Diseases
MICHAEL OSTERHOLM, University of Minnesota Academic Health Center, Minneapolis, MN

Emerging Vectorborne Disease: The Case of Yellow Fever
C.J. PETERS, University of Texas Medical Branch, Galveston, TX

Session 74

Slide Session

Emerging Zoonoses II
Tuesday, March 26, 2:45 p.m. – 4:15 p.m.

Centennial Ballroom I

Moderators:
JANE KOEHLER, University of California, San Francisco, CA

TOM KSIAZEK, CDC, Atlanta, GA

Emerging Rickettsioses of the Thai-Myanmar Border
P. Parola[1,2,3], R. S. Miller[2], P. McDaniel[4], P. E. Fournier[3], D. Raoult[3], **S. R. Telford, III**[1], C. Wongsrichanalai[2]

[1]Harvard School of Public Health, Boston, MA, [2]Armed Forces Institute of Medical Sciences (AFRIMS), Bangkok, THAILAND, [3]Unite des Rickettsies, Marseille, FRANCE, [4]Kwai River Christian Hospital, Sangkhlaburi, THAILAND

Clinical Management and Outcomes of Lyme Disease in Wisconsin
D. R. O'Leary[1], E. Belongia[2], K. Orloski[1], P. Chyou [2], C. Gale[2], M. Finkel[3], E. B. Hayes[1]

[1]CDC, Fort Collins, CO, [2]Marshfield Medical Research Foundation, Marshfield, WI, [3]Mayo-Midelfort Clinic, Eau Claire, WI

A Neighborhood Outbreak of Q Fever Linked to a Goat Ranch in California
M. T. Jay[1], J. Douglas[2], K. Carter[1], J. D. Miller[3], J. McQuiston[3], G. Rishwain[4], E. Schneider[4], H. Thompson[3], D. Kelaita[2]

[1]California Department of Health Services, Sacramento, CA, [2]Calaveras Public Health Department, San Andreas, CA, [3]CDC, Atlanta, GA, [4]Stockton Medical Groups, Stockton, CA

Q fever in the United States: Experience of Infectious Disease Consultants and Comparison to National Reporting during 2000
J. H. McQuiston[1], L. J. Strausbaugh2, D. B. Jernigan[1], L. A. Liedtke2, J. E. Childs[1], H. A. Thompson[1]

[1]CDC, Atlanta, GA, [2]VA Medical Center, Portland, OR

Session 74 continued

Emerging Zoonoses: A Novel Epizootic of Skunks Infected with a Bat Variant of Rabies

M. J. Leslie[1], C. Hanlon[2], J. Smith[2], R. Rohde[3], R. Cheshier[1], C. Rupprecht[2]

[1]Arizona Department of Health Services, Phoenix, AZ, [2]CDC, Atlanta, GA, [3]Texas Department of Health, Austin, TX

Epidemiology of Raccoon and Skunk Rabies in the Eastern United States

M. A. Guerra, A. T. Curns, W. Ivy, III, C. A. Hanlon, C. E. Rupprecht, J. W. Krebs, J. E. Childs

CDC, Atlanta, GA

Session 75

Slide Session

Foodborne and Waterborne Illness II

Tuesday, March 26, 2:45 p.m. – 4:15 p.m.

Centennial Ballroom II

Moderators:

PATRICIA GRIFFIN, CDC, Atlanta, GA

LEE RILEY, University of California–Berkeley, School of Public Health, Berkeley California

Three Outbreaks of *E. coli* O157 Infections Due to Retail Ground Beef in Minnesota, 2000: Detection, Investigation, and Characteristics

K. Smith, **E. Swanson**, E. Wagstrom, F. Leano, D. Boxrud, J. Adams, J. Besser, R. Danila, H. F. Hull

Minnesota Department of Health, Minneapolis, MN

Epidemiology of Shiga Toxin–Producing *Escherichia coli* (STEC)Infections in Connecticut, February 1, 2000–January 31, 2001

Q. Phan[1], T. McCarthy[2], P. Mshar[1], C. Welles[3], R. Howard[3], T. Rabatsky-Ehr[4], J. L. Hadler[1]

[1]Connecticut Department of Public Health, Epidemiology Section, Hartford, CT, [2]CDC, Atlanta, GA, [3]Connecticut Department of Public Health, Laboratory Division, Hartford, CT, [4]Connecticut Emerging Infections Program, Yale University, New Haven, CT

Microbiologic Testing to Identify Shiga Toxin-producing *E. coli* in HUS Patients: FoodNet 1997-2001

C. R. Braden[1], J. C. Lay[1], E. Boothe[2], D. J. Vugia[3], N. Dumas[4], B. Shiferaw[5], E. Wagstrom[6], S. Tong[7], S. Burnite[8], S. M. Thomas[9], S. Hurd[10], and the EIP FoodNet Working Group[1]

[1]CDC, Atlanta, GA, [2]Tennessee Department of Health, Nashville, TN, [3]California Department of Health Services, Berkeley, CA, [4]New York State Department of Health, Albany, NY, [5]Oregon Department of Human Services, Portland, OR, [6]Minnesota Department of Health, Minneapolis, MN, [7]Maryland Department of Health and Mental Hygiene, Baltimore, MD, [8]Colorado Department of Public Health and Environment, Denver, CO, [9]Georgia Division of Public Health, Baltimore, MD, [10]Connecticut Emerging Infections Program, Yale University, New Haven, CT

Risk Factors for Sporadic *Escherichia coli* O157 Infections in the United States: A Case-control Study in FoodNet Sites, 1999-2000

M. H. Kennedy[1], T. Rabatsky-Ehr[2], S. M. Thomas[3], S. Lance-Parker[3], J. Mohle-Boetani[4], K. Smith[5], W. Keene[6], P. Sparling[7], F. P. Hardnett[1], P. S. Mead[1], and the EIP FoodNet Working Group[1]

[1]CDC, Atlanta, GA, [2]Connecticut Emerging Infections Program, Yale University, New Haven, CT, [3]Georgia Division of Public Health, Atlanta, GA, [4]California Department of Health Services, San Francisco, CA, [5]Minnesota Department of Health, Minneapolis, MN, [6]Oregon Department of Human Services, Portland, OR, [7]USDA, Food Safety and Inspection Service, Washington, DC

Re-Estimating the Global Burden of Typhoid Fever

J. A. Crump, S. P. Luby, E. D. Mintz

CDC, Atlanta, GA

Yersinia enterocolitica Surveillance in Minnesota

J. Scheftel[1], J. Bender[2], F. Leano[1], D. Boxrud[1], K. Smith[1]

[1]Minnesota Department of Health, Minneapolis, MN, [2]University of Minnesota College of Veterinary Medicine, Saint Paul, MN

Session 76

Slide Session

Antimicrobial Resistance II

Tuesday, March 26, 2:45 p.m. – 4:15 p.m.

Centennial Ballroom III

Moderators:

ANNE SCHUCHAT, CDC, Atlanta, GA

FRED TENOVER, CDC, Atlanta, GA

Randomized Trial of Day Care Staff Education to Improve Parent Knowledge and Attitudes Regarding Appropriate Antibiotic Use

D. R. Croft[1], E. Belongia[2], M. Knobloch[2], P. Chyou[2], R. Besser[3], J. P. Davis[4]

[1]Wisconsin Division of Public Health and CDC, Madison, WI, [2]Marshfield Medical Research Foundation, Marshfield, WI, [3]CDC, Atlanta, GA, [4]Wisconsin Division of Public Health, Madison, WI

Quinupristin/Dalfopristin-Resistant *Enterococcus faecium* Isolated from Human Stools, Retail Chicken, and Retail Pork: EIP Enterococci Project

K. Gay, K. Joyce, J. E. Stevenson, F. J. Angulo, T. Barrett, and the NARMS Working Group

CDC, Atlanta, GA

Antimicrobial Resistance in *Salmonella* Serotype Typhimurium, R-Type ACSSuT, is Associated with Bacteremia: NARMS 1996-2000

K. Molbak[1], J. K. Varma[2], S. Rossiter[2], J. C. Lay[2], K. Joyce[2], K. Stamey[2], F. J. Angulo[2], and the NARMS Working Group[2]

1Statens Serum Institut, Copenhagen, DENMARK, [2]CDC, Atlanta, GA

Antimicrobial Resistance in *Salmonella* Is Associated with Increased Hospitalization: NARMS 1996-2000

J. K. Varma[1], K. Mølbak[2], S. Rossiter[1], M. A. Hawkins[3], T. F. Jones[4], S. H. Mauvais[5], T. Rabatsky-Ehr[6], S. Stenzel[7], D. J. Vugia[8], M. Park[9], K. Joyce[1], K. Stamey[1], H. Chang[10], F. J. Angulo[1], and the EIP FoodNet Working Group[1]

[1]CDC, Atlanta, GA, [2]Staten Serum Institut, Copenhagen, DENMARK, [3]University of Maryland School of Medicine, Baltimore, MD, [4]Tennessee Department of Health, Nashville, TN, [5]Oregon Department of Human Services, Portland, OR, [6]Connecticut Emerging Infections Program, Yale University, New Haven, CT, [7]Minnesota Department of Health, Minneapolis, MN, [8]California Department of Health Services, Berkeley, CA, [9]Georgia Division of Public Health, Atlanta, GA, [10]New York State Department of Health, Albany, NY

Emerging Fluoroquinolone Resistance among Non-Typhoidal *Salmonella* in the United States: NARMS 1996-2000

S. Rossiter, J. McClellan, T. Barrett, K. Joyce, A. D. Anderson, and the NARMS Working Group

CDC, Atlanta, GA

Prevalence of *Salmonella* spp. and *Campylobacter* spp. Following the Discontinued Use of Antimicrobial Growth Promoters in Broilers and Swine in Denmark

M. C. Evans, H. C. Wegener

Danish Zoonosis Centre, Danish Veterinary Institute, Copenhagen, DENMARK

Session 77

Slide Session

Vectorborne Diseases II

Tuesday, March 26, 2:45 p.m. – 4:15 p.m.

Centennial Ballroom IV

Moderators:

C. J. PETERS, University of Texas Medical Branch, Galveston, TX

BOB SWANEPOEL, National Institute for Virology, Sandringham, SOUTH AFRICA

A Greenhouse Study to Model Potential Field Use of Genetically Modified Bacterial Symbionts for Chagas Disease Control

P. Sen[1,2], E. M. Dotson[1], A. Betz[1], J. Anderson[1], G. Groner[1], O. Kruglov[3], R. V. Durvasula[3], C. B. Beard[1]

[1]CDC, Atlanta, GA, [2]Association of Public Health Laboratories, Washington, DC, [3]Yale University School of Medicine, New Haven, CT

Ecological Niche Modeling and Differentiation of Populations of *Triatoma brasiliensis* Neiva, 1911, the Most Important Chagas Disease Vector in Northeastern Brazil (Hemiptera, Reduviidae, Triatominae)

J. Costa[1], A. Townsend Peterson[2], C. Ben Beard[1]

[1]CDC, Atlanta, GA, [2]The University of Kansas, Lawrence, KS

In vivo Sensitivity of *Plasmodium falciparum* to Chloroquine and Sulfadoxine/Pyrimethamine During an Outbreak of Malaria in Burundi, 2001

F. Dantoine

EPICENTRE, Paris, FRANCE

Risk Factors for Lyme Borreliosis: A German Case-Control Study

J. Fitzner[1], **A. Ammon**[1], I. Baumann[2], T. Talaska[3], A. Schönberg[4], K. Stoebel[4], V. Fingerle[5], B. Wilske[5], L. R. Petersen[6]

[1]Robert Koch Institute, Berlin, GERMANY, [2]Gesundheitsamt Oder-Spree, Beeskow, GERMANY, [3]Beratergruppe Lyme Borreliose Oder-Spree, Lindow, GERMANY, [4]Federal Institute for Health Protection of Consumers and Veterinary Medicine, Berlin, GERMANY, [5]Max v. Pettenkofer Institute, Ludwigs-Maximilians-Universität, Munich, GERMANY, [6]CDC, Fort Collins, CO

Dengue Fever Outbreak in Hawaii – 2001

P. Effler[1], L. Pang[2], P. Kitsutani[3], M. Nakata[1], K. Mills[2], V. Vorndam[4], K. Street[2], J. Elm[1], T. Tom[1], P. Reiter[4], J. Rigau[4], J. M. Hayes[4], D. Sasaki[1], M. Napier[5], G. Clark[4], D. Gubler[6]

[1]State of Hawaii Department of Health, Honolulu, HI, [2]Maui District Health Office, Wailuku, HI, [3]CDC, Atlanta, GA, [4]CDC, San Juan, PR, [5]Pacific Disaster Center, Kihei, HI, [6]CDC, Fort Collins, CO

Re-Introduction of Dengue 3 in Aragua, Venezuela: Clinical, Epidemiological and Laboratory Features of a New Outbreak

G. Comach[1], M. Jimenez[1,2], M. De Quintana[1,2], D. Camacho[1,2], M. Salcedo[1], A. Chiarello[1,2], M. Bracho[1], M. Alvarez[1], M. Soler[1], G. Sierra[1], E. Sanchez[1], I. Villalobos[3], J. Duarte[3], E. Rojas[2], F. Herrera[1], L. Urdaneta[1], R. Barrios[1], N. Zoghbi[1], Y. Rubio[4], N. Uzcategui[5], R. Cuello De Uzcategui[6], E. C. Holmes[7], E. A. Gould[5], F. Liprandi[8], A. P. Goncalvez[8]

[1]LARDIDEV-BIOMED, Universidad de Carabobo, Maracay, VENEZUELA, [2]Corposalud Aragua, Maracay, VENEZUELA, [3]Hospital Central de Maracay, Maracay, VENEZUELA, [4]IAESP-MSDS, Maracay, VENEZUELA, [5]Centre of Ecology and Hydrology (CEH), Oxford, UNITED KINGDOM, [6]Centro Microbiologia y Biologia Celular, IVIC, Caracas, VENEZUELA, [7]Department of Zoology, University of Oxford, Oxford, UNITED KINGDOM, [8]Laboratorio de Biologia de Virus, IVIC, Caracas, VENEZUELA

Session 78

Slide Session

Prevention and Control Strategies

Tuesday, March 26, 2:45 p.m. – 4:15 p.m.

Regency Ballroom V

Moderators:

LEIGH SAWYER, NIH, Bethesda, MD

LARRY SCHONBERGER, CDC, Atlanta, GA

An Evaluation of an Educational Videotape to Prevent Botulism Among Alaska Natives

C. Dentinger[1], A. Horn[2], L. Chiou[3], D. Dahlberg[2], T. Hennessy[1], J. Butler[1]

[1]CDC, Anchorage, AK, [2]Bristol Bay Area Health Corporation, Dillingham, AK, [3]University of Washington, School of Medicine, Seattle, WA

Session 78 continued

Active Laboratory Surveillance in Massachusetts

B. Bolstorff, G. Conidi, J. Daniel, L. Glenn, G. Hamilton, D. Heisey, T. LaPorte, J. Nsubuga, B. Matyas

Massachusetts Department of Public Health, Jamaica Plain, MA

The Emergence of Serogroup Y Disease and the Epidemiology of Invasive Meningococcal Disease in Colorado, 1997 - 2001

L. M. Hammond, K. A. Gershman

Colorado Department of Public Health and Environment, Denver, CO

Transmission of the Main Viral Pathogens Causing Gastroenteritis, NLV, SLV and Rotavirus

M. A. de Wit, M. P. Koopmans, **Y. T. van Duynhoven**

National Institute of Public Health and the Environment, Bilthoven, NETHERLANDS

Improving Influenza and Pneumococcal Vaccination Rates for People 65+ in Rhode Island through Coalition Building Efforts

T. E. Bertrand

Rhode Island Department of Health, Providence, RI

Evidence of Effectiveness of Egg Quality Assurance Programs, Mandatory Refrigeration, and Traceback Investigations To Mitigate Egg-Associated *Salmonella enteritidis* Infections in the United States

G. A. Mumma, P. M. Griffin, M. I. Meltzer, C. R. Braden, R. V. Tauxe

CDC, Atlanta, GA

Session 79

Slide Session

Molecular Diagnostics and Epidemiology II

Tuesday, March 26, 4:30 p.m. – 6:00 p.m.

Centennial Ballroom I

Moderators:

MARY GILCHRIST, Iowa State Health Department, Iowa City, IA

BALASUBR A. SWAMINATHAN, CDC, Atlanta, GA

Detection of La Crosse Virus in Cerebrospinal Fluid and Tissues by Reverse Transcription-Polymerase Chain Reaction

B. Slater[1], K. Bloch[2], T. F. Jones[3], G. Woodlief[4], T. McPherson[4], C. Huang[1]

[1]New York State Department of Health, Slingerlands, NY, [2]Vanderbilt University Medical Center, Nashville, TN, [3]Tennessee Department of Health, Nashville, TN, [4]North Carolina State Laboratory of Public Health, Raleigh, NC

Real-time Fluorescence PCR Assays for the Detection and Characterization of Heat-labile and Heat-stable Enterotoxin Genes from Enterotoxigenic *Escherichia coli*

M. Youssef[1], N. Strockbine[1], N. Lehn[2], U. Reischl[2]

[1]CDC, Atlanta, GA, [2]Institute of Medical Microbiology and Hygiene, University of Regensburg, Regensburg, GERMANY

Development and Evaluation of PCR-based Diagnostics for Identification of *Salmonella* O Antigens Based on the rfb Locus

R. Sherwood, **C. Fitzgerald**, L. Gheesling, P. I. Fields

CDC, Atlanta, GA

PulseNet Experience: Software Changes and Improvements to Online *E. coli* National Database

S. B. Hunter, K. A. Kubota, E. M. Ribot, B. Swaminathan

CDC, Atlanta, GA

Molecular Characterisation of a Multiresistant Strain of *Salmonella enterica* Serotype Typhimurium DT204b Responsible for an International Outbreak of Salmonellosis

E. J. Threlfall[1], E. A. Lindsay[1], A. J. Lawson[1], R. A. Walker[1], L. R. Ward[1], H. R. Smith[1], F. W. Scott[1], S. J. O'Brien[2], I. S. T. Fisher[2], P. D. Crook[2], D. Wilson[3], D. J. Brown[4], H. Hardardottir[5], W. J. B. Wannet[6], H. Tschäpe[7]

[1]Central Public Health Laboratory, London, UNITED KINGDOM, [2]PHLS Communicable Diseases Surveillance Centre, London, UNITED KINGDOM, [3]County Durham and Darlington Health Authority, Durham, UNITED KINGDOM, [4]North Glasgow Univeristy Hospitals NHS Trust, Glasgow, UNITED KINGDOM, [5]Landspitali University Hosptial, Reykjavik, ICELAND, [6]National Institute of Public Health and the Environment, Bilthoven, NETHERLANDS, [7]Robert-Koch Institut, Werningerode/Harz, GERMANY

Determination of Allelic Diversity in the *mec* Operon of Methicillin-Resistant *Staphylococcus aureus* in Wisconsin

S. K. Shukla[1], M. E. Stemper[1], J. M. Conradt[1], R. A. Reich[2], S. V. Ramaswamy[2], E. A. Graviss[2], K. D. Reed[1]

[1]Marshfield Medical Research Foundation, Marshfield, WI, [2]Baylor College of Medicine, Houston, TX

Session 80

Slide Session

Surveillance and Information Systems

Tuesday, March 26, 4:30 p.m. – 6:00 p.m.

Centennial Ballroom II

Moderators:

JAMES GIBSON, South Carolina Department of Health, Columbia, SC

MICHAEL GREGG, Private Consultant in Epidemiology, Guilford, VT

Analysis of a Health Indicator Surveillance System: Its Ability To Detect Annual Influenza Activity for the 1999-2000 and 2000-2001 Seasons Compared to Traditional Surveillance Systems

J. Lee, J. Pavlin, Y. Elbert, P. Kelley

Department of Defense Global Emerging Infections System, Silver Spring, MD

Lessons Learned from Implementing Electronic Laboratory Reporting, New York State

P. F. Smith, M. Davisson, J. M. Fuhrman, H. Chang, I. J. Gotham, G. Birkhead, D. L. Morse

New York State Department of Health, Albany, NY

Outbreak Surveillance: An Important Tool for Controlling Communicable Diseases

M. G. Baker, C. N. Thornley

ESR, Wellington, NEW ZEALAND

Lyme Disease Incidence in Wisconsin: A Comparison of State Reported Rates with Rates from a Population-Based Cohort

A. Naleway[1], E. Belongia[1], J. Kazmierczak[2], R. Greenlee[1], J. Davis[2]

[1]Marshfield Medical Research Foundation, Marshfield, WI, [2]Wisconsin Division of Health, Madison, WI

Surveillance for Patients with Acute Febrile Illness in Egypt

S. Afifi[1], M. A. Azab[1], F. G. Youssef[1], H. El Sakka[1], K. Earhart[1], S. El Oun[2], F. Mahoney[1,3]

[1]U.S. Naval Medical Research Unit No. 3, Cairo, EGYPT, [2]Ministry of Health and Population, Cairo, EGYPT, [3]Centers for Disease Control and Prevention, Atlanta, GA

Foodborne Viruses in Europe: Web-Based Technologies for Investigation of Transnational Outbreaks of Viral Gastroenteritis

M. Koopmans[1], B. A. Lopman[2], H. Vennema[1], M. Reacher[2], J. Carrique-Mas[3], Y. van Duynhoven[4], F. Hanon[5], D. W. Brown[2]

[1]Research Laboratory for Infectious Diseases, National Institute for Public Health and the Environment (RIVM), Bilthoven, NETHERLANDS, [2]Public Health Laboratory Service, London, UNITED KINGDOM, [3]Swedish Institute for Infectious Disease Control, Solna, SWEDEN, [4]2Research Laboratory for Infectious Diseases, National Institute for Public Health and the Environment (RIVM), Bilthoven, NETHERLANDS, [5]Statens Serum Institute, Copenhagen, DENMARK

Session 81

Slide Session

Influenza

Tuesday, March 26, 4:30 p.m. – 6:00 p.m.

Regency Ballroom V

Moderators:

JANE SIEGEL, University of Texas Southwestern Medical Center, Dallas, TX

ROBERT WEBSTER, St. Jude Children's Research Hospital, Memphis, TN

PER.C6: A Human Designer Cell Line Providing a Pandemic Proof Platform for the Manufacturing of Safe Influenza Vaccines

M. Pau, C. Ophorst, M. Oerlemans, A. Vooys, J. Pasma, R. Lonsdale, G. Marzio, C. Tuijn, **F. G. UytdeHaag**

Crucell Holland BV, Leiden, NETHERLANDS

Acute Respiratory Virus Surveillance in Cairo and Alexandria, Egypt, July 2000 to June 2001

D. E. Salman[1], S. Lewis[1], E. Aoun[2], C. Fayez[1], H. M. Esmat[2], B. Botros1, A. K. Soliman[1], G. D. Chapman[1], R. R. Graham[1]

[1]U. S. Naval Medical Research Unit No. 3, Cairo, EGYPT, [2]Ministry of Health and Population, Cairo, EGYPT

Influenza Surveillance in New York State, 1998-2001

M. Kacica, V. Randle

New York State Department of Health, Albany, NY

Geographical Coherence of Influenza Epidemics in the US, France and Australia: 1978-98

C. Viboud[1], A. Flahault[1,2]

[1]INSERM U444, Paris cedex 12, FRANCE, [2]Centre-Hospitalier Saint-Antoine, Paris cedex 12, FRANCE

A DoD Global Influenza Surveillance Program

L. C. Canas, J. S. Neville, A. R. Krull, M. J. Rodriguez, L. T. Daum

Brooks Air Force Base, San Antonio, TX

Using CUSUM Techniques To Identify Influenza Outbreaks

V. Foster[1], J. Matheson[1], **M. Stoto**[2]

[1]George Washington University School of Public Health & Health Services, Washington, DC, [2]The RAND Corporation, Arlington, VA

Session 82

Slide Session

Global Health and GIS

Tuesday, March 26, 4:30 p.m. – 6:00 p.m.

Centennial Ballroom IV

Moderators:

HARRISON SPENCER, Association of Schools of Public Health, Washington, DC

MARY WILSON, Harvard University, Boston, MA

Tuberculosis Status Among Iranian and Afghan patients Admitted to the National Research Institute of Tuberculosis and Lung Disease (1998-2000)

M. Yazdanpanah, M. R. Masjedi, H. Masjedi, M. Hosseini, A. Velayati

National Research Institute of Tuberculosis and Lung Disease, Tehran, IRAN

Modeling Tuberculosis Dissemination in Harris County, Texas, 1995-1998, with Spatial Analysis and Geographic Information Systems (GIS)

M. L. Stone[1], E. A. Graviss[2], L. Teeter[2]

[1]University of Texas-Houston, School of Public Health, Houston, TX, [2]Baylor College of Medicine, Houston, TX

Mapping of West Nile Virus Risk in the Northeast United States Using Multi-Temporal Meteorological Satellite Data

P. Backenson[1], D. J. White[1], M. Eidson[1], P. F. Smith[1], L. D. Kramer[1], D. L. Morse[1], C. J. Tucker[2], M. F. Myers[3], S. I. Hay[4], S. E. Randolph[4], D. J. Rogers[4]

[1]New York State Department of Health, Albany, NY, [2]NASA, Greenbelt, MD, [3]International Research Partnership for Infectious Diseases, Greenbelt, MD, [4]Oxford University, Oxford, UNITED KINGDOM

Session 82 continued

Investigation of Q Fever in Bosnia-Herzegovina, 2000: An Example of International Cooperation

J. H. McQuiston[1], W. L. Nicholson[1], R. Velic[2], R. V. Gibbons[1], L. Castrodale[1], S. H. Wainwright[3], T. J. Vannieuwenhoven[3], E. W. Morgan[4], L. Arapovic[2], A. Delilic[2], P. Puvacic[5], T. Bajrovic[2]

[1]CDC, Atlanta, GA, [2]Veterinary Faculty, Sarajevo, BOSNIA AND HERZEGOVINA, [3]USDA-APHIS, Riverdale, MD, [4]US Army - SFOR, Sarajevo, BOSNIA AND HERZEGOVINA, [5]Ministry of Health, Sarajevo, BOSNIA AND HERZEGOVINA

A WHO Global Salm-Surv Retrospective Study Examining *Salmonella* Serotypes in South America, 2000: Dominance of *Salmonella* Serotype Enteritidis

WHO Global Salm-Surv South America Working Group[1],WHO Global Salm-Surv[2]

[1]Instituto INEI-ANLIS "Carlos G Malbran", Buenos Aires, ARGENTINA, [2]World Health Organization, Geneva, SWITZERLAND

Recurrent Histoplasmosis Outbreaks in Acapulco, Mexico

Y. A. Roldán, L. E. Soto-Ramírez, G. Rosales, G. R. Pena, J. Sifuentes-Osornio, L. Taylor, **G. M. Ruiz-Palacios**

National Institute of Medical Science and Nutrition, Mexico City, MEXICO

Session 83

Slide Session

Latebreakers II

Tuesday, March 26, 4:30 p.m. – 6:00 p.m.

Centennial Ballroom III

Moderators:

PHILIP BRACHMAN, Emory University, Atlanta, GA

JOHN EISOLD, Attending Physician, U.S. Congress, Washington, DC

Wednesday, March 27

Session 84

Meet-the-Experts

Wednesday, March 27, 7:30 a.m. – 8:15 a.m.

Regency Ballroom VI/VII

Behind the Scenes at the *Emerging Infectious Disease* Journal

PETER DROTMAN, POLY POTTER, BRIAN MAHY, CDC, Atlanta, GA

Prevention Effectiveness

MARTIN MELTZER, CDC, Atlanta, GA

ANNE HADDIX, Emory University, Atlanta, GA

Session 85

Plenary Session V

Wednesday, March 27, 8:30 a.m. – 10:00 a.m.

Centennial Ballroom I/II

Moderators:

HAROLD JAFFE, CDC, Atlanta, GA

JOHN McGOWAN, Rollins School of Public Health, Emory University, Atlanta, GA

Global Drug Resistance: The Case of *Streptococcus pneumoniae*

KEITH KLUGMAN, Emory University, Atlanta, GA

Use of Antiretroviral Agents in Developing Countries

PETER MUGYENYI, Joint Clinical Research Center, Kampala, UGANDA

Session 86

Plenary Session VI

Wednesday, March 27, 8:30 a.m. – 10:00 a.m.

Centennial Ballroom III/IV

Moderators:

NANCY COX, CDC, Atlanta, GA

ALTAF LAL, CDC, Atlanta, GA

Virology of 1918 Flu Pandemic

ANN REID, Armed Forces Institute of Pathology, Rockville, MD

Genetic Susceptibility to Infectious Diseases

JANET MCNICOLL, CDC, Atlanta, GA

Session 89

Invited Panel

Emerging Vaccines for Emerging Diseases

Wednesday, March 27, 10:30 a.m. – 12:00 noon

Centennial Ballroom I

Conveners/Moderators:

IRENE GLOWINSKI, NIH, Bethesda, MD

MELINDA WHARTON, CDC, Atlanta, GA

Rotavirus Vaccines in Development

RAJIV BAHN, All India Institute of Medical Sciences, New Delhi, INDIA

Group B Meningococcal Vaccines

GUSTAVO SIERRA, Finlay Institute, Habana, CUBA

New Technologies and Vaccine Development

MARGARET ANN LIU, Bill and Melinda Gates Foundation, Seattle, WA

Anthrax Vaccines

ARTHUR FRIEDLANDER, U.S. Army Medical Research Institute of Infectious Diseases, Fort Detrick, MD

Session 90

Invited Panel

Anatomy of Emerging Infectious Diseases

Wednesday, March 27, 10:30 a.m. – 12:00 noon

Centennial Ballroom II

Conveners/Moderators:
LINDA DETWILER, U.S. Department of Agriculture, Robbinsville, NJ

RIMA KHABBAZ, CDC, Atlanta, GA

The Agent: Prions as Emerging Infectious Particles
DAVID BOLTON, New York State Institute for Basic Research, Staten Island, NY

The Reservoir: Bovine Spongiform Encephalopathy (BSE) and What's Been Done About It
DAGMAR HEIM, Swiss Federal Veterinary Office, Bern, SWITZERLAND

The Unfolding Variant Creutzfeldt-Jakob Disease (vCJD) Epidemic
ROBERT WILL, Western General Hospital, Edinburgh, UNITED KINGDOM

Impact of the BSE/vCJD Outbreak: U.S. Concerns for TSEs
ERMIAS BELAY, CDC, Atlanta, GA

Session 91

Invited Panel

Antimicrobial Resistance

Wednesday, March 27, 10:30 a.m. – 12:00 noon

Centennial Ballroom III

Conveners/Moderators:
DAVID BELL, CDC, Atlanta, GA

ABIGAIL SALYERS, American Society for Microbiology, Washington, DC

Implications of Gene Transfer and Inducible Resistance for Successful Therapy
ABIGAIL SALYERS, American Society for Microbiology, Washington, DC

Prospects for New Antimicrobial Drug Development: Industry Perspective
GAIL H. CASSELL, Eli Lilly and Company, Indianapolis, IN

Computerized Decision Support for Appropriate Antimicrobial Drug Prescribing
MATTHEW SAMORE, University of Utah, Salt Lake City, UT

Promoting Appropriate Antimicrobial Drug Use in Developing Countries
SAYOMPORN SIRINAVIn, Mahidol University, Bangkok, THAILAND

Session 92

Invited Panel

Infectious Diseases in Aging Populations

Wednesday, March 27, 10:30 a.m. – 12:00 noon

Centennial Ballroom IV

Conveners/Moderators:
JAY BUTLER, CDC, Anchorage, AK

WILLIAM ERSHLER, Institute for Advanced Studies in Aging and Geriatric Medicine, Washington, DC

Biology of Aging
STEVEN CASTLE, University of California at Los Angeles, Los Angeles, CA

Biology of Immune Senescence
RICHARD MILLER, University of Michigan, Ann Arbor, MI

Impact of Aging on the Epidemiology of Infections in Adults
THOMAS YOSHIKAWA, Charles R. Drew University of Medicine and Science, Los Angeles, CA

HIV in the Older Patient
BRADLEY BENDER, University of Florida, Gainesville, FL

Session 93

Invited Panel

Foreign Policy and Infectious Diseases

Wednesday, March 27, 10:30 a.m. – 12:00 noon

Regency Ballroom V

Convener/Moderator:
STEPHEN B. BLOUNT, CDC, Atlanta, GA

Global Fund to Fight HIV/AIDS, TB and Malaria (New Political/Economic Model for Addressing Priority Infectious Diseases)
BILL STEIGER, U.S. Department of Health and Human Services, Washington DC

Infectious Diseases and U.S. Foreign Policy from a State Department Perspective
JACK CHOW, U.S. Department of State, Washington, DC

Infectious Diseases: The World Bank Perspective
OK PANNENBORG, The World Bank, Washington, DC

EXHIBITORS LISTING

The ICEID Exhibit Hall opens on Sunday, March 24 from 12:00 noon – 5:00 p.m., poster presentations are available for viewing all day, authors will be standing at their posters from 3:30 – 5:00 p.m. The Opening Reception, at which substantial hors d'oeuvres and refreshments will be served, will be held in the Exhibit Hall from 7:00 – 9:00 p.m., Late Breaker poster presentations will be held at that time. The Exhibit Hall will also open on Monday, March 25, from 10:00 a.m. to 6:00 p.m. (poster authors available 4:30 – 6:00 p.m.), and Tuesday, March 26, from 8:30 a.m. to 1:00 p.m. (poster authors available 8:30 – 10:00 a.m.).

Academia Book Exhibits — booth 8

7700 Cerro Gordo Road
Gainesville, VA 20144-1929
703/753-2261
acadbkex.com

Academia Book Exhibits organizes and arranges professional combined book and journal displays.

Air Sea Atlanta, Inc. — booth 7

1234 Logan Circle
Atlanta, GA 30318
404/351-8600
www.airseaatlanta.com

Air Sea Atlanta, Inc., is a world-wide supplier of a most comprehensive range of United Nations–certified packaging for transport of infectious or diagnostic specimens, with or without dry ice or cool packs, to the pharmaceutical and biomedical industries. All items are available for immediate shipment, with no minimum order quantity.

American Society for Microbiology — booth 12

1752 N Street, NW
Washington, DC 20036
202/737-3600
www.asmusa.org

The American Society for Microbiology is the oldest and largest single life science membership organization in the world, representing over 42,000 microbiologists throughout the world. ASM represents 25 disciplines of microbiological specialization plus a division for microbiology educators. ASM is comprised of five boards—Education and Training, Meetings, Membership, Public and Scientific Affairs, and Publications, plus the American Academy of Microbiology. ASM Programs represented at ICEID include Meetings and Publications.

Applied Maths, Inc. — booth 18

512 East 11th Street
Suite 207
Austin, TX 78701
512/482-9700
www.Applied-Maths.com

Applied Maths develops innovative software solutions for the biosciences. Areas of specialization are pattern-matching algorithms, clustering and identification methods, and data-mining tools for massive datasets such as microarrays and gene chips. Since 1991, Applied Maths has set the trend for the analysis of fingerprints with the renowned GelCompar package. Today the company continues to be a pioneer in bioinformatics, with BioNumerics, GelCompar II, GeneMaths, and GeneBase.

Armed Forces Institute of Pathology—Public Affairs Office — booth 19

6825 16th Street, NW
Bldg 54, Room 1106
Washington, DC 20306-6000
www.afip.org

The AFIP, a tri-service Institute of the U.S. Department of Defense (DoD) in Washington,DC, presents material highlighting its DoD readiness support. Included are AFIP efforts to identify emerging infections and disease patterns, such as bioterrorism agent detection and collaborative research and surveillance, and sophisticated technology to track environmental toxins and adverse drug reactions. Programs featured include Persian Gulf War Illness studies, expanded DNA research and applications, molecular biology and genetics research programs, and veterinary pathology work.

U.S. Army Healthcare Recruiting — booth 31

1568 Hood Avenue
Forest Park, GA 30297-5104

Career and educational opportunities with the Medical Department of the U..S Army and U.S. Army Reserve.

Association of Public Health Laboratories — booth 14

2025 M Street, NW
Suite 550
Washington, DC 20036-3320
202/822-5227
www.aphl.org

The Association of Public Health Laboratories (APHL) is a professional, non-profit organization representing national, state, and local public health laboratories. APHL collaborates with partners in private and public sectors, advocating and formulating sound public health and environmental health policies, and providing technical assistance and training.

Blackhawk BioSystems, Inc. — booth 9

12945 Alcosta Blvd
San Ramon, CA 94583
800/866-0305
www.blackhawkbiosystems.com

Blackhawk BioSystems is a leading worldwide manufacturer of quality control products for use in laboratories that perform infectious disease testing. Products available include the complete line of VIROTROL® independent quality assurance reagents that are used with commercially available testing procedures for hepatitis, HIV, sexually transmitted diseases, and other test procedures.

Centers for Disease Control and Prevention — booth 5

1600 Clifton Road, NE
Atlanta, GA 30333
www.cdc.gov

In 1995, the Centers for Disease Control and Prevention (CDC) launched a national campaign to reduce antimicrobial resistance through the promotion of more judicious antibiotic use. This campaign is comprehensive and extensive, encompassing public media, professional education, and applied research and surveillance activities. CDC's National Campaign for Appropriate Antibiotic Use has two objectives:

1. Reduce inappropriate antibiotic use
2. Reduce the spread of resistance to antibiotics

To accomplish these objectives, the campaign has several major areas of activity:

- Developing strategies and materials that will lead to changes in risk behaviors related to antibiotic use
- Serving as a resource to groups implementing and

evaluating campaigns and intervention programs

- Forming partnerships to harness the resources of collaborating organizations
- Assessing the impact on antibiotic use, resistance, and patient/provider satisfaction.

Centers for Disease Control and Prevention — Morbidity and Mortality Weekly Report — booth 2

1600 Clifton Road, NE
Atlanta, GA 30333
404/639-3636
www.cdc.gov/mmwr

The office of Scientific and Health Communications (OSHC) mission is to conduct effective scientific and health communications, develop new information concepts and systems such as Multimedia MMWR Epidemic Information Exchange (Epi-X), and provide consultation and training programs.

Centers for Disease Control and Prevention — National Center for Infectious Diseases — booth 13

1600 Clifton Road, NE
Atlanta, GA 30333
404/639-3311
www.cdc.gov

CDC's vision for the future is a world in which all available tools are used to combat today's diseases and prevent those of tomorrow. *Preventing Emerging Infectious Diseases: A Strategy for the 21st Century* describes a strategy for moving towards the fulfillment of this vision. This strategy and other informational and educational literature regarding infectious diseases are available at the exhibit booth.

Cereplex — booth 22

1124 Sorrel Ridge Lane
Oakton, VA 22124
www.cereplex.com

Cereplex provides information technologies to hospitals and clinics to help them automate disease detection and reporting (both routine and for bioterrorism detection), address nosocomial infections and antibiotic resistance, and improve the quality of care they provide.

U.S. Department of Agriculture — Animal and Plant Health Inspection Service — booth 30

555 South Howes Street
Fort Collins, CO 80521
www.aphis.usda.gov

The U.S. Department of Agriculture's (USDA) Animal and Plant Health Inspection Service (APHIS) provides leadership in ensuring the health and care of animals and plants. APHIS safeguards resources from exotic invasive pests and diseases, monitors and manages agricultural pests and diseases existing in the United States, resolves and manages trade issues related to animal or plant health, and ensures the humane care and treatment of animals.

U.S. Department of Defense — Global Emerging Infections System — booth 26

503 Robert Grant Avenue
Silver Springs, MD 20910-7500
301/319-9072
www.geis.ha.osd.mil

The mission of the DoD-GEIS is to implement the Presidential Directive on emerging infections through an international, coordinated, joint Service Program focused on timely recognition and control of emerging and re-emerging infections. The means include systematic surveillance (especially laboratory-based), research, response, training, and capacity building. This mission is executed in two primary settings: the DoD's unique overseas laboratory network and the service-specific hubs.

ESRI — booth 1

380 New York Street
Redlands, CA 92373
909/793-2853
www.esri.com/industry/health

ESRI develops computer software that maps health data. ArcView, ESRI's most well known geographic information systems (GIS) software is used by over 5,000 health organizations world wide, in areas such as epidemiology, in-home service routing, marketing, research and Internet mapping. Visit ESRI on the web at www.esri.com/industry/health.

EXAKT Technologies, Inc. — booth 16

7416 N Broadway Extension
Suite E
Oklahoma City, OK 73116-9066
405/848-5800
www.exaktpak.com

Whether you're shipping vials, jars, Petri dishes, or even medical devices, EXAKT offers infectious substance and diagnostic specimen packaging tailored to fit your specific shipping needs. Our packaging approach gives us the flexibility to provide a customized packaging solution to best match your unique shipping requirements. Visit our website at www.exaktpak.com and take our 5Q test, or contact us by e-mail at infopak@exaktusa.com or call toll-free 800/866-7172.

Focus Technologies — booth 28-29

10703 Progress Way
Cypress, CA 90630

At Focus Technologies, formerly MRL, our world revolves around one thing—infectious disease. Our full-service infectious disease laboratory offers over 1200 assays. Our diagnostics group sells serological products worldwide for rare and emerging diseases, as well as type-specific kits for HSV-1 and HSV-2, HerpeSelect™. Focus is also a leader in antimicrobial drug resistance surveillance with TSN—the world's largest antimicrobial susceptibility database.

Fogarty International Center — National Institutes of Health — booth 25

31 Center Drive
MSC 2220
Bethesda, MD 20892-2220

The Fogarty International Center has been a critical component of the NIH international effort since 1968. The Center's mission is to reduce global health disparities by supporting and promoting research and to prepare the current and future generation of international and U.S. scientists to meet global health needs.

Gen-Probe — booth 23

10210 Genetic Center Drive
San Diego, CA 92121
800/523-5001
www.gen-probe.com

Gen-Probe, the recognized world leader in the development, manufacture, and commercialization of genetic probe tests for diagnosing human disease, has been a pioneer in bringing DNA probe assays to the clinical laboratory. Its advanced amplification technologies continue to lead the industry. Representatives will be available to discuss the new APTIMA® Combo 2 Assay, PACE Systems for STDs, and assays for AMPLIFIED™ MTD and GASDirect™.

MIDI, Inc. booth 17
125 Sandy Drive
Newark, DE 19713
302/737-4297
www.midi-inc.com

MIDI, Inc. is dedicated to developing microbial identifcation products and services for research and diagnostic purposes. MIDI develops, manufactures, and sells the Sherlock Microbial Identificaton System worldwide. The Sherlock System identifies bacteria and yeast based on gas chromatographic analysis of their whole cell fatty acid content. Additionally, MIDI provides a Bioterrorism database with each system capable of identifying key agents of biological warfare, including *Bacillus anthracis*.

National Institute of Allergy and Infectious Diseases booth 24
31 Center Drive, Bldg 31, Room 7A-50
MSC 2520
Bethesda, MD 20892-2520
www.niaid.nih.gov

Institute staff will provide materials and information for health care professionals and the general public on NIAID biomedical research areas. These areas include allergic, immunologic, and infectious diseases.

Packard Instrument Company booth 15
800 Research Pkwy
Meriden, CT 06450

Packard Instrument Company is a subsidiary of Packard Bioscience Company, a leading developer, manufacturer, and marketer of analytical instruments and related products and services for use in the drug discovery and molecular biology segments of the life sciences industry and in the nuclear instrumentation industry. Primary products incude the following: automated liquid handling and sample preparation systems, microwell plate readers and plate imaging systems, drug screening and detection reagents, biochip systems, and bioanalytical scintillation instrumentation.

PANBIO, Inc. booth 6
9075 Guilford Road
Columbia, MD 21406
410/381-8550
www.panbio.com.au

Established in 1987, PANBIO, Inc. is a globally focused Australian biotechnology company which specializes in the development, manufacturing, and marketing of diagnostic kits for infectious diseases. With the acquisition of Integrated Diagnostics, Inc. USA (INDX) in 1999 and Stellar Bio Systems, Inc. in 2001, PANBIO's product range includes more than 60 diagnostic assays with a core focus on arbovirus and tick-borne diseases and high quality mouse serum and mouse serum proteins. It has an FDA-approved facility in Columbia, MD.

Pfizer, Inc. booth 11

Public Health Foundation booth 33
1220 L Street, NW
Suite 350
Washington, DC 20005
202/898-5600
www.phf.org

The Public Health Foundation is a national nonprofit organization, which works in partnership with the Centers for Disease Control and Prevention, to provide training and resource materials to public health and clinical professionals. Topics include bioterrorism and emergency preparedness, appropriate antibiotic use, epidemiology, immunizations, influenza, travel medicine, and infectious diseases. PHF also has a free on-line clearinghouse of distance learning courses at www.TrainingFinder.org.

Purified div Germfree Labs booth 10
7435 NW 41st Street
Miami, FL 33166
800/888-5357
www.purified.com

Purified microEnvironments a Division of Germfree Laboratories, Inc., has been manufacturing biological and chemical safety equipment for over 40 years. We specialize in transportable high containment class III gloveboxes and related NBC filtration systems. New products include rapid containment systems for the first responder.

Response Biomedical Corporation booth 21
8855 Northbrook Court
Burnaby, BC, Canada V5J 5J1
604/681-4101
www.responsebio.com

Response Biomedical develops diagnostic tests for use with its FDA cleared RAMP Reader for use in clinical, STAT-lab, and point-of-care applications, as well as rapid on-site environmental testing for biological agents. The RAMP System delivers accurate and reliable results in less than fifteen minutes, and has the potential to be used with more than 250 medical and non-medical tests currently performed in laboratories.

Thermo Forma booth 32
P.O. Box 649
Marietta, OH 45750
800/848-3080
www.thermoforma.com

Thermo Formo is a leading manufacturer of controlled-environment equipment for the educational, biomedical, pharmaceutical, clinical, and industrial research markets. Product lines include cell culture incubators, ultra-low temperature freezers, biological safety cabinets, orbital shakers, LN2 cryopreservation equipment, laboratory refrigerators/freezers, blood bank equipment, and custom-designed products. Stop by our booth for complete details.

Saunders/Mosby/Churchill booth 20
Atlanta, GA
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1 Bioterrorism

Sunday, March 24, 12:00 noon
Grand Hall East

Board 1. Boston's Early Warning Surveillance System for Bioterrorism: September 11 - November 11

J. E. Gunn[1], V. McKenna[1], K. H. Brinsfield[2], K. S. Dyer[2], M. A. Barry[1], Surveillance Task Force[1]

[1]Boston Public Health Commission, Boston, MA, [2]Boston Emergency Medical Services, Boston, MA

Objective: Traditional surveillance systems based in the reporting of specific diseases have limited potential for early detection of mass casualty events such as bioterrorism or pandemic influenza. Prior to 9/11, an electronic real time volume based surveillance system was developed to identify a potential bioterrorism related event in Boston. We report our experience with this surveillance system from 9/11-11/11. **Methods:** Every 24 hours volume data from Boston hospitals was sent electronically to a secure web site. Volume data included urgent care visits and pediatric (PED) and adult (AED) emergency department visits. Using 2000 data, monthly averages of site specific volume were obtained. Adjustments for day of the week were done based on site specific usage patterns. A binomial distribution was used to calculate 99% confidence intervals (CI). The upper 99% CI was compared with daily volume in 2000 to detect excess activity. On days exceeding threshold, rapid on site follow-up was done to identify potential infectious disease clusters. **Results:** From 9/11-11/11 daily volume data was obtained from 9 hospitals which included 11 sites (9 AED, 2 PED, and 1 urgent care center). For all sites a total of 17 days exceeded threshold with at least 2 sites exceeding threshold on 3 days. Combined volume data identified 4 sites exceeding threshold on 10/15 (3 AED and 1 PED). This correlated with reports of anthrax exposures in FL, DC and NYC. Follow-up with sites identified persons seeking nasal swabs and antibiotics for anthrax as the cause of increased activity despite the fact that no anthrax cases or anthrax contaminated environmental specimens had been identified in Massachusetts. **Conclusions:** Volume based surveillance is a feasible method for the early identification of mass morbidity events. In Boston, information from this system was used in October to design public health messages for the general public. A rapid follow-up system is a critical component to understand initial signals. Additional research is needed to define the sensitivity of the individual or combined measures being used and the optimal combination to detect significant activity.

Board 2. The Electronic Surveillance System for the Early Notification of Community-based Epidemics (ESSENCE): GIS Modeling in an Early Detection Surveillance System for Bioterrorist and Natural Disease Threats

C. S. Polyak, Y. Elbert, J. A. Pavlin, P. W. Kelley

Department of Defense Global Emerging Infections System (DoD-GEIS), Washington, DC

Introduction: Current infectious disease surveillance systems are usually not automated, often depend on laboratory confirmation and rely on passive information. ESSENCE, the Electronic Surveillance System for the Early Notification of Community-based Epidemics, is an early detection system for bioterrorist and natural disease threats using syndromic surveillance in the greater Washington, DC area. This automated system provides earlier indication of disease outbreaks in military treatment facilities (MTF) and defines geographically aberrant clinical patterns at the community level allowing for rapid epidemiologic-based targeting of limited response assets. Several agents likely to be used in a bioterrorist attack, such as the causative agents of anthrax, plague and smallpox, initially present as a non-specific flu-like syndrome. In order to assess ESSENCE's ability to geographically track the community-wide patterns of non-specific flu-like syndrome in the greater Washington, DC area, we evaluated data during two influenza outbreaks in 1999 and 2000. Geospatial characteristics of the respiratory syndrome group were used to track the spread of flu-like illness through the community and to assess the utility of incorporating GIS into ESSENCE.

Methods: All military personnel, retirees and beneficiaries located within a 50-mile radius of the National Capital Area (NCA) were included in the study population. Population densities were mapped for those eligible for care at MTFs by residence zip code using ArcView®, a GIS program. The study period incorporates January 1999 to November 2001, including two influenza outbreak periods, defined as October through April of each year (1999/2000; 2000/1). Outpatient clinical information, collected from each clinic and matched to existing demographic databases, was categorized by ICD9 diagnosis into seven separate syndrome groups.

Results & Discussion: A total of 26 MTF's with 106 primary care or emergency clinics serve a population of 400,000 within the NCA. There were a total of 485, 965 respiratory syndrome cases in the study period with a significantly higher number of cases ($p<0.001$) during the influenza outbreak periods. Respiratory syndrome data was examined by day, week, month and season and combined with NCA population data which was classified by zip code, community and city. Rates of respiratory illness were calculated for the combinations and mapped using ArcView®. The average rate of respiratory illness per zip code parcel was greater in the 2000/1 flu season (214/1000 population) than in the 1999/2000 season (154/1000 population). Preliminary analyses determined that clustering based on merged zip code parcels, which depended on population density, have the greatest accuracy. Automatic geospatial analyses, including GIS maps, are a valuable analysis tool and will be incorporated into ESSENCE.

Board 3. A Mathematical Model of the Potential Spread of Smallpox via Air Travel

R. Freeman[1], J. H. Ellis[1], G. E. Glass[2]

[1]Johns Hopkins University, Baltimore, MD, [2]Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD

Of potential pathogens likely to be used as biological weapons, smallpox (variola) may pose one of the greatest risks. Many experts now believe that there are supplies of smallpox outside the confines of the CDC and the Russian State Research Center of Virology and Biotechnology. Although the probability of an intentional release of smallpox is small, if it were to occur, the results would potentially be disastrous.

If a release of the virus were to occur in a US city, smallpox would likely spread both within the city and the US via the transportation network. Over one million travelers board planes every day within the continental US magnifying the potential threat of disease spread. Thus, quarantine of an urban area where smallpox was detected may be a key aspect of disease control strategies. However, the cessation of air travel on September 11 significantly impacted the airline industry and the nation's economy. Stopping

air travel within the US for an extended period to contain the spread of smallpox would have extraordinary consequences. Mathematical models of the potential spread of smallpox may provide insight for preparedness plans and disaster management. Simulations can help identify the possible lag time for intervention and areas where more refined information may improve public health preparedness.

The objective of this research was to explore the potential spread of smallpox via air travel within the US. The purpose is to determine the likelihood of inter-city dispersal of smallpox following secondary infection within Washington, D.C. and the feasibility of air travel quarantine in disease containment strategies. We developed a compartmental model on the basis of previous research concerning the spread of influenza via air travel. 116 US cities were examined in the analysis with a time horizon of one year. We present the results of a series of simulations examining differences in assumptions concerning population susceptibility, transmission rate, initial city of release, airport closure policies and season of virus release.

The results of our simulation suggest that: 1) there is a clear benefit to stopping air travel in and out of cities after one case of the disease is reported; 2) forecast epidemic peak and total case magnitude depends upon the initial city of release in addition to population size; 3) the time lag for action after one case has been reported is very short; 4) season of release plays a potentially important role in epidemic spread and expected cases; and 5) the results of these simulations also highlight the importance of refining estimates concerning the number of secondary cases produced from a single index case and the percentage of persons susceptible.

Board 4. Laboratory-Confirmed Influenza Illness in a Highly Immunized Population

K. M. McNeill[1], B. L. Watts[2], M. B. Goldenbaum[2], Y. Li[3], R. K. Poropatich[4], J. C. Gaydos[5]

[1]Bureau of Disease Control, SC Department of Health and Environmental Control, Columbia, SC, [2]Division of Preventive Medicine, Walter Reed Army Institute of Research, Silver Spring, MD, [3]Allied Technology Group, Inc., Rockville, MD, [4]Department of Medicine, Walter Reed Army Medical Center, Washington, DC, [5]Department of Defense Global Emerging Infections Surveillance and Reponse System, Walter Reed Army Institute of Research, Silver Spring, MD

Background: The Advisory Committee on Immunization Practices (ACIP) estimates the efficacy of influenza vaccine in preventing influenza in healthy individuals under 65 years of age to be about 70-90%. The possibility of respiratory illness in individuals who are currently immunized against influenza is important to consider in assessing the potential value of influenza immunization in the reduction of influenza-like illness (ILI) that might be confused clinically with inhalational anthrax. The US military population is an excellent group in which to study breakthrough illness due to its high rate of influenza immunization. A recent study of febrile acute respiratory disease (ARD) in young, healthy soldiers provided information on breakthrough influenza. **Methods:** During April 1, 1997-March 31, 1999, virus cultures were performed on 340 Army soldier trainees (median age 19 years, 80.3% males) hospitalized with ARD at Fort Gordon, GA. Febrile ARD was defined as fever (100.5° F or higher) with one or more symptoms or signs of a respiratory infection (predominantly cough and sore throat). All individuals had received the current influenza vaccine at least 10 weeks prior to the onset of their illness. Pharyngeal swabs were submitted for virus culture on each patient. **Results:** A virus was cultured from 164 (48.2%) of the soldiers. A total of 29 (8.5%) individuals had influenza virus isolates, including 23 with isolates of influenza A and six with isolates of influenza B. Influenza was second only to adenovirus (98 isolates, 28.8%) as a cause of febrile ARD. Age, gender and temperature were similar for patients with an influenza virus isolate and others hospitalized with ARD. **Conclusion:** Among 340 otherwise healthy young soldiers who had been immunized for influenza and subsequently hospitalized for ARD, 8.5% had an influenza A or B virus isolated; 39.7% had other viruses isolated. For purposes of comparison, the case definition of febrile ARD used in this study closely mirrors that of the CDC ILI case definition (fever of 100° F or higher with cough and/or sore throat). Even though influenza vaccine is highly valued as a public health intervention in the control of influenza, cases of ARD or ILI may occur in highly immunized populations. This situation may result because the vaccine is less than 100% efficacious and many naturally occurring microbes other than influenza are capable of causing ARD or ILI. Objective clinical and laboratory expertise should be used in timely fashion to establish the correct diagnoses. These data support the CDC position that influenza vaccination should not be advocated for the general population solely to reduce the incidence of ILI that might be confused clinically with inhalational anthrax. More intensive laboratory-based surveillance for breakthrough influenza should be performed in military populations to monitor vaccine effectiveness.

Board 5. Modularized Service-Oriented Guidelines in a Distributed Web-Based Environment : A Data Model and Architecture for Managing Bioterrorism and Its Continuous Surveillance

A. Kumar, S. Quaglini, P. Ciccarese, M. Stefanelli

University of Pavia, Pavia, ITALY

The immediate management of the bioterrorism has to be followed by a long term planning in terms of continuous surveillance for bioterrorism and predetermined management methods. The amount of human, material and financial resources, utilized in the management of the current emergencies in bioterrorism clearly determine that a long term expenditure of resources at the current scale is either unfeasible or extremely exhaustive at the national and international levels. The paper defines a new architecture based on knowledge management concepts, for representing and implementing clinical practice guidelines, taking the anthrax emergency as the bench-test. They would help in providing a common platform not only for interaction among different pathologies, but also between various individuals and institutions involved in the health care in general, and infectious disease based bioterrorism in particular.

Health Risk Assessments have always been based on focused questionnaires which neither provide the complete health assessment nor such common platform. The classical view of looking at the guidelines is pathology based. For example, usually the guidelines depict the management of Hepatitis, Anthrax etc. or certain predetermined combinations.

In the proposed architecture we have divided the knowledge into reusable objects called services. This takes into account the conventional medical classification into symptoms, signs, laboratory tests, treatment etc., as well as the universal standards of object orientation in the sector of information technology.

In the non-emergency situations, various reusable guideline modules would run at the level of different institutions involved in the health care. In this case the guidelines become the object flow models, inside which the non-atomic tasks(activities) are divided into reusable atomic actions.

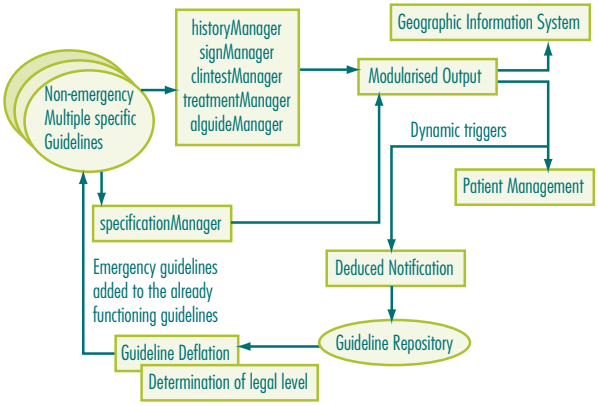
Further, in this scenario, the role of federal bodies, including CDC and ODP, will be to maintain certain guideline repositories and to define the legal level for the compulsion of the implementation of a particular guideline by the health care providers in a particular situation. The emergency guidelines can be released for the nation-wide use in the situations of certain triggers, which in turn, could come from different sources, like general practitioners, hospitals etc.

To mention the main points, this paper deals with:

I. The basis for the system architecture: conventional view of guidelines compared with the modular architecture.

II. The federal action: CDC's and ODP's current approach

III. The new system architecture and data model application in the present setup, taking the anthrax emergency as the bench-test.



The non-emergency guidelines already function in a modularised form divided into signs, symptoms, tests, treatment, alternate guideline modules and the module specific to that particular guideline. When triggered, emergency guidelines are released and added to the already functioning guidelines, with a predetermined legal level for implementation.

Board 6. Tularemia Surveillance - United States, 1990-2000

S. L. Marshall, K. A. Feldman, D. T. Dennis, E. B. Hayes

Centers for Disease Control and Prevention, Fort Collins, CO

Background: Tularemia is a zoonotic disease, caused by the gram-negative coccobacillus *Francisella tularensis*. Although tularemia was removed from the list of nationally notifiable diseases in 1995, it was reinstated in 2000, primarily because of the potential for *F. tularensis* to be used as a bioterrorism agent. However, many states reported tularemia without interruption. This report summarizes the tularemia cases reported to CDC from 1990 - 2000.

Methods: Reported tularemia cases were submitted electronically by state health departments to CDC through the National Electronic Telecommunications System for Surveillance. As of 2000, tularemia was reportable in 46 states. For surveillance, confirmed and probable tularemia cases are clinically compatible illnesses with confirmatory (culture of *F. tularensis* from a clinical specimen or 4-fold change in serum antibody titer) or presumptive (antigen detection by fluorescent assay or single elevated titer) laboratory results, respectively. Reported data included county and state of residence, age, sex, race, date of illness onset, and case status. Incidence rates were calculated using 1995 population estimates. Analysis was performed in Epi-Info.

Results: From 1990-2000, 1368 tularemia cases (average 124 cases annually) were reported from 44 states. Case status was confirmed for 59% of cases, probable for 6%, and unknown for 35%. The incidence did not decrease substantially during 1995-1999, but an increase was noted in 2000 when notifiable status was restored. More than 50% of all cases were reported from four states (AR, MO, OK, SD). Seventeen percent of U.S. counties reported at least one case of tularemia during 1990-2000.

Males had a higher incidence than females in all age categories. The age distribution of reported cases is bimodal, with the highest incidence in persons aged 5-9 years and 75-84 years. Incidence was highest among Native Americans (0.50/100,000), compared with 0.04/100,000 among whites, 0.01/100,000 among blacks, and <0.01 in Asians and Pacific Islanders. Seventy percent of cases reported onset of illness in the late spring and summer months.

Discussion: Although tularemia occurs throughout the U.S., it is consistently reported in greater numbers from AR, MO, OK, and SD. Most cases occur in the summer months and are associated with tick bites. The bimodal age distribution and preponderance of males may be due to differential exposure to infective animals or ticks, differential use of personal protective measures, or to reporting bias. The high incidence among Native Americans may be due to an increased exposure risk. By understanding the occurrence of tularemia in the U.S. over the past decade, clinicians and public health practitioners will be better able to recognize unusual occurrences of tularemia including possible bioterrorist events.

Board 7. Albany County Emergency Department Surveillance: a Pilot Study Using State and Local Public Health Systems for Rapid Detection and Notification of Bioterrorism Events and Disease Outbreak

L. H. Le[1], R. G. Westphal[1], I. Gotham[1], C. Stetson[1], T. Q. Nguyen[2], J. Crucetti[3]

[1]New York State Department of Health, Albany, NY, [2]SUNY at Albany School of Public Health, Albany, NY, [3]Albany County Department of Health, Albany, NY

Recent infectious disease and bioterrorism events in New York and elsewhere point out the critical need to strengthen public health surveillance systems to provide for rapid detection of disease outbreaks and timely notification of public health agencies and health care providers. We have developed an ongoing collaborative project between the New York State Department of Health, the Albany County Department of Health and the hospitals in Albany County, instituting a pilot electronic surveillance system using daily passive reporting of emergency department visit data via a secure website. Based on signal detection theory, this system provides for rapid detection and notification of disease outbreaks, which initiates a hierarchical active surveillance system for more complete investigation of the triggering event. Experiences from this pilot study are being used to improve regional and state-wide surveillance systems and to develop a more robust, multiply-regressed mathematical model for event detection.

Board 8. Rapid Influenza-like Illness Syndromic Surveillance is Possible Using ICD-9 Codes from a Large Health Maintenance Organization

H. Kassenborg[1], M. Hadidi[1], J. Nordin[2], G. Amundson[2], B. Miller[1], R. Danila[1]

[1]Minnesota Department of Health (MDH), Minneapolis, MN, [2]Health Partners Medical Group (HPMG), Minneapolis, MN

Issue: Potential bioterrorism agents will likely first present as an influenza-like illness. Conventional infectious disease surveillance mechanisms that rely on passive reporting are too slow and insensitive to rapidly detect a large scale infectious disease outbreak; the time from patient presentation to specific disease diagnosis to reporting of the diagnosis to MDH currently takes days to weeks. In the event of a large-scale bioterrorism event, the window of opportunity for initiating effective post-exposure prophylaxis is extremely short. In order to minimize the damage to public health, rapid, real-time, syndrome-based surveillance mechanisms are needed. In order to set up such a system in Minnesota, three criteria needed to be met in order for such a surveillance system to be practical and effective. First, due to resource limitations, the surveillance data of interest must be collected for reasons other than bioterrorism and exist in a digital format. Second, the surveillance data need to be entered into a database in a timely fashion (within 24-72 hours). Third, the data and the method for analysis need to be capable of detecting an outbreak. **Program:** HealthPartners is a large health maintenance orginazation with Health Partners Medical Group (HPMG) delivering primary care to over 240,000 persons in the Minneapolis/St. Paul metropolitan area. Ninety-eight percent of patient encounter data including ICD-9 coding are entered into HPMG database within 24 hours of clinic visit.

Thirty-one ICD-9 codes that could code for influenza-like illness were chosen from "check-off" sheets used within HPMG clinics. **Outcome:** Non-identifying demographic and ICD-9 data from encounters that include one of the relevant ICD-9 codes are sent to MDH after posting to HPMG central database. Each evening, this data is automatically extracted and sent to MDH File Transfer Protocol server where the data file is picked up and processed to analyze the ICD-9 codes and demographic information in relation to data from the same year and previous years. **Lessons learned:** This system demonstrates that rapid, near real-time syndromic surveillance can be accomplished using existing data. Aberration detection methods for outbreak detection need development and refinement.

Board 9. Differentiation of Bacterial Agents of Bioterrorism from Routine Clinical Isolates Using Cellular Fatty Acid Analysis

G. Osterhout[1], C. Allan[2], S. Redus[2], J. Teska[3], M. Romagnoli[4], J. Dick[4], M. Sasser[1]

[1]MIDI, Inc., Newark, DE, [2]Anteon Corp., Frederick, MD, [3]USAMRIID, Frederick, MD, [4]Johns Hopkins Hospital, Baltimore, MD

Specimens submitted to the clinical microbiology laboratory generally may not be accompanied with a high index of suspicion for containing potentially contagious/dangerous agents. Routine microbiology screening protocols including various staining techniques and use of selective/differential media provide preliminary impressions suggestive of groups of organisms. Rapid biochemical tests can provide further narrowing of possible bacterial identifications but this frequently requires extensive workup for confirmation. Fastidious or infrequently encountered bacteria often are unreactive in these conventional test systems or present with no discernible pattern. Additionally, many nonpathogenic species, or species of low pathogenicity may exhibit very similar reactions in conventional test systems. We developed a database based on cellular fatty acid (CFA) content that can quickly screen for both the presumptive bacterial agents of bioterrorism (BA) and other less virulent taxonomic relatives. Reference strains of *Bacillus anthracis* (60), *Burkholderia mallei* (12), *B. pseudomallei* (16), *Brucella melitensis* (22), *Francisella tularensis* (20), and *Yersinia pestis* (12) as well as species genetically related to each agent (e.g. *B. cereus, Y. pseudotuberculosis*), were cultured on appropriate media. Cells were processed to generate methyl esters of fatty acids, derived from cellular membranes, for analysis by gas liquid chromatography. Chromatographic peaks were quantified and identified using pattern recognition software. Composite entries were generated and a library entry created for each species. Routine clinical isolates and additional reference strains of each database entry were processed in an identical manner and used to challenge the database. All challenge strains of the agents of bioterrorism were successfully identified by the database. Overlap was noted for several strains of the genetically related species with the corresponding BA. Additional strains of nondatabase entries were properly designated as either "No Match" or an unacceptably low match to the Bioterrorism library. The system allows the simultaneous searching of additional libraries consisting of hundreds of other common clinical species. When searched with the Sherlock® Microbial Identification Clinical database, these isolates were most commonly identified as *B. megaterium, B. licheniformis, B. subtilis,* or *B. circulans*. Batches of specimens can be automatically analyzed with a run time for each specimen being ca. 20 minutes. The same protocol can be applied to all samples minimizing sample handling and potential exposure. This methodology represents an effective approach for simultaneous identification of BA and related organisms.

Board 10. Modeling Results of Exposure to Weaponized Bacterial and Viral Pathogens During Bioterrorism Attack

G. H. Yoakum

BioTechnologies, Inc., Windermere, FL

Modeling the effects of Biological Warfare Agents (BWA) will assist in strategic defense planning and tactical evaluation, if public health systems are engaged by BWA events. We have developed a matrix-analysis model of BWA events based on standard vaccination evaluation data. The Centers for Disease Control (CDC) and The Johns Hopkins Center For Civilian Biodefense Studies reviewed the status of preparations for an attack with aerosol of anthrax spores or smallpox virus as Biological Warfare Agents. The U.S. has a protein-based vaccine that protects monkeys against aerosol anthrax challenge between 8 and 38 weeks following vaccination. This vaccine has been shown to provide experimental animals 88% protection after 100 weeks. A limited supply of this vaccine is now available for military use. Public health plans are underway to prepare material for vaccination against smallpox. Current planning is based on public health data that assess the response of populations to natural diseases. The protective effect of immunization results from a decrease in the number of days needed during secondary response to a disease agent, an increase in the titer of total antibody bound when challenged by disease agent, and the length of time the immune system responds to a new challenge. Natural exposure to pathogens is different from expectations of BWA events. BWA munitions exposure will frequently involve many more infective particles per exposure, and may involve enhanced chemical or genetic factors that increase pathogenic activity. The matrix-model presented here predicts a substantial decriment of protection by primary immunization, if populations are exposed to BWA munitions in these tactical circumstances. This model also develops and applies Q-factors to identify biologically distinct BWA munitions in the field, and assist in developing effective defensive measures. Model results indicate that detections of BWA, at or before exposure, is an important part of a BWA defense strategy.

Board 11. Rapid Identification of Bacillus anthracis Directly from Simulated Positive Blood Culture Bottles by PNA FISH

H. Stender[1], G. Haase[2], K. Oliveira[1], J. J. Hyldig-Nielsen[1], J. Coull[1]

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The definitive diagnosis of anthrax is based on identification of *Bacillus anthracis* e.g. in positive blood cultures. However, standard methods require subculture, overnight incubation and a series of analysis for phenotypic characteristics and thus take at least 24-48 hours. Fluorescence in situ hybridization (FISH) using peptide nucleic acid (PNA) probes targeting rRNA is a novel method for identification of organisms directly from simulated positive blood culture bottles. In this study, we applied fluorescein-labeled PNA probes targeting 23S rRNA of *Bacillus anthracis* to PNA FISH to identify *B. anthracis* directly from simulated positive blood cultures with gram-positive rods. The PNA probe was added to smears made directly from the blood culture bottle and incubated for 10 min at 80°C and subsequently for 90 min at 55°C. Unhybridized PNA probe was removed by washing (30 min) and the smears were examined by fluorescence microscopy and thus provided results within 2.5 hours. Evaluation using reference strains representing eleven *Bacillus* species, including all other type strains of the *B. cereus* complex, i.e. *B. cereus*, *B. thuringiensis*, *B. mycoides*, *B. weihenstephaniensis* and *B. pseudomycoides*, and four other bacterium and yeast species commonly found in blood cultures showed 100% sensitivity and specificity. Studies using clinical isolates are ongoing. Potentially, PNA FISH will be a valuable and powerful tool in the bioterrorism preparedness of clinical microbiology laboratories used for both rapid diagnosis of anthrax and rapid screening of environmental specimens for spores

of *B. anthracis*, since also these morphological forms can be visualized by PNA FISH.

Board 12. Rapid International Assessment of Laboratory Capacity to Test for *Bacillus anthracis* via WHO Global Salm-Surv, 2001

B. C. Imhoff[1], E. D. Mintz[1], M. Jouan[2], P. Braam[3], H. C. Wegener[4], F. J. Angulo[1], WHO Global Salm-Surv[3]

[1]Centers for Disease Control and Prevention, Atlanta, GA, [2]Institut Pasteur, Paris, FRANCE, [3]World Health Organization, Geneva, SWITZERLAND, [4]Danish Veterinary Institute, Copenhagen, DENMARK

Background: Initiated in January 2000, World Health Organization (WHO) Global Salm-Surv is a network of more than 400 individuals from over 100 countries involved in *Salmonella* surveillance. Members include representatives from national and regional public health, veterinary, and food reference laboratories. Several free services aimed at enhancing laboratory capacity, including training, an external quality assurance system, and enrollment in a moderated electronic discussion group, are available for WHO Global Salm-Surv members. In response to WHO Global Salm-Surv member inquiries regarding information about anthrax, we sent a message listing resources for information about anthrax (e.g. anthrax laboratory protocol, facts about anthrax) to the electronic discussion group in October 2001. Also in October 2001, WHO requested WHO Global Salm-Surv conduct a rapid assessment of its members to identify laboratories that are willing and able to test environmental specimens for the presence of *B. anthracis*. **Methods:** A ten-question questionnaire was sent to WHO Global Slam-Surv members via the electronic discussion group on October 31, 2001. This message requested information about laboratory capacity to isolate *B. anthracis*, the methods used to test for *B. anthracis*, whether the laboratory was a national reference laboratory for *B. anthracis*, and whether the laboratory was willing to test samples from countries that do not have the capacity to test for *B. anthracis*. **Results:** Within 23 days, we received responses from 50 WHO Global Salm-Surv members from 40 countries; we received most responses within 7 days. Eighty percent (n=40) of responding laboratories reported capability to isolate and identify *B. anthracis* using culture methods. These 40 laboratories use conventional phenotypic methods (motility and hemolysis) to identify suspect *B. anthracis* strains. Only 66% (n=33) use India ink stain and 32% (n=16) use PCR. Laboratories from the following regions reported having the capacity to isolate and identify *B. anthracis*: 3/3 (100%) from Africa, 3/3 (100%) from the Eastern Mediterranean, 17/23 (74%) from Europe, 10/12 (83%) from the Americas, 2/2 (100%) from South-East Asia, and 5/7 (71%) from the Western Pacific. Of the 40 responding laboratories with the capacity to test for *B. anthracis*, 25 (63%) are national reference laboratories for anthrax testing and 21 (53%) are willing to perform testing for countries that do not have the capacity to isolate and identify *B. anthracis*. **Conclusion:** The WHO Global Salm-Surv electronic discussion group proved to be a valuable means to rapidly identify laboratories willing and able to perform *B. anthracis* testing. These data will be used to create bioterrorism preparedness plans and response systems for regional WHO offices. More information is needed to understand these laboratories' capacities to perform confirmatory testing for *B. anthracis*.

2 Tuberculosis

Sunday, March 24, 12:00 noon
Grand Hall East

Board 13. Evaluation of Pulmonary Tuberculosis Status in Iran: Bijar Pilot 1999-2000

M. R. Masjedi, M. Yazdanpanah, H. Masjedi, M. Hosseini, S. Salek, R. Taghizadeh, A. Velayati

National Research Institute of Tuberculosis and Lung Disease, Tehran, IRAN

Objectives: According to the annual reports of the Ministry of Health of Iran the incidence of Tuberculosis and smear positive pulmonary TB in 2000, were 18.7 per 100,000 and 8.46 per 100,000 respectively. However, WHO has estimated the incidence of different types of TB in Iran to be 54 per 100000 and the incidence of smear positive pulmonary TB, 31 per 100000. Accordingly, Iran was evaluated to have a relatively high prevalence of TB! Having different reports on the incidence rate of TB in Iran, and also in order to initiate systematic study of TB in Iran, a pilot survey was conducted. **Method:** A survay was conducted in urban population of Bijar, Kordestan, in March 2000. Cough condition of everyone in the household were asked by visiting all the households in the city. Then cases with cough ≥ 3 weeks referred to the city hospital. With these two groups were matched on the basis of sex, age and neighbourhood, who had no cough or cough ≤ 3 weeks. All the referred cases were examined; PPD test, sputum smear (3 times), chest X-ray and sputum culture were carried out. Results:In this household survey in Bijar, initially 45,834 were asked for any cough. 50.9% were male and 49.1% females. Amongst people who referred to the city hospital, after clinical examination, PPD test, chest X-ray, sputum smear and sputum culture, 3 new cases were diagnosed as smear positive pulmonary TB. And 2 cases as culture positive. **Conclusions:** According to the reports of health care system of Bijar, 4 new cases were diagnosed as smear positive by March 2000. With 3 new cases who were found in this study, 7 new cases were diagnosed as smear positive pulmonary TB (March 1999- March 2000). So, the incidence rate of smear positive pulmonary TB was estimated to be 15.5 per 100,000. Since, there are places with higher and lower incidence of TB in Iran, it seems that the incidence rate of smear positive pulmonary TB is about 18-20 per 100,000. And then the rate of different types of TB is estimated to be about 40 per 100,000 nation wide. Thus the present study reveals that Iran has a relatively low prevalence of TB.

Board 14. Species Determination of Mycobacteria Isolated from AIDs Patients in India by 16s rRNA Sequencing

S. Shahdad

All India Institute of Medical Sciences, New Delhi, INDIA

In developing countries the most common mycobacterial infection as per reports till now, in persons with AIDS is reported to be tuberculosis as oppposed to MAI infections in the developed countries. The diagnosis of tuberculosis in developing countries is predominantly made after clinical and radiological examination; microbiology services are often underutilized. Smear examination alone can only indicate that acid fast bacilli are present and cannot give any indication of the species of mycobacteria. Since patients with AIDS may suffer from mycobacterial infection different from *M. tuberculosis*, it is essential that the species identification should be attempted whenever possible. Determination of Species identification is necessary if we are to avoid misidentification and mislabeling of cases. Phenotypic methods have proved to be unreliable while sequencing of 16s rRNA has been shown to give definitive

and unambiguous results and be the method of choice, at least in the reference centers.

Fourteen strains from patients testing positive for HIV antibodies were investigated on this study. Clinically all patients were suspected to be suffering from tuberculosis and put on antituberculosis treatment. PCR amplification of 1 Kb region of 16s rRNA was positive for all 14 strains. After sequencing of hypervariable region A and region B using primer 244 and 259 respectively, 7 isolates were identified as *M. tuberculosis* complex, 3 strains as MAI, 2 strains as *M. fortuitum*, 1 as *M. smegmatis*, and one isolate as *M. smegmatis*.

Board 15. The Emergence of Tuberculous Meningitis in Egypt: Clinical and Epidemiological Features

F. G. Youssef[1], M. A. Azab[1], S. Afifi[1], H. El Sakka[1], K. Earhart[1], S. El Oun[2], F. Mahoney[1],[3]

[1]U.S. Naval Medical Research Unit No. 3, Cairo, EGYPT, [2]Ministry of Health and Population, Cairo, EGYPT, [3]Centers for Disease Control and Prevention, Atlanta, GA

Introduction: *Mycobacterium tuberculosis* meningitis (TB-M) has emerged as a significant cause of meningitis in Egypt with a high rate of complications and death. We report the features of TB-M in a cohort of Egyptian patients. **Methods:** TB-M was studied as part of ongoing surveillance of meningitis in a network of twelve infectious disease hospitals in Egypt. Patients suspected of having TB meningitis received lumbar puncture for analysis of cell count, glucose, protein, and culture on Lowenstein Jensen's media. Clinical data from patients with TB-M was compared with data from patients with other causes of culture positive bacterial meningitis. **Results:** Of the 6868 patients evaluated in the surveillance network, 691 had culture confirmed bacterial meningitis including 106 patients with TB-M. TB-M occurred in all age groups with a mean age of 22 years (range 5 months to 56 yrs). 60/106 cases (57%) occurred in patients greater than 20 years. In patients >20 years the causes of bacterial meningitis were *S. pneumoniae* (31.7%), *Mycobacterium tuberculosis* (28%), *Neisseria meningitides* (22%) and all other bacteria (18%). The case fatality ratio (CFR) for patients with TB meningitis (46.2%) was higher than that for all other causes of bacterial meningitis (21.7%). Among patients who survived, the mean length of hospitalization was 27.5 days (range 1-78) compared to 12 days (range 1 - 71) for patients with other bacterial causes. Characteristic CSF findings included elevated CSF WBC count (mean 360 WBC /mm^3, range 0-2830), decreased glucose (mean 31.6 mg/ml, range 0 - 100), elevated protein (mean 135 mg/ml, range 15-650) and percent of WBCs that were lymphocytes (mean 29% range 0-92). Prodrome prior to admission was much longer in the TB-M cases (mean 13 days, range 1-95). **Conclusions:** Three clinical and laboratory features proved to be most prevalent in cases of TB-M when compared with the non-TB-M culture positive cases: 1) prodrome interval ≥ 5 days (OR=7.3), 2) CSF leukocyte ≤ 1000 cells/mm3 (OR 10.3), and 3) lymphocytes ≥ 50% (OR=6.8). With enhanced surveillance and diagnostic capabilities TB-M has emerged as a significant cause of bacterial meningitis in Egypt. In adults over age 20, TB-M is second only to pneumococcus as the leading cause of bacterial meningitis in Egypt.

Board 16. Evaluation of an Automated Method for IS6110 RFLP Fingerprinting of *Mycobacterium tuberculosis*

K. Dupnik[1], J. Hansen[2], C. Campus[1], T. Dambaugh[2], D. Toney[1]

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Molecular typing of *Mycobacterium tuberculosis* (Mtb) isolates using IS6110 RFLP is a useful tool for the epidemiologic tracking of tuberculosis clusters in the community and is currently considered the "gold standard" for DNA typing of Mtb. Widespread use by public health laboratories has been limited due to the considerable time and expertise required to perform the testing and issues of pattern reproducibility and standardization. The availability of an automated method for IS6110 RFLP would eliminate many of the problems associated with manual IS6110 RFLP and would make it more plausible for public health laboratories to provide this testing as a routine service for state and local tuberculosis control programs. The current study investigated the use of the QualiconTM RiboPrinter® Microbial Characterization System for IS6110-RFLP analysis of *M. tuberculosis*. Modification of the RiboPrinter® platform to include PvuII digestion and IS6110 probe hybridization allowed for the generation of a RFLP fingerprint pattern from DNA in 8 hours as compared to an average of 3-4 days using manual IS6110 RFLP. Automated typing of 75 clinical Mtb isolates resulted in the generation of 51 extractable patterns, 43 of which represented unique DNA fingerprints. Failure to extract patterns resulted from either insufficient sample DNA concentrations or MW marker inconsistencies which prevented the automated extraction of fingerprint data. Repeated RiboPrinter® typing of 7 Mtb isolates on multiple independent batch runs (n=3-6) resulted in 100% pattern reproducibility. Automated typing of Mtb isolates from selected epidemiologically-linked clusters of tuberculosis generated indistinguishable RFLP fingerprint patterns for each cluster, strongly supporting the epidemiologic findings. Manual IS6110 typing of the same clusters performed at a reference laboratory also generated an indistinguishable fingerprint pattern for each cluster. Comparison of manual and RiboPrinter® IS6110 fingerprint patterns from 15 Mtb isolates resulted in the generation of patterns with the same number of bands and ratios of distances between bands; however, RiboPrinter®-generated fingerprints possessed less band separation and differentiation, especially at the lower molecular weights. Limitations of this system currently under evaluation include the inability of the software to allow for user modification of data collection and analysis. The results of this study suggest that automated IS6110 RFLP of Mtb using the RiboPrinter® System could provide a fast, efficient, and practical tool for public health laboratories to identify, track, and compare clusters of tuberculosis within the community.

3 Disease Eradication

Sunday, March 24, 12:00 noon
Grand Hall East

Board 17. Prevalence of 1999 Laboratory-Confirmed Neurosyphilis Among All 1999 High Titer Syphilis Cases in a Southeastern Public Hospital System

E. S. Safran, J. R. Drayton, P. Kloda

Morehouse School of Medicine, Atlanta, GA

Neurosyphilis is usually considered a disease of the past. However, in the largest public hospital system in Atlanta, in 1999, there were 11 CSF VDRL+ cases. According to the 1998 CDC guidelines for STDs, a reactive VDRL in CSF is considered diagnostic of neurosyphilis. In the same year, there were 184 high titer laboratory-confirmed syphilis cases — namely, all cases age one year or older where the RPR titer is greater or equal to 32, and there is a documented treponemal IgG positive test. Therefore, the annual prevalence for VDRL+ neurosyphilis in 1999 within this hospital system is 11/184 or 5.98%. Eight out of the 11 (73%) VDRL+ neurosyphilis cases were documented HIV+, while the remaining three cases did not have any HIV testing recorded. Of these eleven cases, there were three cases of RPR=32, three cases of RPR=64, four cases of RPR=128 and one case of RPR=256.

Board 18. Efficacy of *Balanites aegyptiaca*(L.) DEL Balanitaceae as Anthelminthic and Molluscicid Used by Traditional Healers in Burkina Faso

T. H. Hamidou[1], H. Kabore[1], O. Ouattara[1,2], S. Ouédraogo[2], I.P Guissou[2], L. Sawadogo[3]

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Fast growing prices of modern veterinary drugs, more resistance occurring frequently to current medicinal molecules, commonly used by veterinary practitioners and persistence of major diseases as constrains to animal production in rural areas in most of underdeveloped countries, particularly in Burkina Faso (West Africa), explains the importance given nowadays to indigenous knowledge systems about pharmacopoeia both for humans and animals. The recipes, generally based on plants, are found around the village or watershed area, very well known by healers, less expensive, efficient and culturally accepted and integrated by populations into their day-to-day life. *Balanites aegyptiaca* is a sahelian tree of six to nine meters high. Its organs (ie: leaves, bark, kernel) are widely used in Burkina Faso by vet-healers and livestock owners for animal parasitic diseases treatments. The aim of the present study was to experimentally assess the anthelminthic and molluscicidal activities of its kernel powder. The *in vivo* experiment on goats (in village flocks and on - station animals) with doses of 30 mg/kg, 40 mg/kg and 60 mg/kg showed a partial reduction of parasitic eggs out-pout in faeces. The *in vitro* pharmacological study of acetonic, ethanolic and aqueous extracts of powdered kernels led to a complete helminth eggs development inhibition. Total larvae mortality was obtained and LC50 values reached 27.24; 5.82 and 129.02 ppm for acetonic, ethanolic and aqueous extracts, respectively. It also showed a complete lethality on freshwater snails of *Biomphalaria pfeifferi*. LC50 values were 60 ppm; 172,40 ppm and 84,15 ppm for crude kernels powder, acetonic and ethanolic extracts, respectively. Further studies will address confirmation of efficacy and therapeutic doses, which are recommended at village level uses.

Board 19. A Combination of Lamivudine and IFN Adopting a Different Timing-Schedule in the Treatment of B Chronic Hepatitis E Antigen-Negative

G. Tarantino, P. Conca, P. Sorrentino, P. Ragucci, A. Perrella, E. D'Avanzo

Dpt of Clinical and Experimental Medicine Federico II University Medical School, Naples, ITALY

B chronic hepatitis e antigen-negative (BCHe-) among other HBV-related liver diseases is common in our area and is generally poor responsive to canonical IFN therapy. Recently, lamivudine (L) has been found to be an useful tool in treating virus B infection alone or in combination, taking in account the possibility of the so called YMDD variant. To assess the efficacy of a combined regimen, we selected 2 cohorts of BCHe- pts with high viral replication, non responder (NR) or relapser (R) to a previous IFN cycle. Fourteen pts (Group A, 7 females, 12 NR) were randomly enrolled after a histological evaluation (sec. Knodell, grading 6-10 and sec. Scheuer, staging 1-3) and treated by L (100 mg/day) for 6 mths, followed by natural leukocyte IFN alfa-n3 6 MU s. c. at alternate day lasting 12 mths. Group B comprehended 13 pts (8 males, 10 NR), grading (7-9), staging (1-2) and received simultaneously L and IFN (for 6 mths), followed by a twelve mth-course of IFN, at the same previously described doses. The response rate was significantly superior in group A (10/14 versus 2/13) at chi-square, by measuring the undetectability of HBV DNA (PCR) at the end of therapy cycle. Noteworthily, at 6 mths serum HBV DNA in group A was absent in 12/14, meanwhile in group B only 6 out 13 did not showed a positivity of HBV one. At log regression the negativity of HBV DNA during the first 6 mths was an independent factor in foreseeing the complete response (persistently normal ALT levels, undetectable HBV DNA). None was characterized by a loss of HbsAg. Significant life-style changes in examined cohorts were not observed during treatment, nor severest side effects (excluding some degrees of leukopenia) were faced. Three out 10 responders underwent successive liver biopsy evidencing a decrease of their previous grading score (minus 50%). It is our opinion that an abating of viraemia after L makes IFN, successively administered, more active because it deals with a very low viraemic levels that last also in the successive course thanks to an immuno- modulating action of IFN. During the entire treatment (18 mths) unfortunately some pts (group A: 2 versus group B: 4), after having had a viral clearance, displayed a presence of HBV at low-medium levels more pronounced in group B. YMDD variants were not discovered probably *due* to few pts studied.

4 Emerging Nosocomial Infections

Sunday, March 24, 12:00 noon
Grand Hall East

Board 20. Two Epidemiological Patterns of Norwalk-Like Virus Outbreaks: England and Wales, 1992 - 2000

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Public Health Laboratory Service, London, UNITED KINGDOM

Introduction: Norwalk-like viruses (NLVs) cause outbreaks of acute gastroenteritis via a number of routes including foodborne and person-to-person transmission. Outbreaks occur in a range of settings, though outbreaks in healthcare institutions may be particularly common. NLVs are the number one reported cause of hospital outbreaks in England and Wales. **Methods:** Data from the national surveillance for outbreaks of infectious intestinal disease in England and Wales will be presented. NLV outbreaks that occurred in healthcare settings (hospitals and residential facilities) were compared with outbreaks that occurred in other settings. **Results:** From 1992 to 2000, there were 1877 outbreaks reported that were caused by NLV, the majority of which occurred in hospitals (40%) and residential facilities (39%), affecting 13195 and 15545 persons, respectively. The remaining 21% of outbreaks occurred in a range of settings including schools (6%), hotels (8%) and food outlets (6%). Pronounced wintertime seasonality was observed in healthcare institution outbreaks whereas no such peak was seen in outbreaks in other settings ($p < 0.0001$). Person-to-person transmission was more common in healthcare institutions and outbreaks were smaller, more prolonged and had different attack rates compared to outbreaks in other settings. **Conclusions:** There are two distinct epidemiological patterns of NLV outbreaks: those that occur in semi-closed healthcare institutions and those that occur in more open settings. Underlying reasons may include clinical and virological influences. The population at-risk in healthcare institutions has an annual increase in number in wintertime due to influenza. And, certain strains of virus may be particularly adapted to causing infection in semi-closed settings.

Board 21. Emergence of Resistant Pathogens in Egypt: Antimicrobial Evaluation of Community and Hospital Acquired Infections

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Background: Identifying the emergence of resistant pathogens is a key component of disease surveillance. Since 1998, NAMRU-3 has collaborated with the Egyptian Ministry of Health to establish a surveillance network of infectious disease hospitals to evaluate patients with meningitis, acute febrile illness, and diarrheal disease. More recently, the laboratory has supported the surveillance for patients with hospital-acquired infections. Data from these studies is reviewed to evaluate antimicrobial resistance patterns throughout Egypt. **Methods:** Patients with meningitis, acute febrile illness, and diarrheal disease undergo a standardized clinical and laboratory evaluation. Bacterial isolates are archived and characterized further at NAMRU-3. Surveillance efforts have been recently expanded to include support in evaluating nosocomial pathogens from intensive care units. Respiratory, Intestinal, and nosocomial pathogens collected are culture confirmed and tested for antimicrobial resistance by Kirby-Bauer disk diffusion and E-test methods using standard NCCLS criteria. Strains were classified as extended spectrum beta lactamase (ESBL) producing organisms based on a disk diffusion method comparing between disks with and without clavulanic acid. **Results:** Antimicrobial susceptibility data indicates moderate levels of resistance of respiratory and enteric pathogens to commonly used antibiotics for community-acquired infections (Table 1). Data on nosocomial-acquired bloodstream infections (BSI) reveals high levels of resistance to broad spectrum antibiotics and the emergence of extended spectrum beta lactamase producing organisms (ESBL) (Table 2). ESBLs were present in >30% of *K. pneumoniae* isolates. **Conclusion:** Antimicrobial resistance is emerging as an important public health problem in Egypt. Surveillance efforts are being used to guide antimicrobial therapy. The high degree of resistance in nosocomial pathogens suggests that more accurate molecular assays at detecting ESBLs would yield even greater presence. The emergence of ESBLs warrants further investigation and institution of infection control practices.

Board 22. Outbreak of *Pseudomonas aeruginosa* Associated with a Design Change in Specific Models of Bronchoscopes

D. L. Kirschke[1], T. F. Jones[2], A. S. Craig[2], P. Chu[3], G. Mayernick[4], P. Patel4, W. Schaffner[3]

[1]CDC/DAPHT/EPO/EIS/State Branch/Tennessee, Nashville, TN, [2]Tennessee Department of Health, Nashville, TN, [3]Vanderbilt University School of Medicine, Nashville, TN, [4]Skyline Medical Center, Nashville, TN

Introduction: *Pseudomonas* species are commonly implicated in endoscope-related nosocomial outbreaks because they thrive in moist hospital environments. We investigated a series of reports of *Pseudomonas aeruginosa* obtained during bronchoscopy at a community hospital. **Methods:** We reviewed hospital records of patients undergoing bronchoscopy at the community hospital during June-October 2001. Environmental samples were obtained from bronchoscopes and the hospital endoscopy suite. Pulsed-field gel electrophoresis (PFGE) was performed on isolates of *P. aeruginosa.* **Results:** Two new bronchoscopes began use on July 13 and July 24, respectively; both were associated with positive culture results on the second day of use. During the period that these bronchoscopes were used, between July 13 and August 14, 2001, bronchoscopy was performed on 32 patients; 18 (56%) had specimens that grew *P. aeruginosa*. Six (33%) specimens with *P. aeruginosa* also grew *Serratia marcescens*. Among the 26 procedures performed with the new bronchoscopes, 18 (69%) were associated with positive cultures for *P. aeruginosa* versus none of six procedures performed with older models of bronchoscopes during this period ($p<0.01$). One case-patient developed pneumonia eight days after bronchoscopy and the sputum grew *P. aeruginosa*. *P. aeruginosa* and S. marcescens were cultured from a biopsy port of one of the new bronchoscopes before and after routine disinfection procedures. *P. aeruginosa* was cultured from a vacuum trap and cleaning solution in an endoscopy cleaning room. PFGE patterns of isolates from the bronchoscopes, patients, and environmental samples were indistinguishable, and different from strains of *P. aeruginosa* from patients elsewhere in the same hospital. In September, the implicated bronchoscopes were replaced with identical models. Shortly thereafter, three endoscopy procedures resulted in positive *P. aeruginosa* cultures, with a strain matching the initial cluster. The caps of the biopsy ports on all implicated bronchoscopes were easily removed by investigators, despite information from the manufacturer indicating that they should be permanently affixed. The manufacturer had made design changes in 1998 to make that cap easier to remove during repair. **Conclusions:** This outbreak of *P. aeruginosa*, associated with numerous positive cultures and at least one clinical illness, resulted from contaminated bronchoscopes. Environmental contamination within the endoscopy suite likely led to seeding of the bronchoscopes. A design change in the bronchoscopes appeared to allow persistence of contamination in an area not readily amenable to disinfection.

Board 23. Three Laboratory-Associated Infections of *Escherichia coli* O157:H7, New York State 1999-2000

N. L. Spina[1], S. M. Zansky[1], N. B. Dumas[2], S. F. Kondracki[1]

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Background: Transmission of shiga-toxin producing *Escherichia coli* O157:H7 (EC) occurs mainly by the ingestion of undercooked beef, raw milk or contaminated water. Laboratory acquired infection of EC was first documented in 1993. The small infectious dose (as few as 10 organisms) of EC and its prolonged survival on environmental surfaces may be contributing factors to laboratory-acquired infections. This report summarizes three laboratory-associated cases of EC in New York State within a one-year period. **Methods:** The investigation included: 1) a review of lab procedures, 2) case interviews to identify potential sources of exposure and 3) comparison of Pulsed-Field Gel Electrophoresis (PFGE) results of the case isolates to laboratory isolates temporally associated with their exposures. **Results:** Two cases occurred in Medical Technologists (MT) and a third in a child of a lab worker. Each case was associated with a different Microbiology laboratory. Two were temporally related to a large county fair outbreak. MT#1 developed bloody diarrhea 3-4 days after initial exposure to working with an outbreak patient's EC isolate. MT#1's PFGE pattern matched the isolate of a fair attendee identified in this lab. MT#2 did not become infected herself, but her one-year old son developed symptoms of fever and diarrhea 7 days following the mother's work exposure. The child's PFGE pattern matched one of the main outbreak strains tested by this laboratory. No household member had visited the fair but the child attended a facility-related daycare where his mother nursed him twice daily. No other children attending the day care were symptomatic. The mother was asymptomatic and a stool specimen submitted for culture was negative. MT#3 developed bloody diarrhea 4 days after working with EC isolates. An isolate with a matching PFGE pattern was tested in this laboratory prior to onset of symptoms. A review of laboratory procedures showed no obvious breeches in technique. Neither MT#1 or MT# 2 had frequent work exposure to EC prior to the outbreak. **Conclusions:** The PFGE patterns of the laboratory-associated cases of EC were indistinguishable from isolates handled in the laboratory 3-7 days prior to the onset of illness. We were unable to identify breeches in lab procedures to explain the infections. These cases reinforce the need for meticulous adherence to precautions,

particularly among lab workers who handle large volumes of EC cultures as in an outbreak situation. Further studies are needed to identify protocols that decrease the likelihood of transmission in the laboratory setting.

Board 24. Outpatient Candidemia: A Population-Based Study in Connecticut

S. M. Huie[1], T. Im[1], A. N. Sofair[1], R. A. Hajjeh[2], M. E. Brandt[2]

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Candidemia is currently ranked as the fourth most common inpatient bloodstream infection in the United States. However, candidemia as an outpatient infection is not well described. We conducted a population-based laboratory surveillance study to identify incident cases of candidemia in Connecticut from October 1, 1998 through September 30, 2000. We were able to distinguish patients who had outpatient candidemia (defined as a positive blood culture for *Candida* at or within 48 hours of admission to a hospital, or a positive blood culture for *Candida* without a hospital admission) from those who had inpatient candidemia. During two years of surveillance, 464 cases of candidemia were identified, for an incidence rate of 7.2/100,000. Outpatient candidemia infection occurred in 28.7% (133/464) of cases. The species of *Candida* were different in proportion for outpatient versus inpatient cases. Among outpatient cases the species were *C. albicans* 37%, versus non-albicans 63%. The speciation among inpatient cases were C. albicans 57% versus non-albicans 43% ($p < 0.01$). There were no differences in age, race and gender. Among cases, 62% of outpatients and 43% inpatients had required hospitalization in the three months prior to the diagnosis of candidemia. Although outpatient candidemia cases were less likely than inpatient cases to have an indwelling catheter in place at the time of candidemia the proportion was still large (69% versus 96%). Antecedent use of immunosuppressive therapy was documented among 32% of outpatient and 50% of inpatient cases. Pulmonary disease was present in 56% and 81% of outpatient and inpatient cases respectively. A similar proportion of outpatient candidemia cases and inpatient candidemia cases had co-existing malignancy, diabetes mellitus, cardiac, neurological, renal, or liver disease. The median length of stay for outpatient cases was 11 days (range 0-98 days) compared to 36 days (range 5-497 days) for inpatient cases. The crude mortality rate was 26% for outpatient and 51% for inpatient cases ($p < 0.01$). Outpatient candidemia cases are more likely to be non-albicans, many of which are known to be azole resistant. Although candidemia does occur among outpatients, our findings (the large proportions of persons with catheters, underlying illness and prior hospitalizations) indicate that these infections are still health-care related. Clinicians need to maintain a high index of suspicion for candidemia among high risk outpatients. Additionally, infection control methods that are usually applied in hospitals need to be applied in the outpatient setting in order to prevent these infections.

Board 25. Mycobacterial Spondylitis After Intravesicular Bacille Calmette-GuÈrin Treatment of Bladder Transitional Cell Carcinoma

D. S. Smith[1], R. Wilson[2], M. Burgos[3]

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We report an unusual case of iatrogenic mycobacterial spondylitis (Pott's disease) related to the treatment of bladder cancer with BCG. A 79-year-old man presented to the urology clinic in September 1996 with gross hematuria. A diagnostic cystoscopy revealed papillary transitional cell carcinoma. A cystoscopic transurethral resection of the bladder tumor (TURBT) was performed in October. In January 1997 cystoscopy showed tumor recurrence. In March he began a six-week regimen of intravesicular Bacille Calmette-GuÈrin (BCG) therapy for a total of 18 treatments. The tissue sent in July 1997 revealed mild epithelial hyperplasia and small non-caseating granulomas. Special stains of the bladder tissue for AFB were negative and the granulomas were attributed to the recent BCG therapy. 15 months after the last BCG wash, the patient presented to his physician with back pain diagnosed as radiculopathy and sciatica. He went to physical therapy but had focal weakness, so was referred to neurosurgery clinic. MRI in March 1999 showed L4-5 disc space obliteration and extensive scar tissue formation. A CT-guided needle biopsy of a lesion of L4 and L5 vertebral bodies was consistent with abscess. The pathology of this tissue sample demonstrated granulomas, though AFB and Gram stains were negative. A boosted PPD test was recorded at 15mm. The patient was discharged home on IV cefazolin, pending results of AFB culture. The AFB preliminary culture report was positive in May 1999. An AccuProbe test (Gen-Probe Inc. San Diego, CA) identified Mycobacteria tuberculosis complex one week later and an anti-tuberculosis regimen with four drugs was begun. Susceptibility patterns (pyrazinamide resistance) suggested *M. bovis*. High Performance Liquid Chromatography (HPLC) confirmed *M. bovis*, BCG strain in July 1999. After completing almost one year of ethambutol, rifampin, and isoniazid he made an excellent recovery and is now ambulatory with a cane. BCG therapy has not been associated with Pott's disease, however, the cause of our patient's disease state appears related to the use of BCG in the bladder washes for the following four reasons: 1) the spondylitis was temporally related to the exposure, developing after the bladder treatments, 2) granulomatous changes were observed in the bladder consistent with pathology induced by mycobacteria, and later this was seen in the tissue biopsies from the spine, 3) the organism was isolated and cultured from the affected tissue, and 4) the patient responded clinically to a drug regimen designed to treat the disease state. Thus, bone lesions in the setting of a history of intravesicular BCG therapy should raise suspicions of *M. bovis* osteomyelitis.

Board 26. Secondary Transmission of Invasive Group A Strep in a Group Home for the Disabled

S. Kondracki[1], B. Wallace[1], S. Zansky[1], D. Schoonmaker-Bopp[2]

[1]New York State Department of Health, Albany, NY, [2]Wadsworth Lab, New York State Department of Health, Albany, NY

Background: Although 200 - 300 cases of invasive Group A Streptococcal disease (GAS) are reported in New York State each year, secondary transmission is rare. In February 2001, a group home with 10 residents and 14 employees reported 2 cases of invasive GAS (one resident, one employee). This report describes the epidemiologic investigation and use of chemoprophylaxis to prevent additional cases. **Methods:** A site visit was conducted by representatives of the New York State Department of Health (NYSDOH) to review patient/employee records and interview care providers. Throat cultures were collected from clients and staff. Positive cultures from the clients and the two invasive GAS cases were sent to the NYSDOH laboratory for pulse field gel electrophoresis (PFGE). **Results:** Two cases of invasive GAS meeting the CDC case definition were found. Case 1 involved a 40 year old profoundly retarded male who had onset of fever on February 7th and pneumonia on February 10th, at which time he was hospitalized. He expired on February 13th due to GAS sepsis. The patient's exposure history was unremarkable except for minor dental work on February 7th. Case 2 involved an otherwise healthy 47 year-old visiting nurse, who assisted in collecting throat cultures of other residents at the group home on February 12th. On February 13th, she had fever, chills, shoulder pain, and subsequently was hospitalized and diagnosed with necrotizing fasciitis. The wound site was positive for GAS. She recovered and returned to work. Throat cultures from four (44%) of nine consumers and 0 of 14 employees were positive for GAS. The PFGE

patterns of the throat cultures matched the two invasive cases. **Control Measures:** All residents and employees were treated prophylactically with penicillin G benzathine and rifampin or with azithromycin. No additional cases occurred. **Conclusion:** Secondary transmission of invasive GAS occurred at a group home for the disabled involving one resident and one employee. A follow-up identified four additional residents with throat colonization. All cultures matched by PFGE. No cases occurred following prophylaxis.

5 Waterborne Infections I

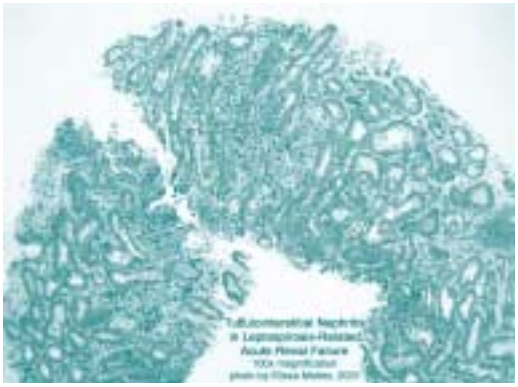
Sunday, March 24, 12:00 noon
Grand Hall East

Board 27. An Outbreak of Leptospirosis following a Houseboat Vacation in California

E. Meites[1], S. Deresinski[2], M. Jay[3], D. Smith[4]

[1]Stanford University School of Medicine, Stanford, CA, [2]Division of Infectious Diseases, Stanford University Medical Center, Stanford University School of Medicine and Santa Clara Valley Medical Center, Stanford, CA, [3]California Department of Health Services, Sacramento, CA, [4]Department of Medicine, Division of ID, Kaiser Permanente Redwood City, Redwood City, CA

We describe an outbreak of human leptospirosis that occurred after a spring houseboating vacation on the New Melones Lake, a popular recreational reservoir in California. This outbreak represents the largest reported common-source outbreak of leptospirosis in California in recent years. Only 3 of 8 men who shared the houseboat reported swimming to a remote cove to hike along a creek that drained into the main reservoir, where they were exposed to muddied waters after an overnight thundershower. Each of these 3 men presented to separate hospitals in Redwood City 10-15 days later with a constellation of signs and symptoms including fever, headache, myalgias, nausea and vomiting. Each developed the salient common clinical feature of renal failure manifested by elevated creatinine levels that in one case required hemodialysis. Renal pathology in one patient showed acute tubulointerstitial nephritis.



Serologic studies for a panel of *Leptospira* serovars performed at the CDC showed the highest titers (1:400 or greater) for *Leptospira* serovars georgia, pomona and javanica in two of the patients. All 3 men received supportive care including antibiotics in hospital settings, and recovered without sequelae. None of the other 5 houseboaters became ill. The following month, a multidisciplinary team conducted an epidemiologic and environmental investigation to determine the source of infection and prevent further exposures. Water specimens were collected from the reservoir and creek using the Moore Swab Technique. Darkfield microscopy of samples from the area where the patients swam was positive for spirochetes, though attempts to culture pathogenic leptospires from these samples were unsuccessful, most likely due to the hot and dry weather conditions at the time of collection. Overall, epidemiologic and environmental evidence strongly suggested that the tributary had been the likely source of the contamination, with possible precipitating factors including the recent rain and warm weather facilitating snowmelt draining through nearby cattle grazing pastures. Public health authorities notified local health care providers, but no further definitive cases were identified. Leptospirosis is the most widespread zoonosis in the world, though it is likely under-diagnosed in the continental United States. The average incidence in California was 4 reported cases per year in 1955-1964, compared to an average of only 1 reported case per year in 1985-1994, when leptospirosis ceased to be a reportable illness. Salient and unusual features in this California outbreak included high fever with uniform renal impairment and only mild hepatitis. Because leptospirosis can progress rapidly if untreated, this re-emerging infection deserves consideration in febrile patients with a history of freshwater exposure, even in states with a low reported incidence of infection.

Board 29. An Increase in Gastrointestinal Illness Associated with Historic Flooding of the Mississippi River: Disease Surveillance from a Randomized Trial of In-Home Drinking Water Treatment

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Background: Recent studies have suggested an association between extreme precipitation and outbreaks of waterborne disease. Since the most frequently observed manifestation of waterborne disease outbreaks, gastrointestinal illness, is relatively common, moderate increases may be difficult to identify. Severe flooding occurred during the spring of 2001 along the Mississippi River. Although finished water continued to meet all treatment standards, untreated sewage and wastewater were discharged directly into the river upstream from the vicinity of Davenport, Iowa for approximately one month during the flood. Peak total and fecal coliform levels in the source water increased at least 10-fold during this period. Since November 2000 we have been collecting daily self-reported GI illness symptoms from 1296 individuals enrolled in a randomized, controlled trial of an in-home drinking water treatment (WET study) in this same area. **Methods:** Rates of illness were determined for the flood period as well as for prior and subsequent seasons. We considered two illness outcomes: "highly credible gastrointestinal illness" (HCGI), a composite of several GI symptoms published previously, and "diarrhea" (three or more loose stools in one day). To determine the impact of the flood illness rates, adjusted for the effect of season, Poisson regression was used. Generalized estimating equations (GEE) were used to account for repeated measures within individuals and the correlation of individuals within households. The predictor variables were the presence of flooding and season. **Results:** The river was above flood stage (>15 feet) between April 14 - May 23, 2000. Based on 519 person-years of observation, the overall rate of HCGI was 2.52 episodes per person-year; and the overall rate of diarrhea was 0.75 episodes per person-year. The highest rates of both HCGI (3.28) and diarrhea (0.95) were in the winter (November-February).

After controlling for season, the flood period was associated (p=0.006) with elevated levels of HCGI (rate ratio=1.23; 95% CI[1.06-1.45]). Diarrhea rates were also elevated during the flood period (rate ratio=1.29; 95% CI[0.98-1.72]), but of borderline statistical significance (p=0.074). **Conclusion:** These data suggest that a significant increase in GI illness occurred during this severe flood. They do not, however, identify the source of this excess illness. We are continuing our examination of the effect of the flooding on GI illness using other community data such as hospital records and a concurrently conducted random digit dialing survey of the population.

Board 30. Spores of UV- Repair Defective *Bacillus subtilus* Strains Exhibit UV Inactivation Kinetics Similar to *Cryptosporidium parvum* and *Encephalitozoon* spp.: Potential for their Use as a Biodosimetry Assay for Evaluation of UV Disinfection Systems

M. M. Marshall

Universtiy of Arizona, Tucson, AZ

Recent reports of protozoan sensitivity to low pressure UV has generated great interest in the North American water industry. UV has many advantages in that it is a proven technology for water and wastewater, and is used widely in Europe for drinking water disinfection. Furthermore, issues related to DBPs do not appear to be a concern for UV. Recent inactivation studies of *Cryptosporidium parvum* oocysts have shown that the oocysts of five different strains are sensitive to low pressure UV light. The Iowa, Moredun, Maine, TAMU and Glasgow strains treated with UV light at 10 mJ/cm2 provided oocyst inactivation at 4 logs. Studies on *Encephalitozoon intestinalis*, *E. cuniculi* and *E. hellem* spores treated with UV light at 20 mJ/cm2 also provided inactivation at 4 logs. Monitoring of UV disinfection systems for optimal inactivation of protozoan parasites relies on a rapid and reproducible bioassay system. In this study we present the development of a UV biodosimeter based on spores of *Bacillus subtilus* mutants defective in the repair of UV damage to DNA, which exhibit UV inactivation kinetics similar to *Cryptosporidium parvum* oocysts and *Encephalitozoon* species spores and which can be thus used as a surrogate system. These non-pathogenic organisms have the following advantages for the water industry: (1) They can be used to evaluate low-pressure UV disinfection systems in situ without the risk of pathogen contamination; (2) They provide a shorter turn around time of < 24 hours as compared to animal infectivity which takes 3-4 weeks for results or cell culture RT-PCR which takes 4-5 days for results; and (3) they are more cost-efficient and rely on standard bacteriological techniques and equipment already available at many existing facilities. Therefore, spores of *B. subtilis* UV-Repair mutants can provide a highly accurate, standardized and reproducible biodosimetry system suitable for municipal-scale applications.

Board 31. Waterborne Epidemic Infections in Ukraine at Last Decade

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Under influences of different ecologic and social factors during the last ten years there is aggravation of epidemiological situation in Ukraine in regards to many infections including waterborne diseases. In August 1991 emerged water outbreak of cholera in towns Vilkovo and Kiliya, situated on river Dunay, where it was revealed 41 patients with illness and 115 - of vibrio-carriers. After that cholera was spread on set of other territories of Nykolaev and Khersoh regions and all around in Ukraine it was revealed 106 patients with cholera and 179 - of vibrio-carriers. Outbreak begun as result of spreading of agents with water of Dunay during freshet from Romania, where cholera was observed. During 1992 - 93 years outbreaks of cholera in Ukraine were not observed. In 1994 year appeared most prominent epidemic of cholera at last 75 years. At that time 845 patients were hospitalized with illness and 600 vibrio-carriers were revealed. By leading factor of infection transmission was water of river South Bug in Nykolaev region, that was polluted by sewage water. Most probable the carry the infection was from Dagestan, where in 1994 year was epidemic of cholera during which 2500 patients were revealed. This epidemic begun one month earlier than in Ukraine and carry the infection was by transport way through Rostov region. In 1995 year there were 525 patients with illness of cholera and 399 of vibrio-carriers and that was a continuation of previous epidemic. After that the cases of cholera were only sporadic, however were connected with deep-seated infection. At that time, there were also continuous outbreaks of other waterborne infectious diseases such as typhoid fever - 6, Flexneri dysentery - 10, Sonne dysentery 3, as well as outbreaks of gastroenterocolitis caused by opportunistic bacteria. Serious problem for Ukraine represents virus hepatitis A and E. During last five years emerged 8 outbreaks of hepatitis A, during which 2972 patients were revealed. All cases were connected with drink water - water-supplies, from shaft wells and reservoirs. Above data evidence about serious danger of emergency of waterborne infection epidemics in Ukraine.

Board 32. Antibodies Against Hepatitis E Virus (HEV) Proteins in Acute Hepatitis and Blood Donors in India

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Background: Hepatitis E virus (HEV), the major cause of viral hepatitis is transmitted by contaminated food and water. It causes large epidemics and sporadic form of disease through out the world. HEV infection is endemic in India. In such an endemic area the diagnostic accuracy and kinetics of IgM anti HEV need to be evaluated. The significance of IgG anti HEV in the endemic population has not been studied. The magnitude of HEV infection among patients with sporadic acute viral hepatitis (AVH) has not been studied as well by sensitive assays for IgM anti HEV detection. Therefore we developed a sensitive ELISA to detect IgM and IgG anti HEV and evaluated its efficacy among healthy blood donors , patients with acute hepatitis in the sporadic and epidemic set up. **Methods:** Development of ELISA for detection of IgG and IgM anti HEV against the 3 recombinant proteins of HEV [full length open reading frame 2 encoded protein (pORF2), full length pORF3 and C terminal end of pORF1 protein]. **Results:** The validation of the test was seen by the high degree of correlation between presence of IgM anti HEV and HEV RNA in serum among the icteric patients (72% and 50% in sporadic and epidemic hepatitis respectively with in the first 2 weeks). The IgM anti HEV was detected against all the 3 proteins in maximum number of cases i.e. 19 of 200 in healthy blood donors, 185 of 266 in sporadic hepatitis, 114 of 221 in epidemic hepatitis and also in 67 of 124 contacts in the epidemic area. The kinetics of IgM anti HEV was studied from the serial samples of 21 patients with acute HEV infection. The IgM antibodies last for about 8 weeks. The IgG anti HEV was found in 30% of normal healthy blood donors and in sporadic cases and 70% in epidemics. **Conclusion:** The IgM anti HEV against all the three proteins of HEV have maximum sensitivity and usually last for 8 weeks. IgG antiHEV may also be short lasting. A significant number of subclinical infections is also seen. In India 45% of acute viral hepatitis is caused due to HEV.

Board 33. Diarrheal Pathogens Other than *E. coli* in Egypt

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Background: Diarrheal disease is a leading cause of morbidity and mortality in the developing world. Previous reports

have documented changing patterns of antibiotic resistance, particularly a resurgence of sensitivity to chloramphenicol (C), tetracycline (TCN) and sulfamethoxazole-trimethoprim (SXT). A surveillance system initiated by the Egyptian Ministry of Health & Population and NAMRU-3 monitors the prevalence of bloody and watery diarrhea at a number of infectious disease hospitals throughout the country. We report the laboratory findings from two hospitals during JAN-JUL 2001. **Methods:** Stool samples or rectal swabs were collected from patients admitted with diarrhea. Samples were cultured on MacConkey, S-S, Hektoen Enteric, TCBS and *Campylobacter* blood agars. Sensitivity testing was performed to standard antibiotics using the disk diffusion method. **Results:** Of 397 stool cultures processed, 80 (20%) were positive for enteric pathogens other than *E.coli*. Etiologies were *Shigella* spp. (51.2%) and *Salmonella* spp. (48.8%). *Shigella* isolates were identified as *Shigella flexneri* (71 %), *S. sonnei* (23 %), *S. dysenteriae* (2.6%) and *S. boydii* (2.6 %). Salmonellae isolates were identified *Salmonella* serogroups B (37%), D (37%), C1 (13%), C2 (8%) and as *S. typhi* (5%). No *V. cholera* or *Campylobacter* isolates were recovered. *S. flexneri* were resistant to C (63%), ampicillin (AM) (63%), SXT (63%) and TCN (79%). 10% of *S. sonnei* were resistant to both C and AM, while most *S. dysenteriae* and *S boydii* were sensitive to all antibiotics tested. While *S. typhi* was sensitive to the antibiotic panel used, 21% of the other *salmonellae* were resistant to C, AM and SXT. No resistance to ciprofloxacin and ceftriaxone was detected. **Conclusion:** *Shigella* and *Salmonella* spp are the most common enteric pathogens other than *E. coli* in patients presenting to hospitals with diarrhea. *S. flexneri* harbors the greatest antibiotic resistance.

6 Emerging Zoonoses I

Sunday, March 24, 12:00 noon
Grand Hall East

Board 34. Human Exposure to Herpes B Seropositive Macaques in Bali, Indonesia

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Herpes B virus is implicated as the cause of nearly forty cases of meningoencephalitis affecting people in direct or indirect contact with laboratory macaques. However, the threat of Herpes B in non-laboratory settings worldwide remains to be addressed. The present study investigates the potential for exposure to Herpes B virus among workers at a "monkey forest" in Bali, Indonesia. A survey eliciting information regarding contact with macaques was administered to 105 workers at the Sangeh monkey forest in Central Bali in July, 2000. Nearly half of those interviewed had either been bitten or scratched by a macaque (*M. fascicularis*). Additionally, serum obtained from 31 of 38 Sangeh macaques contained antibodies to Herpes B virus. We conclude that workers coming into contact with macaques at the Sangeh monkey forest are at risk for exposure to Herpes B virus. Public health implications of these findings are discussed.

Board 35. Cryptosporidiosis in Veterinary Technician Students — An Annual Rite of Passage

A. S. Craig[1], B. Wanamaker[2], D. Gibbs[3], J. Sanders[4], D. Lampley[2], W. Schaffner[5]

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Background: *Cryptosporidium parvum* has emerged as an important cause of human diarrheal disease in the past decade. Cryptosporidiosis has been reported as a cause of commonly occurring "scours" (diarrhea) in calves. Direct zoonotic transmission of disease has been reported though uncommonly. We report an outbreak among veterinary technician students at a local college who participated in a livestock management course. Student activities included feeding, grooming, and taking rectal temperatures on calves three or more days per week. The principal instructor reported that similar outbreaks occurred each fall among students in his class shortly after the arrival of the calves. **Methods:** Students were interviewed regarding gastrointestinal illness and exposures to calves cared for by the class. Human and bovine stools were cultured for *Salmonella*, *Shigella*, *Campylobacter*, and *E. coli* O157. All stools were also examined for parasites by standard microscopic techniques and for *Cryptosporidium parvum* and *Cyclospora cayetenesis* by direct fluorescent antibody (DFA). Three calves had been replaced due to severe diarrhea before they could be cultured. **Results:** Twenty-one (95%) of 22 class members were interviewed. Fifteen (71%) of 21 students reported diarrhea. The average duration of diarrhea was 8 days. Six sought medical attention for their illness; none were hospitalized. Stool cultures were collected from 10 (67%) of 15 ill students and 9 (64%) of 14 calves. All cultures for bacterial pathogens were negative. Three students were DFA positive for *Cryptosporidium parvum*. One calf was DFA positive for *Cryptosporidium parvum*. Five calves were DFA positive for *Giardia lamblia*. There was no association between diarrhea and eating or drinking in the barn or handwashing habits. **Conclusions:** An outbreak of cryptosporidiosis occurred among veterinary technician students at a local college. The students were exposed to at least one calf with cryptosporidiosis and several with giardiasis. It is likely the students contracted *Cryptosporidium* infection via the fecal-oral route due to poor hygiene. Recommendations to prevent this annual rite of passage for students include wearing coveralls, boots and gloves, particularly when caring for ill calves and adhering to meticulous handwashing after class. Future investigations might include follow up of future classes and an assessment of the risk in other veterinary schools.

Board 36. VTalumnNET (VTA) of Virginia Tech: A Program of Distributing Information on Emerging Infectious Diseases (EID) to Virginia Tech Alumni and the General Public

T. E. Toth[1], S. Turner[2], M. Howard[1], J. Phillips[2], C. Zamboni[2]

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VTA is a newly initiated program by the President of Virginia Tech providing an online virtual gateway to lifelong learning. VTA allows easy distribution of knowledge through a wide variety of subjects, asynchronous and instructor led courses to VT alumni and members of the public at large. EID, a one-credit course, is the first on-line (Spring 2001), asynchronous course of the VMRCVM, given by 14 faculty of the VMRCVM and was adapted to the VTA program (Fall 2001). EID defines and discriminates between emerging and other infectious diseases, defines spatial and temporal determinants, host and agent characteristics and risk factors, analyzes social, economical and interna-

tional trade changes, improper uses of antibiotics, multi-drug resistant infectious agents as factors in emerging diseases of humans and animals. Selected emerging food-borne, bacterial, viral and zoonotic diseases of animals and humans are discussed. In all lectures, whether they discuss human or animal diseases, the three-way interaction among the infectious agents and these hosts are emphasized. Content is primarily managed and delivered through the Blackboard course management system and a Real streaming server. The lectures (Powerpoint slides narrated by the instructors) are available by streaming video on RealPlayer in two versions of audio and image delivery for high-, or low bandwidth reception and audio only for the worst reception conditions. In the VTA program, the lectures of EID have been assigned to two main types of self-paced delivery modules: Knowledge Units (1-1.5 hours of content) which contain selected single lectures and Mini Courses (4-8 hours of content) which contain groups of lectures organized to meet pedagogical logic and by presumed interest groups, such as Public Health workers, people interested in horses, swine, poultry, and wild animals. Experience with the reaction of the public to this concept will be included and analyzed at the presentation of the poster. VTalumnNET URL: http://alumni. iddl.vt.edu General Public Direct Link: http://www.vto.vt. edu/vetmed.

Board 37. Prognostic Factors in Moderate to Severe Leptospirosis: An Experience from Kerala, India

D. Unnikrishnan, R. Pisharody, N. Vijayalekshmi

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Background: Leptospirosis, a worldwide zoonosis, has increasing incidence in the state of Kerala, South India. Often mild and self-limited, severe disease can be fatal. **Methods:** 92 patients (74 males, 18 females) with moderate-severe leptospirosis, admitted to Trivandrum Medical College, Kerala, during Jun 1995 - Dec 1996 were studied. Diagnosis was by clinical and laboratory features, and confirmed by IgM ELISA. Demographic, clinical, laboratory and treatment details were analyzed in relation to outcome (mortality). **Results:** 14 of the 92 patients (11 males, 3 females) died, mortality rate 15.2%. Higher mortality was noted in those above age 50 (27.7% vs 12.2%). No difference in mortality was seen when grouped by sex, at-risk occupation or rodent/pet exposure. No significant difference was noted between day of starting antibiotics after initial symptoms and mortality (mean 7.60 $\pm$ 2.95 days in survivors, 8.57 $\pm$ 3.08 in dead). 12 patients had symptoms of Jarish-Herxeimer reaction with penicillin, one died. 46 patients had acute renal failure, 11 underwent hemodialysis. 34 patients had electrocardiographic (EKG) changes: ectopics (24 patients), sinus tachycardia (7), T wave changes (17), atrial fibrillation (3), first-degree block (1), sinus bradycardia (1) and hyperkalemia (1). Clinical, EKG and echocardiographic features of myocarditis was present in 9 patients, 4 of whom died. Those with myocarditis and hypotension had 75% mortality. Abnormal chest X-rays included nodular (12 patients), reticular (7), ground glass (4), consolidation (5) and effusion (6). 3 out of 4 patients with respiratory distress syndrome died. Significant difference ($p<0.05$) among survivors and non-survivors was found in serum CPK (mean 246.21 vs 877.71 u/L), serum sodium (mean 138 vs 127 mEq/L), potassium (mean 4.22 vs 5.21 mEq/L) and platelet count (mean 145,026 vs 80,000/mm3). No significant difference was found in serum bilirubin (mean 8.29 vs 14.92 mg/dL), ALT (98.97 vs 175.86 u/L) or creatinine (2.98 vs 4.04 mg/dL). In logistic regression analysis of organ system dysfunction, bleeding (hemoptysis, gastrointestinal, epistaxis) [OR 17.45, $p=0.003$], cardiac (myocarditis, EKG changes) [OR 15.56, $p=0.02$] and neurological (seizures, altered mentation) [OR 22.12, $p=0.0003$] complications were significant predictors of mortality. Among laboratory variables, CPK >500 u/L ($p=0.0002$) and serum sodium < 130 mEq/L ($p=0.0059$) were significant as predictors of mortality. **Conclusion:** High mortality reflects severe illness in hospitalized patients. Higher numbers of young male patients results from high occupational risk. Bleeding, cardiac, neurologic complications, hyponatremia and high CPKs predict poor outcome. Poor prognostic factors identify patients who need intensive monitoring and treatment. With efficient renal support therapy, other organ dysfunctions account for most deaths in the disease.

Board 38. Acute West Nile Virus Infection of Reptiles and Amphibians

K. Klenk

CDC, Fort Collins, CO

Due to the seasonality of the most important West Nile virus vector, the mosquito, it is presently unknown how the virus can survive periods of mosquito inactivity. One theory suggests reptiles and amphibians may serve as West Nile virus hosts by sustaining infectious viremia for long periods during the winter until mosquito activity resumes in the warmer months. Some reptiles and amphibians are known to develop arbovirus viremia and one species, *Rana ridibunda*, can produce high viremic titers of West Nile virus capable of re-infecting mosquitoes. This present study focuses on the acute viremia titers of three North American species of reptiles and one North American species of amphibian after experimental infection with West Nile virus. The representative species include: *Rana catesbeiana* (bullfrog), *Iguana iguana* (green iguana), *Thamnophis radix* (garter snake), and *Trachemys scripta elegans* (red ear slider). Twenty-one individuals of each species were infected with West Nile virus (NY99) followed by the sacrifice of three individuals of each species each day for viremia determination during 7 consecutive days. Additional animals were maintained longer for evaluation of persistent viremia and/or infection of tissues. These data will be presented and discussed.

Board 40. Pogosta Disease — A Potentially Chronic Arthritis Caused by Virus

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A disease characterised by arthritis, rash and fever was described in the Northern Karelia in Finland 1974 by a local physician and named, acccording to the region, Pogosta disease. When analysing the clinical picture during a later outbreak we found that 93% of the patients had joint inflammation, and 40% of them had polyarthritis. In 8% of the cases the arthritis was severe. Rash was seen in 88% of patients, and 23% had fever. It has been supposed that the disease is mild and self-limiting, but in a follow-up study it turned out that 50% of the patients suffered of chronic joint and muscle pains even more than 2.5 years. Three out of 26 patients had fibromyalgia, six had occasional arthralgia and two had chronic arthritis. One patient developed an erosive disease closely resembling rheumatoid arthritis. There have been several outbreaks of Pogosta disease in the Northern Karelia, where it is considered endemic. The outbreaks seem to occur every seven years. Pogosta disease resembles closely the Ockelbo disease reported from Sweden, and Karelian fever described in Russia. All these three diseases are attributed to Sindbis-related arboviruses. So far the causative virus has not been isolated from Pogosta patients. The vector spreading the infection are mosquitoes, and the virus causing Ockelbo disease was isolated from *Culiseta* late summer mosquitoes. It has been assumed hat Pogosta disease is locally restricted as described for Ockelbo disease and Karelian fever. These diseases affect mainly young to middle aged adults. In an epidemiological study we analysed antibodies in 2250 serum samples, using a semi-purified Sindbis virus as antigen. It turned out

that the prevalence of the disease was much higher than expected, and that positive sera originated from all parts of Finland. Eleven % were positive for IgG class and 0.6% for IgM antibodies. To our surprise, antibodies were frequently found in individuals aged 1 to 20 years. This may indicate that the disease is spreading in an unexpected manner. Pogosta disease is an example of a viral disease the role of which has been underestimated. Pogosta disease may lead to both acute and chronic arthritis or fatigue symptoms. It's occurrence has not been studied outside Scandinavia and Karelia, but mosquitoes may spread it also elsewhere. Pogosta disease should be considered as a differential diagnostic alternative at least in patients with joint symptoms.

Board 41. Wildlife Tuberculosis, Bovine Tuberculosis and Zoonotic Tuberculosis ñ Potential Threats to Human Health in Rural African Communities?

A. Michel

Onderstepoort Veterinary Institute, Onderstepoort, SOUTH AFRICA

Following the implementation of a National Tuberculosis Control and Eradication Scheme in 1969, the prevalence of tuberculosis in South African commercial cattle herds has dropped sharply to around 0.0003%. This does, however, not include cattle herds belonging to rural communities and subsistence farmers. It further excludes the tuberculosis epidemics currently experienced in South Africa's two major game reserves, the Kruger National Park (KNP) and Hluhluwe-Umfolozi Park (HUP). It is estimated that bovine tuberculosis spilled over from cattle to African buffalo (*Syncerus caffer*) in the KNP via the wildlife-livestock interface approximately 40 years ago. It has since spread among buffalo herds in the southern and central regions of KNP and was more recently also diagnosed in the northern areas. With increasing prevalence rates in buffalo, which are regarded as maintenance hosts for tuberculosis, spillover to other animal species such as lion (*Panthera leo*), leopard (*Panthera pardus*), Cheetah (*Acinonyx jubatus*) hyena (*Crocuta crocuta*), chacma baboon (*Papio ursinus*), greater kudu (*Tragelaphus strepsiceros*), warthog ( )and honey badger ( ) became evident. If uncontrolled, this epidemic is expected to spread over the entire areas of both the KNP and HUP, affecting many more species over time. Both parks are mostly bordered by communal farmland of resource poor farming communities and only few commercial farms. Despite the erection of adequate game fencing over the full length of both parks, this barrier can only partially prevent contact between wild animals and domestic livestock. Under these conditions the risk of tuberculosis spillover into domestic livestock outside the parks is increasing and cannot be ignored.As mentioned, communal cattle herds are not regularly tested for bovine tuberculosis. Therefore, once present in a herd, the infection is allowed to progress into the advanced stages of disease, with animals developing open lesions and shedding bacilli mainly in milk and aerosols. These are at the same time the main routes of transmitting zoonotic tuberculosis, in particular because milk is primarily consumed unpasteurised. The high incidence of HIV/AIDS in South Africa is a another complicating factor potentially contributing to the transmission of zoonotic tuberculosis. Immunocompromised patients, especially children, are more likely to contract *M. bovis* infection than healthy individuals. Presently the role of zoonotic tuberculosis in humans in South Africa is unknown, but both the raging HIV/AIDS and wildlife tuberculosis epidemics urge for a joint veterinary/medical approach to assess the current situation.

Board 42. Paleoepidemiology of Hantaviruses

E. J. Bassett

University of Utah, Salt Lake City, UT

Hantaviruses are rodent-borne zoonotic agents with a genetic diversity indicative of significant antiquity. Although Hantavirus Pulmonary Syndrome (HPS) has been described as a re-emergent disease, little is known of past exposure levels. Over six years, a series of replicative maize storage and processing experiments were conducted to evaluate the risk prehistoric agriculturalists living in the North American southwest would have faced from virus-contaminated aerosols of rodent excreta. Twenty-eight traditional, maize pit storage units were constructed and monitored for a year each. Rodents (mostly Peromyscus sp.) infested six of the units (21.4%) with excreta quantified through feces counts and Nessler's reagent for the presence of urine; maize stored by traditional methods would have carried a high load of hantavirus-laden rodent feces, urine, and saliva. Also, areas of reuse were more likely to be reinfested in subsequent years and rodent populations increased over time near storage units, possibly due to an increase in both food and predator cover. A series of replicative maize grinding experiments were conducted to evaluate the potential for aerosolization during maize processing. Sterilized maize rehydrated to average storage moisture was ground with prehistoric groundstone to meal consistency, during which a personal particulate monitor was worn with pre-weighed, low-ash PVC canister filters. Mean inhalable dust was 36 mg/m3 (range 1.1 to 232 mg/m3). During the initial grinding, most particles belonged to the extrathoracic fraction but most later dust was in the respirable fraction with much fugitive dust produced. Historical data indicates ground maize constituted as much as 70% of the diet over two millennia and that adult females spent up to 6 hours a day in its preparation. Similar traditions are discussed for other known areas of HPS, for HFRS in Asia and Eastern Europe, and for arenaviruses, including Lassa fever. These results suggest that among prehistoric maize farmers, HPS exposure would have been very different from the pattern documented during modern times, being common and systematic rather than rare and random; domestic rather than extradomestic; affecting adult females and children more than adult males; and influenced more by cultural practices than by natural or climatic episodes. Higher mortality by reproductive-age females within small breeding populations could have had significant demographic consequences and/or resulted in differential resistance. The clinical recognition of the Sin Nombre strain among non-Native Americans and among Navajos (circa. A.D. 1500 non-agricultural arrivals to the Southwest) and its apparent absence from modern Native Americans who traditionally practiced maize agriculture should be investigated in the light of these conclusions.

Board 43. Anthrax In Kazakhstan

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During 1995-2001, about 150 human anthrax cases were registered, of which over 70% happened in the South Kazakhstan, Jambyl and East Kazakhstan oblasts. These oblasts are known for its cattle raising farms. The South Kazakhstan oblast ‡t present the number of cattle was 264,000, 64% of these were covered with anthrax vaccinations. Sheep and goats numbered 1.·5 million, 29% of them vaccinated, 65,000 horses (31% vaccinated), over 3,000 camels (29% vaccinated) and 3,500 pigs (100% vaccinated). Numerous observations point that man can easily get infected with anthrax through tiny scratches, lesions, etc. This may happen while slaughtering, dressing and skinning anthrax-infected animals, or when wearing fur clothes infected with anthrax spores. There are recorded instances of human infection through the bites of gadflies, flies and mosquitoes, which were in contact with animals infected with anthrax . Basically human anthrax is registered in spring-summer period from May to November with peak July-August. That humans are highly susceptible to infection with anthrax through damaged skin is evidenced by an analysis of an outbreak of the disease in the South Kazakhstan Oblast during 2000-2001. In 74% of the cases the source of infection was cattle, in 14% of the cases it was sheep and goats. 3% of the cases seemed

to get infected through contaminated soil. 9% of the cases had contacts with infected products of animal slaughter. An analysis of data on the outbreaks of anthrax in the SKO in the summer of 2000-2001 allows maintaining: that humans are highly susceptible to the causative agent of anthrax when infected through damaged skin. All people participating in a forced slaughter of farm animals contracted anthrax. They were infected as a result of direct contact with the flesh of anthrax-infected animals. It is necessary to take note of a possibility of getting infected through the transmission way. In the course of the anthrax outbreak one of the patients who died of septicaemic anthrax seem to have contracted infection when using undercooked meat. The possibility of one patient getting infected through the contact with anthrax spores-contaminated soil may not be ruled out.

Board 44. Epidemiological Features of Tularemia Incidence in Kazakstan

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Tularemia is natural-foci zoonotic disease, the wide distribution of that in Kazakhstan is conditioned by the landscape-geographic peculiarities favourable for the causal agent striking root in the natural conditions. The landscape complex of focusing is represented by different types: steppe, flood-lands-marsh, foothills-stream and tugai. Tularemia is registered almost in all the regions of Kazakhstan except South-Kazakhstan and Mangistau oblasts. For the first time tularemia cases were registered in Kazakhstan in 1928 in Uralsk province during the outbreak on the Urals river connected with the purveyance of water vole (*Arvicola terrestris*) skins. From the May 1 till June 9 105 cases in main of bubonic and ulcerous-bubonic forms were registered. Tularemia etiology of the given disease was established by Golov D.A., Kniazevski A.N., Berednikov V.A. and Tiflov V.Y. In summer 1930 a transmissive tularemia outbreak in Karatalsk region of the Taldi-Kurgan oblast (st.Ush-Tobe) was registered. In 1942 16 settlements in the delta of the Volga were enveloped in tularemia. Especially great outbreak was registered in Gvardeiski region of the Taldi-Kurgan oblast in 1947 when 658 people fell ill. Contamination took place as a result of using water from the reservoir infected by water voles secretions and their corpses. The following great outbreak was registered in Karatalsk region in July-October 1949, - 152 human cases were registered. The same year the great outbreak was registered in Norst-Kazakhstan oblast (200 people). In 1954 the greatest outbreak took place in Kazakhstan in Pavlodar oblast in the Irtish flood-lands, 1791 human cases were registered. By its nature it was mixed type; it was started as the trade one, then it became of the transmissive character and took place as a water outbreak type with the considerable number of people who fell ill as a result of the contacts with contaminated water. The increase of the sickness rate in Tselinograd (now Akmolinsk), Karaganda and Semipalatinsk oblast, registered in 1954, 1958-1959 years, was conditioned by the development of long-fallow lands, the migration of large quantity of the not-immunized against tularemia population from the tularemia favourable places. Then (in 1968, 1972) the mass cases were conditioned by stings of blood-sucking Diptera (gnats). The decrease of the sickness rate for some time past was conditioned by the conducted complex of sanitary-hygienic and prophylactic measures. Over all in Kazakhstan since the beginning of the century due to the not total data more than 6000 tularemia cases were registered.

Board 45. Epidemiological Grounds in Russia for Vaccine Prophylaxis of HFRS

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Among zoonotic virus infections and all other natural focus diseases for humans, HFRS with its morbidity rate leads in Russia. A total of 135,222 cases were registered from 1978 to 2000 from 71 out of 89 administrative regions involving 131,192 cases from the European part of Russia. Serological and genetic typing of hantavirus strains as well as wild rodent lung tissue and HFRS patient blood in-dicated the circulation of at least 7 hantavirus types on the territory of Russia: Hantaan, Puumala, Seoul, Dobrava/Belgrade, Tula, Khabarovsk, and Topografov. The first four of them cause HFRS dis-ease in humans. HFRS cases in 52 European regions are etiologically conditioned mainly by Puumala virus type and make up 97% of total number of HFRS cases registered in Russia while 3% have been registered in 4 Far-Eastern regions where HFRS cases are caused mainly by Hantaan and less by Seoul virus types. The sporadic HFRS cases caused by Dobrava/Belgrade virus type were recently detected in European and West Siberian regions of Russia. The highest rate of annual HFRS morbidity occurs in the South East of the European part of Russia, mainly on the territory of Bashkiria with annual average morbidity rate of 58.3 per 100,000 population. Human epidemics are characterized by cycles with a frequency of 3 to 4 years. Periodical and massive reproduction of rodents, with the forming epizootics among them, is the main and determinative factor that influences HFRS epidemics in humans. The prevention of the HFRS disease mainly includes measures aimed at reducing exposure to live rodents and their excreta. However, rodent control measures are expensive and difficult to maintain over long periods because it is practically impossible to eradicate the rodent hosts of the hantaviruses from nature. Hence it is obvious that the most prospective and effective measure for decreasing HFRS morbidity in endemic regions of Russia could be but regular and massive vaccine prophylaxis against the disease. HFRS morbidity may be used as an indicator to estimate the required HFRS vaccine doses for vaccination in Russia: 20 European regions with population of about 45 mln as well as 4 Far-Eastern regions with population of about 5 mln. So, approximately 25% of population of these regions (12.5 mln people) potentially need the vaccination against HFRS.

Board 46. Dysphagia Presenting as an Early Neurologic Complaint in a Fatal Case of West Nile Virus Encephalopathy

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Cases of West Nile virus (WNV) encephalopathy recently reported in the northeastern United States detail numerous neurologic complaints, the most common being weakness, headache and altered mental status. Photophobia, slurred speech and seizures were observed less frequently. Dysphagia was not described. We report the first case of WNV disease in Georgia which occurred in August 2001 in a 71 year old female who resided in inner-city Atlanta. Unlike prior cases, this patient complained of dysphagia early in her clinical course. Interestingly, dysphagia preceded decline in the patient's mental status by approximately 1 day. The patient subsequently developed an aspiration pneumonia which undoubtedly contributed to her eventual demise on hospital day 12. An abnormal barium swallow and EEG confirmed our clinical impression of initial dysphagia and subsequent encephalopathy. WNV diagnosis was confirmed based on established CDC criteria using sera and CSF (EIA and plaque

reduction neutralization assay). The prominence of dysphagia in this case is remarkable because it provides clinical correlation with WNV neuropathologic findings. Specifically, involvement of the brainstem, an area of the brain which is also involved in the swallow reflex, has been noted in multiple WNV cases. Secondly, purely from a clinical viewpoint, this case argues that, in patients in whom one has a high clinical suspicion of WNV encephalopathy, early aggressive airway management is important, especially in the face of unexplained dysphagia.

Board 48. Humoral Immune Responses to Hantavirus Andes in Humans

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The absence of an effective treatment of Hantavirus Pulmonary Syndrome causes mortality rates between 30 and 50%. A number of reports have shown that the passive transfer of neutralizing monoclonal antibodies protects rodents from Hantavirus infection. This has lead several groups to investigate the humoral immune response in patients with different clinical development suggesting that the survival of patients seems to be strongly associated with the titer of neutralizing antibodies. In this work, sera from patients infected with Hantavirus Andes were tested for their neutralizing activity by focus reduction neutralizing tests and assayed for their ability to react with linear epitopes of viral proteins. These epitopes were identified by the use of 120 peptides, each of 13 amino acids in length representing the entire nucleoprotein and the two envelop glycoproteins of the Hantavirus Andes, Chilean isolate CHI99-7913. Analysis of these sera revealed antibodies reacting with epitopes covering the whole nucleoprotein with three immunodominant regions approximately located at aa66 - aa78; aa248 - aa260 and aa326 - aa338. The glycoprotein G1 was highly immunogenic in the N-terminal half which could be divided in four main regions (aa14 - aa26; aa66 - aa104; aa196 - aa234 and aa287 - aa338) whereas in the glycoprotein G2, the regions from aa27 - aa65 and aa79 - aa117 showed strong reactivity with these sera. The production of monoclonal antibodies against these epitopes is in progress.

Board 49. A Single Genotype of *Encephalitozoon intestinalis* Infects Free-Ranging Gorillas and People Sharing Their Habitats, Uganda

T. K. Graczyk[1], J. Bosco-Nizeyi[2], R. B. Innocent[2], A. J. DaSilva[3], N. J. Pieniazek[3], A. H. Lindquist[4], M. R. Cranfield[5]

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For conservation purposes and due to ecotourism free-ranging gorillas of Uganda have been habituated to humans, and molecular epidemiology evidence indicates that this habituation might have enhanced transmission of anthropozoonotic pathogens. Microsporidian spores have been detected by modified trichome and calcofluor stains in fecal samples of 3 gorillas and 2 people sharing gorilla habitats. All spore isolates have been identified by polymerase chain reaction (PCR) with species-specific primers and fluorescent *in situ* hybridization (FISH) to be *Encephalitozoon intestinalis*. Sequencing analysis of the full length SSUrRNA amplified from all isolates were identical to *E. intestinalis* SSUrRNA GenBank SIU09929. In addition sequences generated from the intergenic spacer (ITS) of these isolates were identical to GenBank sequence Y11611 from *E. intestinalis* isolated from European HIV-positive individuals. A single genotype in two genetically distant but geographically united host groups indicates anthropozoonotic transmission of *E. intestinalis*. It is unlikely that infections with genetically identical pathogens were acquired independently, and it is much more likely that one of these two host groups initiated infection of the other group. This may also indicate that ITS region is not infromative for strain differentiation.

Board 50. A Case of Plague Successfully Treated with Ciprofloxacin and Sympathetic Blockade for Gangrene

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Background: Approximately 1800 cases of human plague are reported to the World Health Organization each year worldwide. Roughly 10 cases yearly occur in the southwestern U.S. The recommended antibiotic for this infection, streptomycin, is difficult to obtain in the U.S. Ciprofloxacin has shown good activity against *Yersinia pestis in vitro*, but has not been systematically evaluated in humans with *Y. pestis* infections. This report details the use of ciprofloxacin in a patient with septicemic plague, and sympathetic blockade for gangrene of his lower extremities. Presentation: A 45 year old white male presented with a 2 day history of increasing fever, myalgias, rigors, headache and weakness. He had been camping in an area of Arizona known to be endemic for plague, but had no history of rodent exposure or insect bites. Physical examination revealed an acutely ill man with blood pressure of 85/57 mm Hg, respiratory rate 26, heart rate 117 and temperature 38.5∞C. He had acrocyanosis, severe myalgias and a purpuric rash with evolving gangrene of the nose, ears and extremities. There were no sores, lymphadenopathy or pneumonia. Blood cultures were negative; however, Gram stain of a peripheral blood smear showed Gram-negative rods within leukocytes. Direct fluorescent antibody stains of organisms on the peripheral smear by the Centers for Disease Control were positive for *Y. pestis*. This finding was confirmed by seroconversion for *Y. pestis* using the passive hemagglutination test, with titers rising from negative to 1:1024. **Treatment and Results:** The patient was treated empirically for 15 days with ciprofloxacin because of its spectrum of activity and ability to penetrate leukocytes. He survived with supportive treatment and this antibiotic regimen. He also had progressive gangrene of the extremities. On the fourth hospital day, before the gangrene had completely demarcated, a lumbar epidural infusion catheter was placed. This sympathetic blockade of the lower extremities brought about almost complete resolution of the gangrene involving his feet. He sustained gangrenous damage to his nose and fingers, however, which required plastic surgery reconstruction. Discussion: Septicemic plague can be fulminant and patients often are critically ill when diagnosed; there is a risk of mortality even when appropriate antibiotic treatment is started. Our diagnosis was aided by the observation that peripheral gangrene is more likely to be associated with septicemia due to plague than with other organisms. Ciprofloxacin proved well-tolerated and effective in treating this patient, warranting further investigation in septicemic plague. Sympathetic blockade should be considered for cases of evolving gangrene in patients with good peripheral blood supply.

Board 51. Detection of West Nile Virus RNA in Human Clinical Specimens

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West Nile virus (WNV), a member of the Flaviviruses, was responsible for an outbreak of encephalitis in New York City in 1999. Human WNV infections can be diagnosed by an immunoglobulin M capture enzyme-linked immunosorbent assay. Because of antigenic cross reactivity among members of the Flaviviruses, a plaque reduction neutralization assay is required to confirm infections by WNV. Reverse transcription-PCR (RT-PCR) assays have been developed for the selective detection of several

RNA viruses, including WNV. We have assessed two molecular approaches, a standard RT-PCR and a real-time (TaqMan) RT-PCR, with clinical specimens from confirmed human cases from the New York City outbreak. Thirty-two cerebrospinal fluid (CSF) samples and 4 brain tissue samples from 23 confirmed cases were analyzed. WNV sequences were detected in 12 (52%) and 8 (35%) of patients by two-step RT-PCR and TaqMan assays, respectively. Analyses of CSF samples collected from 4 fatal cases detected WNV in only 1 person who was ill and in all 4 persons postmortem by both standard RT-PCR and TaqMan assays. Analyses of brain tissue samples from the same 4 fatal cases by standard RT-PCR and TaqMan assays detected WNV in all samples with both assays. The quantity of WNV RNA in the brain tissue samples, as determined by the TaqMan assay with *in vitro* transcribed WNV RNA, ranged from 4.8×10^4 to 6.2×10^6 copies per milliliter of 10% brain suspensions. The quantity of WNV RNA in CSF samples from fatal and nonfatal cases ranged from <50 to 3.1×10^4 copies per milliliter. In general, the quantities of WNV RNA in the CSF of nonfatal cases were lower than the quantities detected in fatal cases. Our results independently corroborate the results of other investigators concerning a lower success in the detection of WNV in CSF by RT-PCR and TaqMan compared with serologic detection methods.

Board 52. Clinical and Molecular Investigation of a *Salmonella* Typhimurium DT104 Outbreak Due to Consumption of Raw Beef

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Background: *Salmonella enterica* serotype Typhimurium, definite phage type (DT)104 is a zoonotic pathogen. Since 1990 it has become an increasingly common cause of human gastroenteritis worldwide. In Israel the first human cases were reported in 1994. This strain is frequently associated with multidrug resistance to antimicrobial agents. The common R-type in Israel is ACST (A. ampicillin; C. chloramphenicol; S. streptomycin; T. Tetracycline). **Objectives:** To determine the epidemiological, clinical and molecular characteristics of an outbreak of severe gastroenteritis in a close community of East Asian workers. **Materials and Methods:** A comprehensive epidemiological investigation was carried out by the Ashkelon District Health Office employing interviews and survey of medical records. *Salmonella spp.* isolated from clinical sources and from suspected beef and cow blood samples were identified and tested by classical laboratory methods (serotyping, phagetyping and antibiotic resistance typing). The epidemiological and serological data were complemented by molecular investigation, using pulse field gel electrophoresis (PFGE). **Results:** In July 2001, fifty nine individuals of an East Asian group of workers developed severe diarrhea. Twenty five were hospitalized. Two patients developed secondary bacteremia. *Salmonella* typhimurium DT104 was isolated from the stool of all the 25 patients and the two blood samples. The epidemiological investigation revealed a suspected common source: Raw beef eaten by all on the day before onset of symptoms. The estimated attack rate in the exposed population was 100%. The median incubation time was 18h. The same *S.* typhimurium DT104 was isolated from samples of the suspected beef and cow blood. Application of PFGE with the restriction enzymes *Xba*I and *Avr*II to all isolates revealed the same PFGE pattern for all human and food isolates. The clonality was confirmed by a common drug resistance pattern (ACSTN; N. nalidixic acid). **Conclusions:** The main characteristic of the reported outbreak is its definite focal pattern. We assume that this food borne outbreak is correlated with the specific food handling practice. Similar events have been reported worldwide, emphasizing the global importance of *Salmonella* typhimurium DT104.

Board 53. Simian Foamy Virus (SFV) Infection in Occupationally Exposed Humans: Preliminary Results from a Long-term Follow-up Study

R. S. Boneva, W. M. Switzer, T. Spira, V. Shanmugam, J. E. Cummins, V. B. Bhullar, W. Heneine, T. M. Folks, L. E. Chapman

Centers for Disease Control and Prevention (CDC), Atlanta, GA

Background: Simian foamy virus (SFV) infection has been confirmed by PCR in 11 of 12 seropositive men occupationally exposed to nonhuman primates (NHPs). SFV is strongly cytopathic in cell culture but is not known to cause a disease in its natural hosts, NHPs. The purpose of this cohort study was to investigate whether this infection is transmissibile among humans and whether it constitutes a zoonotic disease. **Methods:** SFV-infected humans and their close contacts are eligible to enroll. Participants respond to a standard questionnaire about demographics, occupational exposures, work practices, health status, and opportunities for transmission. Blood and body fluids (saliva, throat swabs, urine, and semen) are collected annually for clinical, virological, and immunologic testing. Enrolled contacts are tested for SFV infection by serology (Western blot, WB) and PCR. **Results:** Of 11 eligible persons, 6 enrolled (A-F), 2 refused participation; enrollment of the other 3 is pending. Reported occupations of the 6 participants were veterinarian, manager, administrator, animal-care worker (two), and researcher. Participants' mean age at enrollment was 52.5 years (range 41 to 62 years). Reported exposures to NHPs ranged from 4 to 41 years (mean 23.3±13.4 years). A minimum of 107 person-years of seropositivity was retrospectively documented. All 6 reported a history of both mucocutaneous exposures to NHP body fluids and occupational injuries with skin penetration (bites and/or sharp injuries). Complete blood counts, blood chemistry, and liver function tests obtained on participants A-F were within normal limits with the following exceptions: patient D had mild thrombocytopenia and a mildly elevated hemoglobin and hematocrit; patient C had a mildly elevated ALT; and patient E, a diabetic, had high blood glucose and indicators of impaired kidney function. SFV was successfully cultured from participants' A and B peripheral blood mononuclear cells and from a throat swab from participant A; viral cultures from other participants were negative. Four wives of these six participants have been tested and were PCR and seronegative after a mean documented exposure of 18.3 years (range 12 to 22 years, total 73 person-years). Four recipients of cellular blood components, donated by participant A, were SFV-negative by WB and PCR. **Conclusions:** Interim analysis found no evidence of disease attributable to SFV infection and no evidence of person-to-person transmission. Continued follow up (anticipated minimal duration of 5 years) should provide more information regarding the transmissibility and pathogenicity of SFV infection and whether any of the identified minor clinical abnormalities in these participants might be associated with the SFV infection.

7 Evolutionary Potential of Viruses

Sunday, March 24, 12:00 noon
Grand Hall East

Board 54. Outbreak of Aseptic Meningitis Associated with the Emergence of Echovirus 13

D. L. Kirschke[1], T. F. Jones[2], S. C. Buckingham[3], W. Schaffner[4]

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Background. The largest reported outbreak of aseptic meningitis associated with echovirus 13 occurred in Memphis, Tennessee between April 15 and August 15, 2001. Before this outbreak, echovirus 13 accounted for only 65 of approximately 45,000 reported enteroviral isolates in the United States in the past 30 years. Several smaller outbreaks occurred in Europe in 2000. We describe the epidemiology of the outbreak among children in Memphis and the clinical manifestations of those with laboratory confirmed echovirus 13 infection. **Methods.** We examined discharge diagnoses to identify cases of aseptic meningitis at a children's tertiary medical center during the epidemic period. We reviewed the charts of patients with laboratory confirmed echovirus 13 and interviewed the parents by telephone. Historical data from this and five other area hospitals were reviewed. Results. We identified 303 cases of aseptic meningitis at the children's medical center during the epidemic period. The number of hospitalizations peaked in May. Twenty-six percent of cases occurred in infants aged <4 months and 63% were male. Black children had hospitalization rates 2.3 times greater than those of white children ($p<0.01$). Echovirus 13 was isolated in specimens from 37 (80%) of 46 patients with positive viral cultures; 27 from cerebrospinal fluid (CSF) and 10 from stool. Echovirus 18 was isolated in eight specimens and echovirus 6 in one specimen. Of those with laboratory confirmed echovirus 13, 35 (95%) had fever, with a mean maximum temperature of 38.9∞C. Other common symptoms were irritability (88%), vomiting (53%), diarrhea (35%), and cough (29%) in infants; and headache (100%), vomiting (85%), stiff neck (75%), and photophobia (45%) in older children. Thirty-five (95%) patients had normal blood leukocyte counts. The median CSF leukocyte count was 230 with a predominance of polymorphonuclear cells in 23 (62%) patients. Thirty-six (97%) had CSF glucose levels >40 mg/ml and 34 (92%) had CSF protein levels <100 mg/dL. One infant had hepatitis as well as echovirus 13 meningitis. There were no objectively verified sequelae and no deaths. We estimated the hospital charges associated with this outbreak to be $900,000. **Conclusions**. This outbreak, and others associated with echovirus 13 in the United States and Europe, occurred earlier than is typical for enteroviruses in temperate climates. With these outbreaks, echovirus 13 has emerged as a predominant strain of enterovirus associated with aseptic meningitis. Past experience indicates that echovirus 13 will likely spread to other areas of the United States and the world during the next few years.

8 Food Safety I

Sunday, March 24, 12:00 noon
Grand Hall East

Board 55. Survival and Growth of Alkali-Stressed *Listeria monocytogenes* on Beef Frankfurters and Thermotolerance in Frankfurter Exudates

P. J. Taormina, **L. R. Beuchat**

Center for Food Safety, University of Georgia, Griffin, GA

Contamination of processed, ready-to-eat foods with *Listeria monocytogenes* as a result of exposure to processing environments is a concern. Survival of *L. monocytogenes* in these environments suggests that some cells may survive exposure to chemical cleaners and sanitizers. Surviving cells may be injured as a result of this exposure but subsequently resuscitate, contaminate processed meat products, and grow. Routine washing of food processing equipment, floors, walls, or drains with water and application of cleaning chemicals, often with alkaline pH, is followed by application of sanitizers. The influence of alkaline pH on viability of *L. monocytogenes* and development of cross protection against other environmental stresses such as vacuum packaging of meat has not been reported. This study was done to determine the behavior of *L. monocytogenes* on frankfurters after exposure to two commercial alkaline cleaners used in meat processing environments. A second objective was to determine the thermotolerance of alkaline stressed *L. monocytogenes* cells suspended in frankfurter exudates. Cells of *L. monocytogenes* exposed at 4°C to 1% solutions of two alkaline cleaners or alkali-adapted in tryptose phosphate broth (pH 10.0) at 37°C for 45 min, followed by 4°C for 48 h, were inoculated onto beef frankfurters containing high fat (16 g) and high sodium (550 mg) or low fat (8 g) and low sodium (250 mg) per 57-g serving. Frankfurters were surface-inoculated (2.0 log10 CFU/g), vacuum packaged, stored at -20, 4, or 12°C, and analyzed for populations of *L. monocytogenes* at 2-day to 2-week intervals. Populations did not change significantly on frankfurters stored at -20oC for up to 12 weeks. After storage at 4oC for 6 weeks (1 week before the end of shelf life), populations of control cells and cells exposed to alkaline cleaners were ca. 6.0 log10 CFU/g of low fat, low sodium (LFLS) frankfurters and ca. 3.5 $\log_{10}$ CFU/g of high fat, high sodium (HFHS) frankfurters. Growth of alkali-adapted cells on both types of frankfurters was retarded at 4°C but a delay in growth of alkali-adapted cells on HFHS and LFLS frankfurters was evident during the first 9 and 6 days, respectively. Alkali-adapted cells had a significantly ($P\leq 0.05$) lower logistic D59°C value than alkaline cleaner exposed cells but the D59°C value was not different than that of control cells. Growth characteristics of *L. monocytogenes* inoculated onto the surface of frankfurters may be altered by previous exposure to alkaline environments. Differences in growth characteristics of *L. monocytogenes* on HFHS versus LFLS beef frankfurters stored at refrigeration temperature indicate that composition influences the behavior of both alkaline stressed and control cells.

Board 56. Mild Heat Treatment of Lettuce Enhances Growth of *Listeria monocytogenes* During Subsequent Storage at 5oC or 15oC

Y. Li[1], R. E. Brackett[2], J. Chen[1], **L. R. Beuchat**[1]

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Listeria monocytogenes has been isolated from a wide range of raw vegetables. Because of the widespread distribution of *L. monocytogenes* in soil and on plant surfaces, it is important to understand the ability of the pathogen to survive and grow under

conditions associated with processing, distribution, and storage of raw fruits and vegetables. Researchers have observed that dipping fresh-cut lettuce in water at 45°C or 55°C inhibits phenylalanine ammonia lyase activity, which leads to brown discoloration. We have studied the survival and growth of *Escherichia coli* O157:H7 inoculated onto cut lettuce before or after heating in chlorinated water. Mild heat treatment retarded discoloration but growth of *E. coli* O157:H7 was enhanced. Investigations to determine the effect of mild heat treatment on survival and growth of *L. monocytogenes* have not been reported. We undertook a study to determine the effects of heat treatment, storage temperature, and storage time on the survival and growth of *L. monocytogenes* inoculated onto cut iceberg lettuce. The efficacy of treatment of lettuce with 20 mg/l free chlorine in killing the pathogen was also determined. Before or after inoculation with *L. monocytogenes*, cut iceberg lettuce leaves were dipped in water (20°C or 50°C) containing or not containing 20 mg/l chlorine for 90 sec, then stored at 5°C for up to 18 days or 15°C for up to 7 days. The presence of 20 mg/l chlorine in treatment water did not significantly (P £ 0.05) affect populations of the pathogen, regardless of other test parameters. The population of *L. monocytogenes* on lettuce treated at 50°C steadily increased throughout storage at 5°C for up to 18 days. At day 10 and thereafter, populations were 1.7 - 2.3 $\log_{10}$ CFU/g higher on lettuce treated at 50°C after inoculation compared to untreated lettuce or lettuce treated at 20°C, regardless of chlorine treatment. The population of *L. monocytogenes* increased rapidly on lettuce stored at 15oC. At 2 and 4 days, significantly higher populations were detected on lettuce that had been treated at 50°C, compared to respective samples that had been treated at 20°C, regardless of inoculation before or after treatment or the presence of 20 mg/l chlorine in the treatment water. Results clearly demonstrated that mild heat treatment of cut lettuce leave enhances the growth of *L. monocytogenes* during subsequent storage at 5°C or 15°C. Mild heat treatment of cut lettuce may result in a prolonged shelf life as a result of delaying the development of brown discoloration. However, heat treatment also facilitates the growth of *L. monocytogenes* during storage at refrigeration temperature, thereby increasing the potential risk of causing listeriosis.

Board 57. Epidemiologic Analysis of Statewide Restaurant Inspection Scores in Tennessee

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Background: Virtually every licensed restaurant in the United States is inspected regularly to ensure adherence to food safety guidelines. Despite this, few data exist regarding restaurant inspection scores or their correlation with foodborne illness. **Methods:** We analyzed restaurant inspection data from July 1993 through June 2000. Routine inspections of all restaurants holding permits during this period for preparing and serving food were included in the analysis. Inspections were performed by state or regional health department employees using standardized forms with a scale of 0-100. Data were entered in a centrally-maintained database. **Results:** In Tennessee, over 19,500 hours of inspector time are spent each year on routine inspections of approximately 17,000 restaurants. The average scores of individual inspectors were distributed in a bell-shaped curve with a median of 82 and a range from 69 to 92. Mean scores by county ranged from 75 to 88. From 1993 to 2000, the mean inspection score rose steadily from 80.2 to 83.8, and the average number of violations cited per inspection fell from 11.1 to 9.9. None of the 12 most commonly cited violations were among those designated as "critical" food safety hazards. While restaurants with a score over 60 tended to have fairly stable scores on subsequent inspections, establishments scoring under 60 had a mean improvement of 16 points on the subsequent routine inspection, with an additional mean increase of 5 on the following inspection. Fast-food restaurants (mean score=79.9) had slightly lower mean scores than independent (80.9) or chain (82.1) full-service restaurants. Some variation was noted in mean scores of restaurants serving certain types of cuisine, such as barbecue (82.9), pizza (82.3), Chinese (77.7) and Mexican (77.4) foods. **Conclusions:** Restaurant inspection scores vary substantially over time and by region and inspector. The most commonly cited violations are not those believed to be most important in maintaining food safety. Being cited for a poor score does appear to lead to some sustained improvement. These data suggest that restaurant inspections may not be performed uniformly even within a single state, and that substantial resources may be invested in monitoring issues which do not directly affect food safety. A recent study in Dade County found that restaurant inspection scores did not predict outbreaks there. Given the tremendous resources expended in regulating this huge industry, food safety agencies should consider ways to improve the utility of restaurant inspections in preventing foodborne illness.

Board 59. Demographic Factors Associated with the Consumption of Sprouts Among California Women

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Background: Alfalfa sprouts are considered by many to be a healthful food and the consumption of sprouts has increased greatly in the United States in the past 30 years. Ironically, in California in the past 5 years, there have been more than 10 outbreaks of salmonellosis or *E. coli* O157:H7 infections due to contaminated alfalfa or clover sprouts and involving predominantly adult women. **Methods:** To evaluate demographic factors associated with alfalfa sprout consumption, we used data from the 1999 California Women's Health Study Survey (CWHS), an on-going monthly telephone survey which collects information on a wide variety of health-related behaviors and attitudes from a sample of randomly selected adult women who reside in California. We conducted a logistic regression using the software Stata. Eating alfalfa sprouts in the past year was the outcome variable. **Results:** Of the 3858 women in the study, 45% ate sprouts in the 12 months prior to the interview. Consumption of sprouts varied by race/ethnic group: among whites 52% ate sprouts vs. 39% of Blacks, 31% of Hispanics, and 48% of Asians. The proportion consuming alfalfa sprouts increased with household income. Consumption of sprouts also varied by age group with the highest sprout consumption in the middle age groups (median age 44). Overall 23% had heard that sprouts can cause foodborne illness. In the logistic regression model we found that, for all race/ethnic groups other than Asian, increasing income is associated with a greater odds of eating sprouts. For Asian women there is no income effect. At lower income levels Asians and Whites have a higher odds of eating sprouts than Hispanics while at the highest income level (>$50K) there is no race/ethnicity difference. Among 44 year olds at the lowest income level (<$10K), Asians have a higher odds of eating sprouts than whites (OR=2.35, 95% CI= 1.1-5.3), but at the highest income level, they have a lower odds of eating sprouts (OR=0.67, 95% CI= 0.47-0.97). Knowledge of the risk of the consumption of sprouts did not significantly improve the logistic regression model. **Discussion:** Sprout-related outbreaks in California have involved predominantly adult women. Our study shows that, among California women, sprout consumption increases with higher incomes and is more common among Asians and whites compared to Hispanics. However, knowledge of sprouts as a hazardous food did not correlate with consumption. Better prevention strategies targeted at women eating sprouts are needed.

Board 60. Microbiological Quality of Food in Relation to HACCP and Food Hygiene Training in Catering and Retail Premises in the United Kingdom

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There is growing acceptance in many countries of the value of hazard analysis and critical control point (HACCP) principles in ensuring the microbiological safety of foods. Most of the product specific European Community (EC) directives as well as the Directive on the Hygiene of Foodstuffs (93/43/EEC), place obligations on industry and food business operators to adopt HACCP principles as the basis for their product safety management systems. Food hygiene training and instruction for all staff handling food is also a legal requirement. Catering and retail premises in five UK food microbiological studies (butchery products and butchers' premises; cold ready-to-eat meats from catering premises; ready-to-eat quiche from retail premises; ready-to-eat burgers sampled at the point of sale; ready-to-eat food to which spices have been added) carried out between 1997 to 1999 were surveyed to determine the microbiological quality of food and the extent to which they comply with the legal requirements. Among the 11,044 premises visited, almost three-quarters (74%; 8222) were catering premises and 25% (2822) were retail premises. Significantly almost twice as many samples of ready-to-eat foods from catering premises (21%; 1822/8568) were of unsatisfactory or unacceptable microbiological quality compared to those from retail premises (11%; 516/4705) ($P<0.0001$). Almost two-thirds (64%; 1809/2822) of retail premises visited had hazard analysis in place compared with 53% (4398/8222) of catering premises visited ($P<0.0001$). In most (82%; 2315/2822) retail premises visited the manager had received some form of food hygiene training compared with 76% (6254/8222) of catering premises visited ($P<0.0001$). Food safety procedures such as the hazard analysis system were more likely to be in place where the manager of the premises had received some form of food hygiene training. Retail premises where the managers had received some form of food hygiene training were more likely to have hazard analysis systems in place, either documented or undocumented, in premises compared to managers of catering premises that had not received food hygiene training ($P<0.0001$). Evidence from these studies suggests that the lower microbiological quality of ready-to-eat foods from catering premises compared with those collected from retail premises, may reflect differences in management food hygiene training and the presence of a hazard analysis system. Government initiatives across the food chain have encouraged food businesses to introduce HACCP based controls. However, in some sectors the levels of HACCP awareness, understanding and uptake remain low. The importance of adequate training for food handlers and managers as a pre-requisite for effective HACCP based controls is recognised.

Board 61. Detection of Viral Contamination in Food

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International spread of viruses through foodstuff has been increasingly recognized especially since sensitive detection methods have been introduced. In particular, Norwalk-like virus (NLV) and hepatitis A have been found to cause infections via fresh produce like vegetables and berries. Especially frozen raspberries seem to have caused numerous outbreaks. Transnational outbreaks due to international food distribution have been documented by tracing the virus in the population and epidemiological study. However, the pathogen detection in the incriminated food, other than shellfish, is still rare. Based on previously described methods for shellfish analysis, different protocols were compared on artificially contaminated lettuce and raspberries. For lettuce, elution and PEG precipitation and then extraction using Qiagen plant kit gave the best results (one log more sensitive than direct extraction using trizol). For berries, different elution buffers were compared (PBS, Tris/NaCl/CaCl2, glycin buffer pH12), and then nucleic acid extraction using tripure or Qiagen plant kit. Several problems were encountered (low pH, pectin from the seeds, viscosity.) and thus the sensitivity is still very low. Even if some improvements are still needed the development of such methods will help to further monitor global food safety in coordination with surveillance of viral gastroenteritis outbreaks.

Board 62. Decline in Staphylococcal Foodborne Disease Outbreaks in the United States, 1973-1997

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Background: *Staphylococcus aureus*, a gram-positive coccus, is a well recognized cause of foodborne outbreaks in most regions of the world. *S. aureus* produces an endotoxin that, when ingested, can cause rapid onset of illness characterized by severe nausea and vomiting. When *S. aureus* is present in food that is kept at room temperature, the organisms multiply and produce the toxin. **Methods:** We reviewed *S. aureus* outbreaks reported through CDC's Foodborne Disease Outbreak Surveillance System between 1973 and 1997. Etiologic confirmation of an *S. aureus* outbreak requires either isolation of *S. aureus* of the same phage type from stool or vomitus of two or more ill persons or detection of enterotoxin in epidemiologically implicated food. Trends were analyzed using least squares regression. **Results:** Between 1973 and 1997, 462 *S. aureus* foodborne disease outbreaks were reported in the United States. These outbreaks resulted in 20,389 illnesses and 5 deaths. The number of outbreaks per year declined significantly from 19 in 1973 to 10 in 1997 (slope -1.33, $p<0.0001$). The median number of cases per outbreak remained fairly stable; 50 in the 1970s, 36 in the 1980s, and 33 in the 1990s. Meat products, including beef, poultry and pork, were identified as the confirmed vehicle in 50% of *S. aureus* outbreaks, with ham or ham products implicated as the vehicle in 24.7% of outbreaks, and poultry products implicated in 13.4%. The location of food preparation was reported for 452 outbreaks; preparing the food item(s) at home (23%) or in a restaurant (25%) was most frequently reported compared with preparing the food item(s) in a delicatessen, cafeteria, institution or by a caterer. Among the 452 outbreaks that reported one or more contributing factors, 322 (71%) were attributed to improper food storage or handling and 145 (32%) to poor personal hygiene of a food worker. **Conclusions:** In the United States, reported staphylococcus foodborne outbreaks have declined substantially, dropping by almost 50% between 1973 and 1997. A similar decline in the number of *S. aureus* foodborne outbreaks has been documented in Japan between 1970 and 2000. Although the cause of the decline remains unknown, improved methods in food handling and food storage may be partly responsible for the decline in *S. aureus* foodborne outbreaks.

Board 63. Environmental Health Specialists Network (EHS-Net) — The Development and Implementation of a Systems Approach To Investigate Foodborne Illness

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The Environmental Health Specialists Network (EHS-Net) is composed of environmental health specialists and epidemiologists located at the federal, state and local levels. Based on a sys-

tems approach, this collaboration is to improve the understanding of the underlying causes and interactions of factors that lead to foodborne illness and to use the knowledge gained to prevent future cases of such illness. The EHS-Net activities are conducted in conjunction with the Centers for Disease Control and Prevention's (CDC) Foodborne Diseases Active Surveillance Network (FoodNet). A component of CDC's Emerging Infections Program (EIP), FoodNet is a collaborative project of CDC, nine EIP sites, the U.S. Department of Agriculture, and the Food and Drug Administration (FDA). FoodNet consists of active surveillance and studies designed to help public health officials gain a better understanding of the epidemiology of foodborne diseases in the United States. The EHS-Net is a combined effort between the FDA, CDC, and eight of the nine EIP sites. In collaboration with FoodNet activities, EHS-Net projects will provide insights to understanding the environmental causes of foodborne illness. Current EHS-Net activities describe food safety systems in restaurants and other establishments where food is eaten outside the home. Survey tools have been designed by EHS-Net to collect data in both outbreak and non-outbreak settings. Data collection encompasses the entire food preparation process from delivery of ingredients, through preparation and cooking, to the actual service of the food item. Both univariate and multivariate analyses are used to assess potential risks present in food establishments. By documenting the entire food preparation process, such as bare-hand contact with food, preparation of raw meats and poultry, and egg handling practices, we will be able to analyze the role of food handling and preparation practices, in foodborne illness. On the basis of this information, data may support existing food handling guidelines as well as suggest revision of current guidelines and policy where necessary to improve food handling and preparation practices. The data gathered will provide a unique opportunity to explore associations between eating outside the home and the occurrence of foodborne illness from agents such as *E. coli* O157:H7, *Salmonella*, and *Campylobacter*. Thus, the EHS-Net project will aid in understanding FoodNet results and provide a more effective approach to reducing foodborne-related illness.

Board 64. Genetic Diversity of *Salmonella* and E.coli in Irrigation Water and Sediments Along the Texas-Mexico Border

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The Texas-Mexico border region along the Rio Grande River is one of the most heavily impacted regions in the United States as a result of increasing human population. The Rio Grande serves as the primary source of drinking water and irrigation water in this region. Vegetable production in Texas is concentrated in this region and is supported by a large network of open canals and drains. The objective of this study was to determine the genetic diversity of *Salmonella* and *E.coli* isolates isolated from selected irrigation water, canal sediment and vegetable samples adjacent to specific population centers. The underlying hypothesis was that multiple sources of contamination exists even within a single location and that microbial contaminants can persist for extended periods of time within the irrigation system. Thirty three (33) *Salmonella* isolates and 50 *E.coli* isolates collected from irrigation water and sediments were genotyped using PFGE. Additionally, 33 *Salmonella* isolates from carrots (field, truck and packing shed) were also genotyped and classified on their basis of similarities. The isolates were obtained over a period of 4 months. There were 6 defined *Salmonella* genotypes (<90% similarity) from Weslaco compared to 4 genotypes in Laredo, and 12 genotypes in Presidio. There were 25 different *E.coli* genotypes in Weslaco, 11 genotypes in Presidio and 4 genotypes in the El Paso region. Some isolates obtained on successive months showed similar genotype patterns. Among carrot samples, the farm isolate was significantly different compared to the truck and packing-shed isolates. There were 3 distinct genotypes among the truck samples. These results indicate that the irrigation water and the sediment are contaminated and potentially serve as a source of produce contamination. There are multiple sources of contamination and data suggest that the contaminants can persist for prolonged periods. The results indicate that produce can get contaminated at the field, during transport, and in the packing shed. Management practices that limit pathogen contamination needs to be carefully implemented.

Board 65. Effects of Climate on Prevalence of *Campylobacter* spp. in Humans and Broilers in Denmark

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Introduction: In Denmark, rates of human *campylobacteriosis* have risen steadily since 1992, reaching a peak of 82 cases per 100,000 population in 2000. Studies have shown poultry to be a source of *Campylobacter* infection in humans. A recent survey of Danish broiler flocks found a prevalence of nearly 40%. Both human and broiler infections appear to follow the same seasonal trend. We investigated the role of climate on the number of reported human *Campylobacter* cases and the prevalence of *Campylobacter* in Danish broilers at slaughter. **Methods:** Reports of human *Campylobacter* cases between 1991 and 2000 were provided by the Statens Serum Institut. Since 1998, the Danish Veterinary Institute has examined ten birds from every broiler flock for *Campylobacter* by cloacal swabs at slaughter. National climate data (maximum and mean temperature, mm of precipitation, % relative humidity, and hours of sunlight) by week was provided by the Danish Meterological Institute. Number of human cases and broiler prevalence were compared to climatic factors using lag dependence functions, locally fitted linear models, and cross-validation methods. **Results:** Humans: A model including maximum temperature and precipitation 3-4 weeks prior to reported *Campylobacter* infection showed that the highest incidence occurred during temperatures above 20°C and precipitation around 20mm per week. Maximum weekly temperature 3-4 weeks before infection was the best single predictor. Using cross-validation, average temperature 6-8 weeks before infection was the best predictor, explaining 85% of the variation. Adding precipitation to the model only slightly improved the result. Broilers: A model including maximum temperature, precipitation and relative humidity three weeks prior to slaughter was the best estimator of broiler prevalence. Maximum weekly temperature 4 weeks prior to slaughter was the best single predictor. Using cross-validation, average temperature was the best single predictor and a model including average temperature and either precipitation or maximum temperature 3-4 weeks prior to slaughter further improved the estimate, explaining 81% of the variation. **Conclusion:** As shown in previous studies, we found that temperature does play a role in *Campylobacter* infections in both humans and broilers. To our knowledge, this is the first time that the combined effect of temperature with other climatic factors such as precipitation and relative humidity was shown to predict infection; however, more work is needed to support these findings. Future research should address conditions in the broiler environment that may be susceptible to climate, and examine micro-climatic data on and around broiler farms. Investigations into the effect of climate on human infections must take into account the role of broilers as a source of *Campylobacter*, as well as food consumption or preparation practices that may vary by season.

Board 66. Sources of Human *Campylobacter* Infection—The Contribution of Strain Typing to a Challenging Problem

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Campylobacter has been the most commonly reported cause of bacterial gastro-intestinal infection since 1981. *Campylobacter* spp. were the most commonly isolated bacterial pathogens in the study of Infectious Intestinal Disease carried out in England between 1993 and 1996, being found in 12% of cases but only 0.7% of controls. This study estimated that, for every case reported to national laboratory surveillance, there were a further seven cases not reported: approaching 500,000 cases per annum. In contrast, the widespread carriage of *campylobacter* in food producing animals is rarely accompanied by any pathology. The widespread distribution of *Campylobacter* spp. through the food chain, and the low number of reported outbreaks of *campylobacter* infection make tracing sources and vehicles of human infection difficult. The extraordinary range of variation seen in this organism compounds these difficulties. Both microbiological and epidemiological studies indicate that poultry is not the only source of human infection. Although a wide range of typing techniques has been applied to *C. jejuni* and *C. coli*, few have been applied systematically on a large scale. All methods however indicate that isolates from human infection consist of a small number of stable clones which are widely distributed on a global scale, a large number of isolates which can be uniquely identified in any particular study, and the majority of isolates which comprise a number of closely inter-related ëtypes'. The implications of these observations for epidemiological studies aimed at characterising isolates from human infection will be described with reference to studies carried out in the *Campylobacter* Reference Unit (CRU). Since 1997 between 7,000 and 12,000 isolates from human infection in the United Kingdom have been referred to CRU each year for typing. Approximately 5,000 isolates from foods and food animals have been studied during the same time period. All have been serotyped and phagetyped and screened for resistance to a range of antimicrobial drugs. A proportion have also been typed by Pulsed Field Gel Electrophoresis, Single enzyme Amplified Fragment Length Polymorphism and Fluorescent Amplified Fragment Length Polymorphism. The necessity for large scale studies, the choice of method and the sampling strategy employed will be discussed with reference to the above experience.

Board 67. The Microbiological Status of Ready to Eat Fruit and Vegetables

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In the year 2000, six of 95 (6%) foodborne general outbreaks of infectious intestinal disease reported to the PHLS Communicable Disease Surveillance Centre were associated with consumption of salad, fruit and vegetables. Two notable outbreaks occurred: in August 174 cases of infection caused by *S.* Typhimurium DT 104 associated with the consumption of lettuce in food items bought from fast food outlets and 124 cases of *S.* Typhimurium DT 204b infection linked with the consumption of lettuce. The latter outbreak appeared to be part of an international outbreak also affecting Iceland, Scotland, the Netherlands and Germany. In response to these two large outbreaks the PHLS organised a number of studies of ready-to-eat salad items in collaboration with the Local Authority Co-ordinating Body on Food and Trading Standards (LACOTS). No pathogens were recovered from a study of 3,200 of Ready to Eat Organic Fruit and Vegetables. The majority (99.5%) of samples were found to be of satisfactory/acceptable microbiological quality whilst only 15 (0.5%) were of unsatisfactory microbiological quality. Unsatisfactory results were due to *Escherichia coli* and *Listeria* spp. (not *L. monocytogenes*) levels in excess of 100 c.f.u. g-1. The absence of pathogens (*L. monocytogenes*, *Salmonella*, *Campylobacter*, and *E. coli* O157) and the low incidence (1.5%) of *E. coli* and *Listeria* spp. associated with these organic vegetables indicates that overall agricultural, hygiene, harvesting, and production practices were good. As a follow up, two further studies were conducted in 2001: A study of 3,581 Retail Prepared Prepacked Ready-to-Eat Salad Vegetables detected *Salmonella* spp. in 5 samples. No *E.coli* O157 or *Campylobacter* spp. were detected. *L.monocytogenes* was recovered at very low levels (<20 c.f.u. g^{1}) in 25% of samples. A small number of cases of *Salmonella* Newport occurred linked with one of the affected products but swift removal of this product prevented a much larger outbreak. No pathogens have so far been found in a subsequent study of around 4,000 Open Prepared Ready-to-Eat Salad Vegetables from Catering & Retail Premises. The results of both latter studies are still being collected and analysed and will be presented.

Board 68. Prevalence of *Escherichia coli* O157:H7 in Ground Beef, United States, 1995-2000

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Escherichia coli O157:H7 is an important human pathogen that can be transmitted by food, water or person-to-person. Ground beef has been implicated in foodborne disease outbreaks and as a risk factor for sporadic cases of *E. coli* O157:H7 infection. In 1994, the United States Department of Agriculture, Food Safety and Inspection Service (FSIS) began testing ground beef for *E. coli* O157:H7. Raw ground beef samples obtained from federally inspected processing facilities and retail outlets were analyzed through an ongoing FSIS monitoring and surveillance program. Information regarding the date of sample collection, geographic location of the sampled facility, and test result was available for each sample. From 1995-1997, 25-gram samples of ground beef were tested for the presence of *E. coli* O157:H7 using enrichment, screening ELISA and culture. In 1998, the sample size increased to 325 grams, and in September 1999, immunomagnetic antigen capture techniques and the use of a highly selective plating medium were implemented. Descriptive statistical analyses were completed for tests performed during 1995-2000 for samples from processing facilities and retail outlets. For processing facilities, 47 (0.29%) of 16,366 samples tested positive. The annual prevalence of positive samples for 1995-2000 was 0.08%, 0.09%, 0.09%, 0.22%, 0.28%, and 0.50%, respectively. The number of samples tested annually increased from approximately 1,000 during 1995-1997 to 4,000 during 1998-2000. The prevalence of positive samples varied from 0.0% - 0.52% for 9 geographical regions of the U.S. During June-September 1998-2000, *E. coli* O157:H7 was detected in 27 (0.64%) of 4,228 samples, compared to 17 (0.20%) of 8,667 samples collected during October-May 1998-2000 (p = 0.0001). For retail outlets, 19 (0.24%) of 7,885 samples tested positive. During 1995-2000, *E. coli* O157:H7 was detected in 0.07%, 0.0%, 0.0%, 0.10%, 0.35% and 0.86% of samples, respectively; 1,000-2,000 samples were tested annually. At retail sites, prevalence in 9 regions of the U.S. varied from 0.0% to 0.57%. During June-September 1998-2000, 10 (0.60%) of 1,665 samples tested positive, compared with 8 (0.25%) of 3,180 obtained during remaining months (p = 0.10). This is the first report of a national estimate of the prevalence of *E. coli* O157:H7 in ground beef from processing facilities and retail outlets. An increase in the prevalence of *E. coli* O157:H7 was observed over time. This increase may be due to enhanced sensitivity of the surveillance system due to larger sample sizes and improved test methodology. A seasonal peak in the prevalence of *E. coli* O157:H7 in ground beef was observed for both processing facilities and retail outlets during June-September. This seasonal peak follows a similar pattern

observed in both the incidence of reported human cases and the prevalence of carriage by cattle.

Board 69. Trends in Foodborne Disease Outbreaks Due to Scombrotoxin and Ciguatoxin in the United States, 1973-1997

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Background: The per capita consumption of fish in the United States has increased by approximately 50% since 1970. In addition, climatic changes have produced warmer waters during the 1990s compared with the previous 2 decades, potentially increasing the range of warm water dinoflagellates that produce toxin. Reported scombroid and ciguatera outbreaks were reviewed to identify temporal trends. **Methods:** We reviewed scrombroid and ciguatera outbreaks reported to CDC's Foodborne Disease Outbreak Surveillance System between 1973 and 1997. Etiologic confirmation required either demonstration of histamine or ciguatoxin in epidemiologically implicated fish or the appropriate clinical syndrome among persons who had eaten a type of fish associated with this illness. Trends were analyzed using least squares regression. **Results:** Between 1973 and 1997, there were 361 scombroid (2072 illnesses) and 337 ciguatera (1450 illnesses) outbreaks. The number of scombroid outbreaks increased significantly from 12 in 1973 to 22 in 1997 (slope 0.36, p= 0.028); there was no distinct trend in ciguatera outbreaks. Among scombroid outbreaks, the median number of illnesses was 2 (range 1-232). One fatality occurred in 1988. Among ciguatera outbreaks, the median number of illnesses was 3 (range 1-69). Three fatalities were reported in 1981. California, Florida, Hawaii, New Jersey, New York and Washington reported 10 or more scombroid outbreaks. California, Florida, Hawaii, Puerto Rico, and the Virgin Islands reported more than one ciguatera outbreak. Ciguatera and scombroid outbreaks demonstrated a marked seasonality, peaking in August. However, seasonality varied by geographic region. Outbreaks of scombroid in Pacific coastal states were bimodal, peaking in March and then again in August through September; in Atlantic coastal states outbreaks peaked in August. Outbreaks of ciguatera in Hawaii peaked between July and September, whereas outbreaks in Florida peaked in May; those in tropical regions demonstrated less seasonality. Of the 361 scombroid outbreak investigations reported, 311 (86%) implicated a food vehicle. Ten families of fin fish were identified; Scombroidae (tuna, mackerel and bonitos) accounted for 160 (51%) outbreaks and Coryphaenidae (mahi-mahi) accounted for 89 (29%). Of the 337ciguatera outbreak investigations reported, 247 (73%) implicated a food vehicle. Seventeen fish families were identified; Carangidae (ulua, amberjack) accounted for 65 (26%) outbreaks. **Conclusions:** From 1973 to 1997, scombroid fish poisoning outbreaks increased, while no trend in ciguatera outbreaks was observed. Scombrotoxin and ciguatoxin continue to be a cause of foodborne disease outbreaks in the United States, particularly in coastal areas. Continued monitoring and enforcement of regulations for temperature logs and product testing from commercial fishing operations may help reduce illness.

Board 70. Risk factors for fatal *Vibrio vulnificus* infection in the United States, 1997-2000

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Background: *Vibrio vulnificus* is a natural inhabitant of marine and estuarine environments all over the world. Human infection with this gram-negative bacteria occurs in compromised hosts and is associated with an approximate 30% fatality rate. **Methods:** To determine risk factors for fatal *V. vulnificus* infections we analyzed data from the *Vibrio* Surveillance System at CDC. Participation in this surveillance system is voluntary. Each surveillance report includes the species of *Vibrio*, the site of isolation, patient demographics, clinical history including underlying illness and exposure history. We analyzed *V. vulnificus* infections reported between 1997 and 2000. The analysis was limited to patients who had *V. vulnificus* isolated from blood or wound (i.e., patients at greatest risk for death). Antimicrobial agents were classified as tetracyclines, any cephalosporins, third and fourth generation cephalosporins, aminoglycosides, and quinolones (including fluoroquinolones). Antibiotic dose and duration was not reported. **Results:** Between 1997 and 2000, 287 laboratory-confirmed *V. vulnificus* infections from 23 states were reported. Of these, 203 had complete information and were included in the analysis: 112 (55%) were classified as sepsis and 91 (45%) as wound infections, 184 (91%) were male, the median age was 54 years (range, 13 to 94), and 70 (34%) died. Overall, 195 (96%) patients received antimicrobial treatment and 77 (38%) received at least three antimicrobials. All eight patients who did not receive any antimicrobials died, 21 (25%) of 84 taking quinolones died, 26 (25%) of 102 taking tetracyclines died, 16 (39%) of 41 taking aminoglycosides died, 29 (28%) of 102 taking any cephalosporins died, and 23 (28%) of 82 taking third or fourth generation cephalosporins died. On univariate analysis, residing in a Gulf Coast state (RR=.67, 95% CI=.46-.98) and treatment with quinolones (RR=.61, 95% CI=.39-.95) or tetracylines (RR=.58, 95% CI=.38-.88) were significantly protective against death, whereas age below 54 years (RR=2.09, 95% CI=1.39-3.15), non-white race (RR=1.76, 95% CI=1.21-2.57), and underlying liver disease or alcoholism (RR=3.56, 95% CI=2.08-6.08) were significant risk factors for death. In a logistic regression model, use of tetracyclines remained significantly protective against death (OR=.45, 95% CI=.21-.93) and underlying liver disease or alcoholism remained a significant risk factor (OR=5.26, 95% CI=2.34-11.81). **Conclusion:** This analysis suggests that use of tetracyclines during an illness associated with *V. vulnificus* may be therapeutic. However, without data on antimicrobial dose and duration and antimicrobial resistance, these data should be interpreted with caution. Surveillance data may need to be expanded to capture these data. Public health prevention messages should continue to target persons with underlying liver disease or alcoholism.

Board 71. Investigation of a Senegalese Foodborne Outbreak Caused by *Vibrio* parahaemolyticus in Shrimps

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Foodborne diseases continue to present a major challenge to public health authorities in carrying out the core functions of outbreak detection and control, which rely on timely disease surveillance. Epidemiologic studies have made crucial contribution to the understanding of how outbreaks of food-borne deseases occur and how they can be prevented. On April 14th 1993, Pasteur Institute in Dakar was asked to investigate an outbreak of diarrheas in a hotel with restaurant located a hundred kilometers far from Dakar, Senegal. The main objective of this investigation was to provide informations for the development of appropriate measures for the prevention of future outbreaks. **Background:**The number of consultation for diarrhea done by the resident doctor increased from 1 per week usually to 6 per day on april 12th and april 13th. One hundred fifty seven (157) guests were staying at the hotel during the outbreak, most of them coming from foreign coutries: 108 arrived on april 11th, 29 on april 12th or later and 20 arrived before april 11th. The outbreak affected persons working at the hotel, resident guests and persons who did not stay at the hotel butate at the restaurant on april 11th and april 12th. **Methods:** A case-control on-site investigation was undertaken in order to determine the extent of the outbreak and identify its suspected source. Epidemiological investigation of the outbreak included informations on the number of affected people, causal agents, incriminated foods, place where food was contaminated, factors contibuting

to the outbreak. Stool and food samples were collected for microbiological analysis including phenotypic and molecular characterisation of the suspected pathogen. **Results:** Statistical analysis of epidemiological data including determination of odd-ratios revealed that shrimps was the food vehicle. *Vibrio* parahamolyticus was isolated from suspected shrimps (4 strains from four different samples) and from a stool sample of a guest suffering from diarrhea. Molecular characterization of these strains revealed that all five strains belonged to the same ribotype.

Board 72. A Study of Cleaning Standards and Practices in UK Food Premises

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During September and November 2000 a study was undertaken to determine the microbiological status of surfaces used in the preparation of ready-to-eat foods, and to assess cleaning standards and practices in food premises. Food contact surface samples (6533) were examined from 1502 premises. Cleaning cloths (1132) and chopping board surfaces (2033) were more heavily contaminated with bacteria (Aerobic Colony Count (ACC), Enterobacteriaceae, *E. coli*, and *Staph. aureus*) compared to worktop (2009) and food container (1359) surfaces. *Campylobacter* spp. and *Salmonella* spp. were also detected in two (0.2%) and one (0.1%) of the cleaning cloths. Higher levels of bacteria were found on surfaces that were visually dirty, wet, or cleaned more than 24 hours previously ($P<0.0001$), and boards that were scored or damaged ($P<0.0001$).

A documented hazard analysis system was in place in half (52%) of premises visited. Significantly more samples (surfaces of chopping boards, worktops, and food containers, and cleaning cloths) with ACC levels in excess of 10^3 cfu/cm^2, swab or ml were from premises where there was no hazard analysis system in place (39%) compared to those where a hazard analysis system was in place (27%) ($P<0.0001$). Most managers (89%) had received food hygiene training. Documented cleaning schedules and cleaning records were present in approximately half (55% and 44%, respectively) of the premises. Sixty-one percent of premises had physically separate areas for raw and ready-to-eat food. However, most did not have separate cleaning materials for raw and ready-to-eat food areas (67%), or stored cleaning equipment for high risk areas from those used in low risk areas (70%). Deficiencies in the correct use of cleaning products were identified. Surface samples and cleaning cloths with ACC levels in excess of 10^3 cfu/cm^2, swab or ml were also associated with premises types as well as premises where management did not have food hygiene training or where cleaning schedules or records were not implemented. Recommendations for improving cleaning standards are provided.

Board 73. Examining Publication Bias in Foodborne Outbreak Investigations: Implications for Food Safety Policy

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Background: Systematic national surveillance of general outbreaks of infectious intestinal disease (IID) (i.e. those affecting more than one household) was introduced in England and Wales in 1992, comprising a minimum dataset for each completed investigation. It was designed to provide unbiased information on causative organisms, sources or vehicles of infection and modes of transmission. We compared the information from the surveillance system for general outbreaks of IID between 1st January 1992 and 31st March 1999 with that which appeared in the peer-reviewed literature during the same time period in order to assess the effect of publication bias and consequent implications for food safety policy. **Methods:** We abstracted data on foodborne outbreaks of IID from the national surveillance dataset for England and Wales. We searched PubMed for publications from 1992 onwards using the MESH headings "disease outbreaks" and "food". We excluded outbreaks originating outside England and Wales and family outbreaks. **Results:** Between 1st January 1992 and 31st March 1999 1347 foodborne outbreaks of IID were reported to the Public Health Laboratory Service (PHLS). Forty-five foodborne outbreak reports appeared in the peer-reviewed literature. The minimum interval between outbreak occurrence and the appearance of a peer-reviewed paper was 7 months (maximum 71 months; median 21 months). The minimum interval between outbreak occurrence and receipt of a completed outbreak surveillance form by the PHLS was 1 month (maximum 20 months; median 13 months). Foodborne outbreaks of Shiga toxin-producing *Escherichia coli* O157, *campylobacter* and unusual *Salmonella* species tended to be over-represented in the peer-reviewed literature compared with the national dataset (16% versus 3%; 9% vs. 2% and 13% vs. 4% respectively). Foodborne outbreaks due to Norwalk-like Virus infection were under-represented in the peer-reviewed literature compared with the national dataset (2% vs. 6%). Outbreaks in the peer-reviewed literature overestimated the impact of milk and dairy products and miscellaneous food items, whilst underestimating the impact of poultry, eggs, red meat and fish and shellfish. **Conclusion:** Few of the foodborne outbreaks reported to the PHLS led to peer-reviewed publications. In the quest for originality publications in peer-reviewed journals tend to favour the unusual or novel event. In order to develop rational policies, however, policy-makers and enforcers need to know what is usual as well as what is unusual. It is in dealing with the usual that the greatest health gains are to be made. In the absence of systematic surveillance knowledge of causative organisms, sources or vehicles of infection and modes of transmission in foodborne disease outbreaks gleaned from the peer-reviewed literature would have the potential to distort food safety policy.

Board 74. Knowledge, Attitudes and Practices Regarding Use of Irradiated Meats and Pasteurized Eggs in Health Care Institutions, Universities, and Restaurants in Connecticut

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Background: Contaminated meats and eggs have been implicated as a major source of foodborne diseases. In recent years, several significant food safety technologies have been approved for commercial use: irradiation of meats and pasteurization of both egg-product and in-shell eggs. Widespread use could reduce the occurrence of Shiga toxin-producing *Escherichia coli* infection, salmonellosis, campylobacteriosis, listeriosis and toxoplasmosis by an average of 50%. As a prelude for a public health initiative to promote their use, a survey was undertaken to determine the extent to which these technologies are currently being used in Connecticut. **Methods:** A standardized questionnaire was developed to assess the knowledge and attitudes toward the use of irradiated meats and pasteurized eggs and the extent to which they are currently being purchased and used. The surveys were mailed in February 2001 to the food services of all universities and acute-care hospitals and a representative sampling of long-term care facilities (LTCF) and restaurants in Connecticut. A second mailing to non-respondents was conducted in March 2001. **Results:** Of the 391 surveys sent, 211 (54%) were returned: 24/34 (71%) from hospitals, 113/167 (68%) from LTCFs, 17/40 (43%) from universities and 57/150 (38%) from restaurants. Nearly all respondents reported using hamburger, chicken, and eggs in their operations. Seventy-five percent (75%) of facilities use pasteurized egg product (PEP), but no facility currently uses irradiated hamburger or

poultry, and only 16% use pasteurized in-shell eggs (PSE). Restaurants (14%) and universities (56%) were less likely than LTCF or hospitals (96% each) to use PEP. The majority of respondents requested more information concerning PSE (66%) and most (79%) would be willing to consider buying irradiated meat products if given additional information. Significant predictors ($p<0.05$) of willingness to buy irradiated meat products include being a hospital or LTCF (88% vs 62%), having a manager with >20 years food service experience (89% vs 66%), believing that irradiation kills harmful bacteria (89% vs 63%), and believing that a person will not get irradiation exposure from eating irradiated meat (94% vs 63%). Significant predictors associated with the current use of PSE include having received prior information (44% vs 6%) and belief that consumers will accept the product (22% vs 7%). While 53% of respondents thought that DPH should encourage use of PSE, only 17% thought that DPH should encourage use of irradiated meats. **Conclusions:** Pasteurized egg product is already widely used in hospitals, LTCFs and universities in CT. There is considerable potential to improve the use of irradiated meats and pasteurized in-shell eggs in food service establishments, beginning with provision of more information.

Board 75. Multistate Outbreak of *Salmonella* Poona Infections Associated with Precut Melon

K. K. Carter[1], K. Cummings[2], B. Sun[1], S. B. Werner[2], J. Rosenberg[2], S. Abbott[2], A. Sokoloff[1], J. L. Thomas[1], C. A. Myers[1], M. T. Jay[1]

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Imported cantaloupes or watermelon have been implicated in several outbreaks of salmonellosis in the United States. There were multistate outbreaks of *Salmonella* serotype Poona (SP) associated with imported cantaloupe in 1989, 2000, and 2001. In June 2001, a multistate outbreak of SP infections with isolates indistinguishable by pulsed-field gel electrophoresis (PFGE) was identified in 23 case-patients in the U.S; 19 were residents of one of 11 California counties. Four case-patients were out-of-state residents; three of them had traveled to California during the week prior to the onset of illness. Symptom onsets ranged from June 1 to July 4, 2001. Four patients were hospitalized, but no deaths were reported. The median age of case-patients was 7 years (range 1-88 years) and 13 (56.5%) were female. A case-control study, utilizing a standardized questionnaire telephone-administered to 12 case-patients and 24 age- and telephone prefix- matched controls, found an association between illness and precut melon (cantaloupe, honeydew, or watermelon) consumption. The percentage of case-patients who ate precut cantaloupe (54.5%), precut honeydew (40.0%), or precut watermelon (50.0%) was higher than that of controls (4.2%, 0%, 8.3%, respectively). Exact methods in the statistical software package Egret® were used to calculate the odds ratio (OR, maximum likelihood estimate), 95% confidence intervals (CI), and 2-sided p-values for the test that the OR=1. For precut melon, the OR, CI, and p-values were: infinite, 2.0-∞, p=0.006 (cantaloupe); infinite,1.3-∞, p=0.03 (honeydew); and infinite,1.5-∞, p=0.02 (watermelon). Eating honeydew in general was also implicated; however, all case-patients who recalled the form of honeydew eaten ate precut honeydew. A traceback investigation identified multiple sources of precut melon mixes. The results of this outbreak investigation parallel those of other SP outbreaks and demonstrate the importance of assessing the manner of food preparation, in addition to the type of food consumed, when analyzing food histories. Additional research into safe melon handling and processing procedures is needed to provide science-based guidelines to reduce the risk of *Salmonella* infection.

Board 76. Evaluation of Factors Contributing to Environmental Contamination with *Cryptosporidium parvum* from a Dairy Herd

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Cryptosporidium parvum is an important protozoan pathogen that infects over 75 species of mammals, including humans. *C. parvum* is common in dairy cattle wastes and transmission from cattle to humans has been extensively documented. Little is known about the public health risk posed by animal waste and how that risk is affected by storage and disposal procedures. Assessing the potential role of cattle in human exposure requires understanding the dynamics of factors contributing to environmental contamination. These include host and temporal patterns of shedding, survival of the organism in animal waste, and waste management strategies. The goal of this study was to determine whether dairy cattle significantly contribute to environmental contamination with *Cryptosporidium parvum* oocysts under conditions typical of Illinois dairy farms. A one-year study was conducted to determine the prevalence of *Cryptosporidium parvum* oocysts shedding in fecal samples at a dairy, and identify any seasonal or temporal shedding patterns. In addition, an experiment was performed to determine the survival rate and viability of *C. parvum* oocysts in compost over time. The information gathered was incorporated into a computer simulation model to evaluate the interaction of relevant factors that can be used to predict environmental load of *C. parvum* oocysts. We concluded that dairy herds may be a significant source of environmental contamination with C. parvum, depending on the occurrence of specific events. The actual level of contamination varies over time and is affected by calving pattern, seasonal incidence, and the effectiveness of composting. Based on our model, compost management may be the most important critical control point in preventing environmental contamination with *C. parvum* oocysts. In addition, the actual human health risk is dependent upon a unique sequence of events subsequent to environmental contamination.

Board 77. The Outbreak Investigation at Square One: Submit a Specimen

M. E. Huddle, S. O. Olsen, K. M¯lbak

Centers for Disease Control and Prevention, Atlanta, GA

Background: Despite the discovery of new agents of foodborne disease and improvements in laboratory detection methods, a large percentage of foodborne disease outbreaks in the United States are of unknown etiology. **Methods:** Data from the CDC Foodborne Disease Outbreak Surveillance System were used to characterize foodborne disease outbreaks of unknown etiology that occurred in the United States between 1973 and 1997. A foodborne disease outbreak was defined as the occurrence of two or more cases of a similar illness resulting from the ingestion of a common food. Outbreaks are investigated by local and state health officials and reported to CDC on a standard form. Any outbreak that met the criteria needed for confirmation of a foodborne disease outbreak for one of the many known agents was defined as an outbreak of known etiology [MMWR 2000; 49(SS-1): 54-61]. All other foodborne disease outbreaks were defined as outbreaks of unknown etiology. **Results:** There were 12,846 foodborne disease outbreaks reported; 8,227 (64%) were of unknown etiology. This percentage remained relatively constant when comparing decades: 64.8% from 1973-1979, 63.1% from 1980-1989, 64.6% from 1990-1997. The percentage of foodborne disease outbreaks of unknown etiology varied from month to month with the highest percentage occurring between December and February (range, 71.9% to 74.1%) and the lowest percentage occurring between July and September (range, 53.8% to 54.7%). The median number of persons who became ill in outbreaks of unknown etiology was 6

[interquartile range: (IQR): 3 to 22 persons] compared with 12 persons (IQR: 4 to 34) in outbreaks of known etiology. In 1010 (15.1%) outbreaks of unknown etiology patients were hospitalized and in 20 (0.28%) at least one person died compared with 2125 (56.1%) and 177 (4.4%) in outbreaks of known etiology, respectively. In 2801 (34.1%) foodborne outbreaks of unknown etiology patients submitted specimens for testing compared with 3278 (71.0%) outbreaks of known etiology (RR=0.57, $p<.0001$). In 2341 (28.5%) outbreaks of unknown etiology a vehicle was identified compared with 3307 (71.6%) outbreaks of known etiology (RR=0.51, $p<.0001$). **Conclusions:** Foodborne disease outbreaks of unknown etiology were generally smaller than outbreaks of known etiology but contributed to the overall morbidity of foodborne illness. There was a strong association between the collection of a patient specimen and a known etiology as well as between known etiology and an increased likelihood of identifying the vehicle. Health care workers should be encouraged to collect specimens at the beginning of an outbreak investigation. In addition, further work is needed to identify barriers to obtaining specimens.

Board 78. Risk Factors for Sporadic *Campylobacter* Infections in Maryland

L. A. Klatka[1], M. A. Hawkins[1], M. A. Pass[2], F. J. Angulo[3], D. D. Rohn[4], J. G. Morris[1], and the EIP FoodNet Working Group[3]

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Background: *Campylobacter* is the leading cause of bacterial diarrhea in the United States and among CDC's Foodborne Diseases Active Surveillance Network (FoodNet) sites. Data from FoodNet show that Maryland has a remarkably low incidence of culture-confirmed *Campylobacter* infections, where it is the third reported most common cause of diarrhea. In this analysis, we sought to examine risk factors for sporadic infection in Maryland to determine if differences in exposure may explain the difference between Maryland and other FoodNet sites. **Methods:** Between March 1998 and February 1999, a *Campylobacter* case-control study was conducted in FoodNet sites (Connecticut, Georgia, Minnesota, Oregon, and selected counties in California, Maryland, and New York). A case was defined as a person with *Campylobacter* infection identified by a clinical laboratory; and diarrhea, with onset <10 days before the positive stool culture. Each case was matched with a control from the same age range and telephone exchange. Subjects were interviewed regarding diet, kitchen practices, travel, and animal exposure in the 7 days prior to illness onset (cases) or interview (controls). Risk factors among Marylandës cases and controls were compared using «2 analysis. **Results:** Of 157 cases identified by surveillance in the Baltimore metropolitan area of Maryland, 119 were enrolled. The mean age of the cases was 35.6 years (range 2 months to 93 years); 17 (14.3%) cases were hospitalized. Cases were more likely than controls to be white ($p<0.01$), to have recently eaten in a restaurant ($p=0.01$), traveled internationally ($p=0.01$); eaten chicken luncheon meat ($p=0.03$), or ham ($p<0.01$); had contact with a puppy ($p=0.01$), dog ($p=0.03$) or cat ($p=0.02$); or visited a petting zoo ($p=0.04$). Cases were less likely than controls to have purchased ($p=0.01$), stored ($p=0.01$), or cooked ($p=0.01$) raw chicken. Cases who purchased chicken reported leakage from the package onto other items in their grocery bag more often than controls ($p<0.01$). The remainder of kitchen practices did not differ between groups. **Conclusions:** Except for the handling of raw chicken, Maryland's site-specific analysis identified similar risk factors for *Campylobacter* infection as the analysis of FoodNet-wide data, and previously published reports, suggesting that exposure to poultry and animals, eating outside the home, and international travel are risk factors for disease. The reason for the unusually low incidence of *Campylobacter* infections in Maryland remains unexplained, but suggests exposure to contaminated chicken may be lower. Other factors, including those leading to identification of *Campylobacter* as the etiologic agent in a case of diarrhea, warrant further study to clarify the low incidence of *Campylobacter* infections in Maryland.

Board 79. Foodborne Outbreak Surveillance in Georgia: The Impact of State and Federal Funding, 1995-2000

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Georgia Division of Public Health, Atlanta, GA

Background: Georgia has experienced a dramatic increase in the number of recognized foodborne disease outbreaks at the state level from 1995-2000. The number of reported foodborne outbreaks increased more than tenfold, from 3 in 1995 to 43 in 2000. New federal grants targeting emerging infectious diseases epidemiology and laboratory capacity have provided increased resources to support activities at the state level. New state funding has also boosted epidemiologic capacity in the 19 health districts, providing support for masters trained epidemiologists for 13 districts.

Methods: We calculated the amount of funding received from state and federal sources that focused on general infectious disease investigation and control. Foodborne disease outbreaks reported to the Georgia Division of Public Health during 1995-2000 were compared with the number of infectious disease (ID) epidemiologists at the state level.

Results: Before 1994, federal grant money was focused on specific infectious diseases such as sexually transmitted diseases (STDs), tuberculosis, and AIDS. The amount of federal funding to Georgia devoted to general infectious diseases drastically increased from $63,000 in 1995 to over $1.4 million in 2000. The number of ID epidemiologists increased from 3.5 in 1995 to 16.5 in 2000. During 1995-2000, a total of 106 foodborne outbreaks were reported to the Georgia Division of Public Health. Of these, 3 outbreaks were reported in 1995, 4 outbreaks were reported in 1996, 4 outbreaks were reported in 1997, 17 outbreaks were reported in 1998, 34 outbreaks were reported in 1999, and 43 outbreaks were reported in 2000.

Conclusion: Increased federal and state funding has greatly improved the foodborne disease outbreak surveillance system in Georgia. These funds have allowed an increase in the number of ID epidemiologists at the state and local levels, which in turn has increased the number of reported outbreaks in Georgia each year. This increase is primarily due to improved communication between state, district, and county health departments, and to better ascertainment and reporting of outbreaks at all levels. County, district, and state public health personnel are striving to improve foodborne outbreak reporting, and to develop stronger collaboration and communication between epidemiologists, environmental health specialists, and laboratorians to conduct better outbreak investigations.

Board 80. Interventions at Critical Points Along the Shell Egg Supply Chain to Mitigate Egg-Associated Salmonella Enteritidis in the United States — A Descriptive Analysis

G. A. Mumma, P. M. Griffin, M. I. Meltzer, C. R. Braden, R. V. Tauxe

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Background: Salmonella Enteritidis (SE) emerged as a major cause of foodborne illness in humans in the U.S. in the 1980's. Programs to mitigate SE have focused on reducing SE infection and growth in shell eggs. There is a need to evaluate their effectiveness. However information with which to do so is incomplete.

Objectives: Collect data on SE control programs aimed at reducing SE infection and detering SE growth in eggs, describe them, and identify data that would be needed to evaluate their effectiveness.

Methods: We collected national and state-specific time series data on SE control programs designed to reduce SE infec-

tion at the primary and multiplier-breeding flocks level, shell egg production, and deter SE growth at the retail level. We used these data to describe the programs over time and analyzed them to identify gaps that needed to be filled in order to adequately evaluate their effectiveness. Data were obtained from CDC, USDA, FDA, SE vaccine producers, National Restaurant Association (NRA), and state agricultural and public health officials.

Results: Chicken breeding flocks in the USDA's program to eliminate SE at the breeding level increased from 70% in 1990 to 100% in 1997. The top-twenty egg-producing states in the U.S. produced 81% of eggs between 1995 and 1999. By 1999, 15 of 50 states had adopted EQAPs and they produced 26% of U.S. eggs. The number of doses of SE vaccine for chicken sold in the U.S. increased by 1400% between 1992 and 1999. The proportion of layers that were of one breed of chicken, thought to be relatively resistant to SE, increased from 25% to 77% between 1980 and 1999. Funding for USDA traceback activities was withdrawn in 1995, and the work was taken over by the FDA in 1996. Between 1976 and 1999, states requiring refrigeration for shell eggs at retail increased from 5% to 73%, and those requiring refrigeration at more stages along the egg supply chain increased from 3% to 40%. The number of annual ServSafe Certificates issued by the NRA increased by 892% between 1987 and 1999.

The following data were found to be incomplete and limiting to potential evaluation of programs for effectiveness: state-specific time series data for the source and destination of eggs, eggs produced under each EQAP, compliance rates for each EQAP's requirements and for temperature requirements, SE infection rates in layer flocks and eggs, SE vaccine usage, layer strains, and evidence of training for food service professionals that could be compared to SE reductions. USDA SE Task Force reports from 1993 to 1995 were incomplete, and FDA provided trace back data aggregated around regions.

Conclusions: Although many SE control strategies were instituted since the late 1980's in response to the epidemic of SE illness, records relating to major egg safety programs are difficult to obtain. More complete data and time series analyses are needed to assess the impact of these programs on SE infections and growth in eggs.

9 GIS and Remote Sensing

Sunday, March 24, 12:00 noon
Grand Hall East

Board 81. NASA Remote Sensing Data for Epidemiological Studies

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In response to the need for improved observations of environmental factors to better understand the links between human health and the environment, NASA has established a new program to significantly improve the utilization of NASA's diverse array of data, information, and observations of the Earth for health applications. This initiative, lead by Goddard Space Flight Center (GSFC) has the following goals: (1) To encourage interdisciplinary research on the relationships between environmental parameters (e.g., rainfall, vegetation) and health, (2) Develop practical early warning systems, (3) Create a unique system for the exchange of Earth science and health data, (4) Provide an investigator field support system for customers and partners, (5) Facilitate a system for observation, identification, and surveillance of parameters relevant to environment and health issues. The NASA Environment and Health Program is conducting several interdisciplinary projects to examine applications of remote sensing data and information to a variety of health issues, including studies on malaria, Rift Valley Fever, St. Louis Encephalitis, Dengue Fever, Ebola, African Dust and health, meningitis, asthma, and filariasis. In addition, the NASA program is creating a user-friendly data system to help provide the public health community with easy and timely access to space-based environmental data for epidemiological studies. This NASA data system is being designed to bring land, atmosphere, water and ocean satellite data/products to users not familiar with satellite data/products, but who are knowledgeable in the Geographic Information Systems (GIS) environment. This paper discusses the most recent results of the interdisciplinary environment-health research projects and provides an analysis of the usefulness of the satellite data to epidemiological studies. In addition, there will be a summary of presently-available NASA Earth science data and a description of how it may be obtained.

Board 82. Coordinated Regional Surveillance for West Nile Virus in Metropolitan Washington

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In support of the activities of the Metropolitan Washington Council of Government's West Nile Virus coordinating committee, a geographical information system was set up and analytical maps prepared to describe the evolution of West Nile virus activity in birds during the summer and early autumn of 2001. The region covered by the maps includes the District of Columbia, three counties in Maryland, and five cities, counties, and health districts in Virginia. The maps were intended to inform state and local health departments in the Washington metropolitan area regarding risk and possible cases in humans as well as mosquito spraying decisions, and to inform the public. The exercise was also intended to illustrate benefits of collaboration between academic institutions and public health agencies, and between epidemiology and geography. A geographical information system database was built combining data on dead birds reported, tested, and found positive for West Nile virus in the metropolitan area. Differences across the states and local areas with respect to surveillance and testing procedures were harmonized to the extent possible. Maps were prepared with a greater degree of geographical detail for the health officers of the jurisdictions concerned, and in less detail for the general public so that the specific locations where birds were found were not disclosed. The analyses revealed two clusters of West Nile positive birds in the metropolitan area: a major cluster in the District of Columbia, extending into adjacent parts of two Maryland counties, and a smaller cluster at the border of Arlington County and the City of Alexandria in Virginia. The concentration of birds at this point was such that human risk seemed likely. A comparison of positive and negative birds in the region provided evidence that this cluster was not the result of reporting biases. The first positive bird was found in early July at what would become the center of the major cluster. While the pattern spread throughout the season, it remained centered at this point. The extent and dynamics of the epidemic would not have been apparent without a geographical analysis of this sort. Collaborating across jurisdictional lines provided additional information that would not have been clear to any individual health official.

Board 83. Analysis of the Spatial Distribution of Cryptosporidiosis in AIDS Patients in San Francisco Using Density Equalizing Map Projections (DEMP)

A. Khalakdina[1],[2], S. Selvin[3], D. W. Merrill[4], C. Erdmann[4], J. M. Colford, Jr.[1]

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Background: Environmental transmission of cryptosporidiosis has occurred repeatedly in defined spatial areas during outbreaks of disease attributed, for example, to drinking water contamination. Little work has been done to investigate the possibility of cryptosporidiosis infection in defined spatial areas in non-outbreak (i.e. endemic) settings. This study applies a novel approach to the investigation of the spatial distribution of cryptosporidiosis in AIDS patients in San Francisco. **Methods:** Density equalizing map projection (DEMP) maps were created for nine race/ethnicity-age groups of AIDS patients based on census tract of residence. This technique is illustrated for one category: White, male AIDS cases 10-29 years old in the Figure where (a) shows cases plotted in their respective census tracts on a geopolitical map of San Francisco, and (b) shows the same cases plotted randomly within the same census tracts on a DEMP map.

The study population included 906 AIDS patients with cryptosporidiosis and 15,138 AIDS patients without cryptosporidiosis; the DEMP maps were created using the entire study population. In addition to testing for spatial randomness, census tracts with a "high density" of cryptosporidiosis cases were identified by applying smoothing techniques to the DEMP maps, and included as a covariate in multivariate Poisson regression analyses of other known risk factors for cryptosporidiosis. **Results:** These analyses suggest: (1) cases of cryptosporidiosis among Black and Hispanic AIDS patients, but not among Whites, show a significant non-random spatial distribution ($p < 0.05$) even after adjustment for the underlying spatial distribution of AIDS patients for these demographic groups and (2) the risk of residence in these high density census tracts adjusted for other known risk factors, although slightly elevated, was not statistically significant (relative risk=1.27, 95% confidence interval 0.15, 10.53). **Conclusions:** The results of this investigation do not support an independent effect of spatial distribution on the transmission of cryptosporidiosis among AIDS patients in San Francisco.

Board 84. Predicting Geographic Variation in the Risk of Cutaneous Leishmaniasis Throughout Colombia

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Cutaneous leishmaniasis is a notifiable disease in Colombia, with around 6000 cases reported to the Ministry of Health annually — representing a several-fold increase over the last 20 years. As in other endemic countries, case notifications are likely to significantly underestimate true incidence, and the geographic distribution of reported cases will be biased by the effectiveness of local health services. In this paper, using data from 1994, we investigate the extent to which the geographic distribution of cases (amongst 1080 municipalities of Colombia) can be explained by spatial variability in both land use (using data derived from remotely sensed images) and altitude. Firstly we use logistic regression analysis to model the probability that a municipality has at least one case reported; and then we investigate the extent to which we can predict the variability in incidence amongst these "positive" municipalities. Model fits were tested on data from geographic localities not used to generate the models being tested. As cutaneous leishmaniasis in Colombia is caused by more than one parasite species, and is transmitted by several sandfly vectors, we tested whether the "binary model" fit could be significantly improved by generating separate models for each regionally defined ecotype. The results of the analyses allow us (i) to quantify the effect of changes in land use (such as deforestation); and (ii) to identify areas where we suspect significant under-reporting of cases. The utility of risk maps for determining control decisions depends on the sensitivity and specificity of the predictions. In this paper, we derive these parameter values for different threshold incidence levels (above which control should hypothetically be implemented). To our knowledge this is the first reported study to demonstrate that remotely sensed images can accurately predict the risk of leishmaniasis across a wide geographic area.

10 Health Department Activities

Sunday, March 24, 12:00 noon
Grand Hall East

Board 85. Is Crow Density Reporting Predictive of Human West Nile Virus Cases in Florida?

L. Conti[1], C. Blackmore[2], R. Oliveri[1], L. Stark[3], S. Wiersma[1]

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Florida implemented a dead bird reporting and testing system in April 2000 as a response to the identification of West Nile (WN) virus in the New York City area during 1999. This activity was in addition to Florida's traditional arbovirus surveillance measures of maintaining sentinel chickens, and reporting human and equine vector-borne disease incidence.

The new system first successfully detected WN in a dead crow in North Florida during July 2001. Overall, fewer dead birds were reported once WN was identified in Florida compared with New York State, despite similar state populations. Crow mortality as a proportion of dead bird reports also appears to be lower in Florida (12%) than New York (33% during 1999, and 25% in 2000) and Connecticut (40% in 2000). Avian virus isolation rates were lower in Florida than in the Northeast. In New York, 32% of all birds tested (n=3,976) during 2000 were positive. In comparison, WN virus was isolated in 10% of the birds tested (n=7,163) in Florida during 2001. WN virus was detected in approximately half of the crows tested in both Florida and New York.

The 11 human cases of disease reported from eight of Florida's 67 counties were preceded by crow mortality reports in each instance. Although higher rates of reported crow mortality occurred in counties with intensive WN virus activity, as a general rule, dead crow densities were not useful for estimating the risk for human disease in Florida during 2001.

Board 86. Epidemiology of *Neisseria meningitidis* Infections in New York City, 1989-2000

D. Weiss[1], A. Moura[2], A. Pablos-Mendez[2], M. Layton[1]

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National trends in meningococcal disease have demonstrated a shift in the epidemiology with an increasing median age and proportion of sergroup Y. We undertook an analysis of meningococcal disease in New York City (NYC) over the past 12 years to examine for similar trends. **Methods-** All reports from January 1, 1989 to December 31, 2000 that met the definition for a confirmed case (isolation of N. meningitidis from a normally sterile site) were included in the review. Additional case finding was performed by reviewing records of the NYC Public Health Laboratory and by searching the vital records system for meningococcal deaths. Information abstracted included demographics, outcome and serogroup. Incidence rates were computed using US census estimates for 1990 and 2000. Pearson's Chi Sq, Fischer's exact test and Kruskal-Wallis were used to assess statistical significance of categorical variables and mortality risk. Analyses were performed using SPSS and Epi Info. **Results-** There were 578 confirmed cases of meningococcal disease in NYC during the period for an average annual incidence of 0.63/100,000. Ninety-six case-patients died for a case fatality ratio of 16.6%. One serogroup C institutional outbreak of three cases occurred in 1998. Meningococemia was the most common presentation accounting for 56% of cases with meningitis in 41%, arthritis in 2% and pneumonia in 1%. The median age increased from 16 years in 1989-1991 to 30.5 years in 1998-2000 ($p< 0.001$), as a result of a decline in the incidence among young children. Of the 420 (73%) with a known serogroup; 2% were serogroup A, 32% were serogroup B, 27% were serogroup C, 7% were serogroup W135, 28% were serogroup Y and 4% were other or ungroupable. Serogroup Y increased from 4% of serogrouped cases in 1989-1991 to 48% in 1998-2000. The mortality was lowest in the 5-19 year old group (reference group) and the risk ratio of death was significantly greater for the following age groups: 20-44 years (RR=2.5, 95% CI 1.1-8.1), 45-64 years (RR=3.7, 95% CI 1.6-13.2) and 65 years and older (RR=4.5, 95% CI 2.2-17.4). Children 0-4 years old had a three times greater mortality if they had meningitis (RR=3.1, 95% CI 1.1-9.0) whereas adults over 45 years had a three times greater mortality when presenting with meningococcemia (RR=3.0, 95% CI 1.3-64.0). Conclusion- New York City experienced a trend similar to the national change in the epidemiology of meningococcal infections with an increase in the median age and increasing proportion of serogroup Y. While the incidence rate is low, the case mortality ratio exceeds national levels. Possible explanations for this finding include the exclusion of probable cases from the analysis, differential reporting of severe cases, the presence of virulent clones in the population and factors relating to the timely access of medical care. Further epidemiologic investigation is necessary to evaluate excess meningococcal mortality in NYC.

Board 87. Guide to Surveillance and ReportingóAn Example of Technical Assistance for Local Health Departments in Massachusetts

A. Hackbarth, et al.

Massachusetts Department of Public Health, Boston, MA

Issue: Limited resources have impaired the capacity of many local health departments to conduct adequate surveillance for many infectious diseases. Technical assistance by state health departments can help expand capacity. In Massachusetts, technical assistance in the form of a comprehensive reference manual addressing reporting, investigation and control has been developed for local health departments. Provision of this reference manual, in combination with training, has strengthened local capacity, hopefully leading to more timely recognition and containment of infectious diseases.

Project: The *Guide* is a comprehensive manual for local health departments on how to do surveillance for the infectious diseases reportable to the Massachusetts Department of Public Health (MDPH). It is organized alphabetically into 57 chapters by disease; each contains step-by-step instruction on reporting, investigation and control, including state requirements and an emphasis on those diseases that have higher priority, such as those that are vaccine-preventable or caused by bioterrorist agents. The *Guide* contains an overview of the MDPH infectious disease surveillance system and a copy of case report forms. The *Guide* describes who should be responsible for surveillance and emphasizes a team approach within the local health department and the local community. It was distributed to all local health departments in March 2001. This was followed-up with daylong training programs held at seven locations statewide. The *Guide* also has been posted on the MDPH website.

Results/Lessons Learned: It is clear that a certain level of expertise is needed to carry out infectious disease surveillance. By involving local health departments in the development of this guide and through the statewide daylong training program, the state health department has experienced an increase in timeliness and completeness of reporting, and the ability of some local health departments to handle more on their own. Communication can improve when the state health department provides technical assistance proactively rather than in response to cases or outbreaks. A step-by-step reference manual that emphasizes collaboration (among members of a local health department, among bordering towns, and with the state health department) was adapted from a previous reference manual developed by MDPH (*Foodborne Illness Investigation and Control Reference Manual*) that has proved to be successful in improving foodborne illness response and control.

Board 88. Bacteriological Profile of Septic Abortion Clients: A Study in Southern India

S. K. Korlagunta

S. V. Medical College, Tirupati, INDIA

Objective: To study the bacteriology associated with attempted abortions admitted with sepsis.

Design: Case Study

Participants: 100 respondents admitted for post-abortion sepsis.

Place of study: Government Maternity Hospital, Tirupati town, Chittoor district, Andhra Pradesh, India.

Materials: A total of 100 specimens (pus/exudate/tissue) collected from cases of septic abortion admitted for treatment in maternity hospital.

Methods: Specimens were incubated on blood and Macconckey's agar plate and in Nutrient broth for aerobic organisms, on Neomycin and Robert Cooked Meat medium for anaerobic culture. Organisms were identified by their morphological,cultural and biochemical characterestics.

Results: Anaerobes were isolated from 10% of cases ,while mixed infections involving both aerobes and anaeorobes was observed in 37.5% of cases. Aerobes alone were encountered in 52.5% of specimens. Of anaerobes, anaerobic cocci were predominant (65.6%) followed by bacteroides (25.5%) and different *Clostridium* species (8.7%). Among aerobes, *E.coli* (50%) and *Staphylococcus pyogenus* (29.2%) were dominant.

Conclusions: The prevalence of bacteroides poses a problem in India, as these strains are resistant to less expensive penicillins .

Implication: Alternative cost-effective drugs like metronidazole and gentamycins may be provided in the health service institutions.

11 Infectious Causes of Chronic Diseases

Sunday, March 24, 12:00 noon
Grand Hall East

Board 91. Radiographic Findings and Risk Factors for Bronchiectasis Among Alaska Native Infants Hospitalized with RSV as Infants: 5 Year Follow-Up

R. J. Singleton[1], L. Bulkow[1], G. J. Redding[2], T. C. Lewis[3], P. Martinez[4], J. Butler[1], H. Peters[1], J. Gove[1], B. Morray[2]

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Background: Bronchiectasis has become rare in developed countries and is labeled an orphan disease; however, prevalence of bronchiectasis in one Alaska Native region remains high at 16 cases per 1,000 persons born in 1980-1989. Since infants in this region also have an extremely high rate of RSV hospitalization, we hypothesized that early RSV hospitalization and early repeated pneumonias were risk factors for development of bronchiectasis.

Methods: In 1993-96 we conducted a case control study to evaluate risk for RSV hospitalization. A total of 102 RSV hospitalized cases and 122 non-hospitalized controls were recruited in infancy and studied again 5 years after RSV hospitalization. Chest films since birth were reviewed by two of us (GJR, TCL). If chest films were missing, the radiologist report was reviewed. Chest film diagnosis of bronchiectasis required saccular changes or cylindrical outlines of airways that widened as airways extended into the lung periphery.

Results: 1200 chest films were available from study participants. 102/102 former RSVcases and 89/122 controls had at least 1 chest film (median 4 per child, range 1-42 per child). 24 children (11%) had chest film evidence of bronchiectasis at ≥2 years of age. Former RSV-hospitalized cases were not more likely than controls to have bronchiectasis (13% vs. 9%, p=.393). 124 (56%) of the participants had ≥ 1 infiltrate < 2 yrs of age. These children were more likely to have bronchiectasis on chest film than children with no infiltrates < 2 years of age (16% vs. 4%, p=.004). Also, presence of infiltrates ≥ 3 yrs. of age (67% vs. 18%, p<.001), multiple infiltrate ≥ 3 yrs. of age (38% vs. 6%, p<.001), and atelectasis >3 yrs. of age (50% vs. 5%, p<.001) were more common in children with bronchiectasis. For all chest films, pulmonary infiltrates were more common in chest films taken <2 yrs of age than ≥2 yrs. of age (51% vs. 45%, p=.042), while bronchiectasis was more common in chest films > 2 yrs. of age than < 2 yrs of age (12% vs. 2%, p<.001). The 24 children with bronchiectasis were more likely than other participants to have cough > 1 month (29% vs. 9%, p=.010), productive cough (58% vs. 33%), wheezing (41% vs. 19%), or albuterol use (39% vs. 17%) in the past year, but were not more likely to have environmental and socioeconomic factors such as ≥ 6 persons in the house, household smokers, and flush toilets.

Conclusions: Alaska Native children experience a high prevalence of bronchiectasis. While bronchiectasis was not more common in children hospitalized with RSV as infants, it was more common in children with pulmonary infiltrates before 2 yrs. of age, and those with infiltrates or atelectasis after 3 yrs. of age.

Board 92. The Health and Economic Burden of *Helicobacter pylori* on the US Military

D. A. Blasiole, C. J. Hansen, M. Ryan, K. L. Russell

Naval Health Research Center, San Diego, CA

Background: *Helicobacter pylori*, a bacterial pathogen, is a recognized etiological agent in gastric cancer, chronic gastritis, and peptic ulcer disease. The worldwide infection rate is estimated at nearly 50%, with prevalence ranging from 70-90% in developing countries and 17-20% in developed countries. A review of data on *H. pylori*-related diagnoses among US military personnel and their families was conducted to assess its operational and economic burden in this healthy, young population. **Methods:** Comprehensive medical information systems available to the US military provided detailed information on all inpatient and outpatient medical visits at military and civilian treatment facilities by military families. Cases of *H. pylori* were captured using the International Classification of Diseases, 9th edition, Clinical Modification (ICD-9-CM) code 041.86. The period prevalence of *H. pylori* diagnoses among military personnel was calculated for calendar year 2000. The pharmaceutical cost for treatment was estimated using the average military price of standard triple therapy regimens. **Results:** *H. pylori* was diagnosed in 2429 total cases among military personnel and their families. In active duty military only, 802 cases were diagnosed, yielding a period prevalence of 2.1 cases per 100,000 in the year 2000. The specific diagnosis of *H. pylori* was most commonly associated with diagnoses of gastritis, gastrointestinal hemorrhage, diseases of the esophagus, duodenal ulcer, and gastric ulcer. Using an average cost of pharmaceutical treatment of $106.90 per case, the estimated cost to the US military for 2429 total cases was nearly $260,000. Conclusion: This analysis provides a very conservative estimate of the burden of *H. pylori* disease in the US military community. Presumptive treatment for conditions associated with *H. pylori* likely occurs without documentation of specific *H. pylori* diagnoses. Presumptively treated cases, the cost of maintenance therapy for these and confirmed cases, and the costs of healthcare encounters and diagnostic procedures for *H. pylori*-related illnesses were not included in this analysis. Despite these limitations, available data demonstrate that *H. pylori* appears to have a significant impact on the healthcare system of the US military.

Board 93. Association of *Chlamydia pneumoniae*, but not CMV,with Incident Myocardial Infarction in Male Military Personnel

C. M. Arcari[1], K. E. Nelson[1], M. Krauss[2], C. A. Gaydos[3]

[1]Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, [2]Walter Reed Army Institute of Research, Silver Spring, MD, [3]Johns Hopkins School of Medicine, Baltimore, MD

Despite the progress in prevention, diagnosis, and treatment, coronary heart disease (CHD) still remains the leading cause of death in the United States, and established risk factors are unable to explain fully half of all CHD cases. The role of infections in the pathogenesis of CHD has been postulated. This study addresses the hypothesis that previous *C. pneumoniae* or CMV infection, is a significant independent risk factor for CHD. This cohort is a valuable resource to study the association of previous chronic infections and CHD due to the young age and generally healthy status of the population. Data and specimens were collected from an ongoing and well-established prospective cohort of United States Military active-duty personnel. A nested case-control study was conducted using 300 cases and 300 matched controls. Cases were male, 30-50 years of age, with a medically documented first time hospitalization for acute myocardial infarction (MI), with no history of hospitalization due to CHD. Cases had a serum specimen drawn prior to the time of the acute MI and a health risk appraisal available. Controls were chosen from the same Military active-duty cohort and were individually matched on age, race, and

military rank. Controls had no record of hospitalizations due to cardiovascular reasons prior to the date of the case event. Incidence density sampling was used to identify eligible controls. To be eligible, controls had to have a serum specimen available within 1 month of the date of the case serum. All serum specimens were part of the Department of Defense serum repository. Evidence of past infection with *C. pneumoniae* was based on a ≥1:16 IgG antibody titer, as measured by microimmunofluorescence. Past infection with CMV was measured qualitatively using enzyme immunoassay (Wampole) for IgG antibodies. A total of 300 individually matched pairs were studied. Median age of the pairs at time of case MI was 40.2 years. The race/ethnicity was 29% Black, 59% White, and 12% Other. Serum cholesterol and smoking status was significantly different between cases and controls ($p < 0.05$). Overall prevalences of *C. pneumoniae* (≥1:16) and CMV antibodies in the population were 77% and 57% respectively. Crude analysis using a cut off of ≥1:256 showed an odds ratio of 1.53 (95% C.I.: 1.004, 2.326) for *C. pneumoniae* and 0.89 (95% C.I.: 0.637, 1.244) for CMV. Further multivariate analysis to assess whether high cholesterol level, smoking, hypertension, obesity, and diabetes modify the relationship between *C. pneumoniae* and CMV is ongoing. Results of this study to date demonstrate a significant association between high titer antibody to *C. pneumoniae* and acute MI, but no association between past infection with CMV and acute MI in this cohort. An important challenge is to identify new modifiable risk factors for CHD, which could be used in prevention strategies to reduce the morbidity and mortality associated with CHD.

12 Prevention and Control Programs

Sunday, March 24, 12:00 noon
Grand Hall East

Board 94. Patterns of Measles Current Epidemic Process in Rural Areas

N. Z. Ninashvili

Public Health Department, MoH, Tbilisi, GEORGIA

Introduction: Vaccination against several infectious diseases not only have reduced morbidity rates but also have given us the possibility to eliminate most of them. However, their resurgence in different countries requires consideration of the current epidemic process with its social, geographical and demographical patterns.

After introduction of immunization against measles it became a common infection among adults and already vaccinated persons, including children, especially in rural areas.

According to available literature study of immunization issues in urban and rural areas simultaneously is not highlighted respectively. The lack of such studies is still important.

Methods and Objectives: analytical epidemiological studies using seroepidemiological data were carried out in order to study: 1. Patterns of measles current epidemic process in rural and urban areas; 2.Duration vaccine induced immunity; 3. Immunological efficacy of measles vaccines, simultaneously used in rural and urban areas; 4. Epidemiological effectivnes of vaccination.

Results: Although measles was very frequent among children everywhere in pre-immunization era, the process of "growing up" appeared to be characteristic only in urban areas. Hence, in the category of children's respiratory infectious diseases (such as measles, mumps, pertussis, chicken pox and scarlet fever), measles, which took the first place in the pre-immunization period in rural areas, has moved to the second place after chicken pox in the late 1990s. The number of measles cases has reduced only two-fold (from 56.5% to 27.8%). As for the urban areas, measles took the third place (instead of the first in the pre-immunization era) after scarlet fever and mumps. Despite the low herd immunity against measles in rural areas the infection was more frequently registered among previously immunized persons (48.4%) there than in urban areas (38.6%) where the immunity level was higher.

According to the serological data, the majority of the seronegative persons were from rural areas. Duration of vaccine-induced immunity was longer in urban areas than in rural areas. After 11-15 years since immunization dates the proportion of the previously immunized persons in urban areas was 31.4+2.5%, in rural - 9.5+1.7%. Although immunological efficacy of measles vaccines was equally high in both areas.

Conclusion: High incidence of measles among immunized persons, high level of seronegative persons in rural areas along with other objective reasons are mainly due to shortcomings in vaccination practice there.

Recommendations: 1. Immunizing children in rural areas mostly during the cool period of a year. 2. Reviewing vaccine distribution schedules in accordance with season and electricity supply conditions. 3. Provision rural vaccination points mainly with single dose vaccines.

Board 95. Public Health Laboratories and HIV/AIDS in Sub-Saharan Africa: Efforts in Zimbabwe

B. R. Lall[1], K. V. Shah[1], B. Wilcke, Jr.[2]

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The Association of Public Health Laboratories (APHL) in cooperation with the Centers for Disease Control and Prevention's Global AIDS Program (GAP) has initiated efforts towards working on the laboratory component of the HIV/AIDS epidemic. Our involvement includes strengthening laboratory support for surveillance, diagnosis of HIV/STD/TB and opportunistic infections, and disease monitoring.

APHL has worked on identifying the priority training and functional needs for public health laboratories in Zimbabwe, Cote d'Ivoire, Botswana, and India. This involves in-depth assessment and implementation reports, creating networking opportunities for country laboratory directors abroad and in the U.S., evaluating current methodologies for HIV testing, reviewing laboratory programs, and training laboratory scientists in HIV testing methodologies and quality assurance program plans.

The Zimbabwe Public Health Laboratory System is comprised of 70+ laboratories that need support in several key laboratory areas including quality assurance, management, and training. APHL has provided technical assistance to both the National Microbiology Reference Laboratory and the National TB Reference Laboratory in Zimbabwe. Technical assistance to these laboratories has included the development of Standard Operating Procedures for HIV testing and TB as well as provision of training to laboratorians in U.S. public health laboratories. Assistance has also been provided in Quality Assurance for the public health laboratory system through supplying documents such as CAP checklists for laboratory general services, microbiology, and clinical microscopy.

Setting: The scope of CDC's Global AIDS Program is to support HIV/AIDS prevention program development and technical assistance for 24 countries. These 24 countries were targeted due to the severity of the HIV/AIDS epidemic. APHL's approach towards this effort in Zimbabwe utilizes a multi-faceted APHL team consisting of technical experts, state laboratory directors, and APHL staff to work with in-country partners to further laboratory assistance in Zimbabwe.

Partners: CDC, WHO, and Ministries of Health in project countries.

Conclusions: By assisting with the development of public health laboratories in Zimbabwe, APHL has helped to enhance the

public health laboratories' HIV/AIDS surveillance capabilities and their ability to perform HIV/AIDS testing with the support of quality assurance measures. This sustainable approach to laboratory assistance will lead to better seroprevalence data and thus will aid in the prevention and containment of the HIV/AIDS epidemic.

Additional Authors: Kajari V. Shah, MPH; Burton Wilcke, Jr. PhD

Board 96. Cluster Investigation of Swollen Joints at an Air Force Base in Louisiana

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From April to June 2001, six children enrolled in a daycare center on a United States Air Force Base in Louisiana were medically evaluated for joint pain and swelling. All children were between seven months and four years of age. Concern was raised that these illnesses may be related to a common exposure at the daycare center. **Method:** A case-cohort investigation was conducted. Through a survey administered at the daycare center or by telephone, other potential cases were identified. A case was defined as any adult or child in the daycare center with joint pain or swelling, or any sibling of a child enrolled in the daycare center with joint pain or swelling from April to July 2001. Titers were obtained for lymphocytic choriomeningitis, measles, mumps, cytomegalovirus, Eastern Equine Encephalitis, California Encephalitis, St. Louis Encephalitis, Western Equine Encephalitis, Adenovirus, Influenza Types A and B, Varicella, Coxsackie A and B, Echovirus, Herpes Simplex Virus 1 and 2, Parvovirus, Epstein-Barr Virus, and Lyme Disease. Geographic Imaging System (GIS) software was used to map out room assignments and home addresses of the cases. Environmental assessments were conducted of the daycare center grounds and the Heating, Ventilating, and Air Conditioning (HVAC) system. **Results:** Respondents included 200 enrolled children and daycare workers (N=262) and three siblings. The survey identified 16 additional cases. Multivariate analyses of responses indicated that joint pain and swelling was associated with exposure to ill persons, being febrile, having malaise, and being an adult. There was no association with bug bites, travel history, pets, group activities, or the presence of a rash. Blood samples were obtained for 13 cases; only five had both acute and convalescent titers. Of these, one case seroconverted to cytomegalovirus and another to both Parvovirus and Epstein-Barr virus. GIS identified some clustering of cases in Room 7 of the daycare center (N=4) and by residential zip code. There was no evidence of rodents, ticks, or mosquitoes on the daycare grounds and the HVAC system was in good condition. Conclusion: Although the characteristics of this outbreak are consistent with Parvovirus B19, this could not be confirmed. There were no new cases after 3 June 2001 and the condition was self-limited; hence, the urgency of finding a more definitive etiology waned. Clustering in Room 7 may have been related to age clustering since children were assigned to classrooms by age. It was not necessary to close the daycare to contain the spread of infection, only to stress the importance of good handwashing and hygiene practices.

Board 97. Assessment of Non-Vaccine Acute Respiratory Disease Prevention Interventions (NOVARDPIs) in the US Army

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Introduction: Vaccines have been used extensively to protect against respiratory disease agents such as influenza viruses and adenoviruses. However, vaccines are not always available or may not be effective against the agent threatening an outbreak. NOVARDPIs like personal hygiene (eg, handwashing), administrative controls (eg, allotting adequate floor space/person), engineering controls (eg, indoor air dilution) and personal protective measures (eg, protective face masks) are often considered and sometimes recommended even though scientific evidence of their efficacy is often lacking. The US military has decades of experience with prevention methods, particularly in recruit (initial entry) training. Many strategies were tested and employed in the 1950s and '60s, until the routine use of adenovirus vaccines markedly decreased respiratory disease rates. Since 1999, however,, these vaccines have been depleted and have resulted in recurring outbreaks. The loss of adenovirus vaccines, as well as the potential for non-vaccine epidemic influenza strains to circulate, have renewed interest in NOVARDPIs in the US military.

Methods: We reviewed >140 reports on NOVARDPIs. Interventions covered included handwashing, control of ventilation, barrier protection, prophylactic antibiotics, isolation of individuals and groups, and other methods. Additionally, we surveyed 5 US Army recruit training centers to determine how many had implemented or planned to implement 10 different non-vaccine interventions (handwashing, antimicrobial wipes, 2 space management methods, limiting contact between military units (cohorting), antibiotic prophylaxis, indoor air dilution, increased air filtration, ultraviolet lights and face masks).

Results: Most of the literature addressed theory with some laboratory findings, anecdotes and uncontrolled comparisons. A Navy study found frequent handwashing decreased respiratory disease rates by 45%. An Air Force study noted that antimicrobial wipes decreased respiratory disease clinic visits by 33 to 40%. At each of the 5 surveyed sites, 2 to 7 NOVARDPIs had been or were to be implemented. Costly interventions were avoided. Indoor space management was not possible because of inadequate space. All centers were implementing or planned to implement handwashing programs. None were using or planned to use handwipes.

Conclusion: The effectiveness of NOVARDPIs is poorly addressed in written reports. The many variables that impact on the occurrence of respiratory disease are complex and difficult to study. Costly NOVARDPIs are unlikely to be implemented in the absence of credible effectiveness data. Space limitations prevent space management to reduce crowding. Encouraging frequent handwashing and implementing handwipes to augment handwashing may offer benefits in respiratory disease control, but deserve further study to document efficacy.

Board 98. Evaluating Vulnerabilities and Preparedness for Emerging Infectious Diseases in the Air National Guard

A. M. Likos[1],[2], J. Neville[3], J. C. Gaydos[4],[5]

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Background: Air National Guard (ANG) military units have considerable responsibility for global missions. People in these units live and work in civilian communities but assume military roles one weekend a month or for periods of a week or longer. Even for short periods, ANG members fly to remote parts of the world for humanitarian or other missions. Once their military work is completed, they rapidly return to their civilian communities. We examined demographic and deployment data to assess the extent to which ANG members were exposed to overseas areas, and possibly to novel infectious disease agents. We looked at surveillance and response procedures to determine if an outbreak in an ANG unit would be rapidly detected and an appropriate response would

occur. We focused on medical people who have close contact with ill natives on humanitarian missions.

Methods: Demographic and deployment data were obtained from the Air Force Personnel Center, the National Guard Bureau and the ANG Readiness Center (ANG-RC). Procedures for medical surveillance and outbreak response were identified in interviews with people from the ANG-RC, the Air Force Medical Operations Agency and the Air Force Institute for Environmental, Safety and Occupational Health Risk Analysis. Pertinent documents were studied.

Results: During 1996-2000, ANG medical personnel had 88,976 person-days of overseas exposure; 13,489 (15.2%) person-days were for humanitarian missions. There were 106,433 total ANG members in 91 ANG units, spread over 54 geographical areas. Residence data revealed 9.6% of members did not live in the same state as their assigned unit. The ANG did not participate in Air Force surveillance activities, such as laboratory-based influenza surveillance. Outbreaks occurring while deployed would likely be detected, reported and receive a response. Civilian public health authorities had responsibility for outbreak detection and response after members returned to their communities. Outbreaks occurring after ANG members returned home could be geographically dispersed and undetected. Military-civilian communication was not well established.

Conclusions: ANG members have many opportunities for exposure to novel agents, like influenza or drug resistant enteric organisms, in many areas of the world. An outbreak in an ANG unit, after members have returned to civilian status, could be widely dispersed with delayed detection and response. Reliance upon civilian public health agencies in these situations could result in the ANG unit headquarters not knowing that an outbreak was occurring that might prevent the unit from performing its military mission. ANG units should be included in the military laboratory-based respiratory disease surveillance program. Additionally, ANG public health officers should establish communication links with civilian public health authorities in areas where ANG members live and work.

13 Surveillance and Information Systems Technology

Sunday, March 24, 12:00 noon
Grand Hall East

Board 100. A Unique Medical Surveillance System for Soldiers in Korea that May Have Application in Civil Emergencies

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Introduction: Military forces in Korea may face naturally occurring infectious agents and agents developed by humans. We determined if data could be captured at the lowest medical care level, the battalion aid station (BAS) operated by medical corpsmen, and at the time illness occurred in soldiers in the field. Data collected would be used to identify sentinel events and for ongoing surveillance. **Methods:** BAS activities, e.g., medical documentation and reporting, were analyzed with the goal of making modifications to improve efficiency and eliminate wasteful activities. Next, application of available technology was considered for BAS and field use, and an implementation plan was drafted. Finally, a proof-of-concept system prototype was developed and application of the technology was tested. This occurred in populations served by two BASs in Korea over 4 months. **Results:** At the BASs, corpsmen followed a detailed Ambulatory Patient Care (APC) algorithm and documented symptoms and severity on a standard medical form that was placed in the paper chart. The existing surveillance system used diagnostic information that was independently coded on an ICD9/CPT code bubble sheet and scanned into a central database. The existing data management method was unacceptable for accurate, rapid surveillance because it lacked timeliness, completeness, appropriateness and effectiveness. To improve this situation, a one-write electronic health record that automated the APC algorithm through screen flows was created. A method was also devised to collect information from soldiers on field missions using existing hand-held transmitters. Those who became ill could self-report, or another soldier could report the event, which was plotted by time and location in a Geographic Information System (GIS). All data were rapidly transmitted to a central location for evaluation. Through electronic tracking of events in the BASs and among soldiers in the field, health status could be followed in near real time in a large, command-wide GIS system. The BAS was the epidemiologic unit; all soldiers served by the BAS were the denominator for rate calculations. The standard state of health for the population was defined over time. Deviations from the standard indicated possibly significant health events that required investigation. **Conclusion:** Medical processes in the BASs were made more efficient, benefiting both the primary medical care system and the public health surveillance effort. Corpsman in the BASs and soldiers in the field rapidly adapted to new technologies. Data from the field and from the BASs were married to form a complete picture that helped in determining if a medical event needed rapid and in-depth diagnostic measures. The proof-of-concept test was a success. This military system may have application in medical care systems hastily established for civil emergencies.

Board 101. Developing an Electronic Laboratory Surveillance Network for the Caribbean

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Objective: To strengthen the laboratory surveillance system in the Caribbean, in order to improve national and regional capacity for enhanced disease surveillance. **Design and Methods:** The Caribbean Epidemiology Centre (CAREC/PAHO/WHO), a regional center with a mandate for disease surveillance in 21 Caribbean countries, has been collaborating with the US Centers for Disease Control and Prevention (CDC) and the Walter Reed Army Institute of Research (WRAIR) to develop an appropriate infrastructure. The Public Health Laboratory Information System (PHLIS) software, originally developed by CDC for managing and utilizing laboratory data for surveillance was customized for use in the Caribbean. A feasibility assessment was conducted in each country, to determine the needs and logistics for establishing PHLIS. During training sessions, PHLIS was installed and customized at designated sites and data transmission was tested. Sites then transmitted data on a weekly basis. In 2000, an advanced level PHLIS workshop was convened for selected Ministry of Health employees in order to build national capacity and assure the potential for regional programme sustainability. In 2001, an evaluation of the PHLIS programme was conducted in each country in the network. **Results:** There are currently 11 countries participating in the PHLIS programme in the Caribbean and this year the programme was evaluated in eight of these countries. Feasibility assessments were conducted in another five countries. CAREC has developed three modules, namely Dengue, HIV and Enterics and has established a PHLIS helpdesk. Customization and usage of the software has resulted in the identification of problems related to

specimen management and laboratory capacity. The programme initially experienced data transmission problems due to problems with hardware and telephone lines, but these were all successfully resolved. As at November 16, 2001 the PHLIS database contained 1,829 records. There were 182 dengue records, the majority (91%) of unknown serotype as they were confirmed by IgM. There were 75 HIV records and 1,572 Enteric records (62% Parasites, 26% *Salmonella*, 10% *Shigella* and 2% *Campylobacter*). A serotype was identified in 202 (50%) *Salmonella* records and the greatest proportion of these were *Salmonella* Enteritidis (35%). **Conclusions:** The countries of the Caribbean can successfully utilize the CAREC customized version of PHLIS for surveillance of laboratory data and improved communication between Laboratories and Epidemiology Departments. Ministries of Health and CAREC now have more readily available to them organized laboratory surveillance data, though this is limited by the capacity of the laboratories in the programme. PHLIS however, was not intended to, and cannot function as a laboratory management system

Board 102. A National Surveillance System for West Nile Virus in Zoological Institutions

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In June 2001, the National Zoological Surveillance Working Group* was formed incorporating both human and veterinary health experts from the Centers for Disease Control and Prevention, local and state public health agencies, the United States Department of Agriculture, the American Zoo and Aquarium Association and the American Association of Zoo Veterinarians. A nation-wide surveillance system for detection of West Nile virus in zoos was outlined in a set of guidelines entitled Surveillance for West Nile Virus in Zoological Institutions. A one-year pilot study was initiated in September 2001 and is being implemented in two phases. Phase I consists of the collection and testing of samples from systemically ill or dead at-risk animals on zoo grounds; at-risk animals are defined as animals (from any taxa) housed outside for at least part of the time that may be regularly exposed to mosquitoes. Phase II will be implemented in the winter of 2001 and will consist of surveying archived serum samples from at-risk animals from selected institutions. The Cornell University Veterinary Diagnostic Lab is performing all virus isolation, serology and RT-PCR tests for the system. Preliminary results from the first three months of phase I include data from over 200 animals from 35 participating institutions in 20 states representing all regions of the country. Samples from 150 birds of over 36 species were submitted with 34 sero[or test-]positives still being confirmed and characterized. Forty-five mammals including equids and other hoof stock, big cats, marine mammals, primates and others were tested, as well as 5 reptiles. One hoofed mammal and 1 reptile were seropositive and are being further characterized. All positive animals were from known epizootic areas on the East Coast. These initial results show promise for both increasing the effectiveness of existing national surveillance systems by providing data from previously untapped sources, and for increasing the quality of health monitoring in zoos in the face of a rapidly spreading emerging disease. *Bruce Akey, VA Dept. Agriculture; Wilbur Amand, American Association of Zoo Veterinarians; Robyn Barbiers, Lincoln Park Zoo; Bobby Brown, CDC; Grant Campbell, CDC, DVBID; Pamela Diaz, Chicago Department of Public Health; Cindy Driscoll, MD Dept. Nat. Res.; Ed DuBovi, Cornell College of Veterinary Medicine; Millicent Eidson, NY State Dept. of Health; Amy Glaser, Cornell College of Veterinary Medicine; Thomas Gomez, USDA, APHIS, VS; Duane Gubler, CDC, DVBID; Nicholas Komar, CDC, DVBID; Laura Kramer, NY State Dept. of Health; Bob McLean, USGS, National Wildlife Health Center; Rita McManamon, Zoo Atlanta; Tracey McNamara, Wildlife Conservation Society; Hayley Murphy, Zoo New England; Eileen Ostlund, USDA, NVSL; Mary Grace Stobierski, MI Dept. of Community Health; Scott Terrell, Disney's Animal Kingdom; Kristin Vehrs, American Zoo and Aquarium Association.

Board 104. Using Technology in the Department of Veterans Affairs (VA) to Enhance Screening and Assessment of Patients for Risk of an Emerging Infectious Disease, Hepatitis C

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Hepatitis C disease is of major importance to the United States and specifically the Department of Veterans Affairs (VA). Currently, in over 70,000 unique persons served by the VA are reported as positive for hepatitis C virus antibody (HCVAb). A system of screening and assessment of risk for hepatitis C for each patient coming into the VA system was needed. Therefore, an automated computerized reminder system was implemented at the level of delivery of clinical care with national roll-up of the local data. In the reminder system, there are seven discrete options for resolution. Three are passive and include a previous positive test for HCVAb, a previous negative test for HCVAb or an ICD-9-CM code for hepatitis C infection. If none of these can be found in the local VA computer system, a reminder that the hepatitis C risk assessment needs to be completed is generated at the point of clinical care. Then, a data entry screen providing the 4 remaining resolution options can be utilized by the clinician delivering care. These 4 options are a previous assessment of risk factors for HCV infection (either outside the VA [e.g. had testing done elsewhere] or within the VA but not captured by the computerized system from the electronic medical record [e.g. contained in a written record]), risk factors for HCV infection are present, no risk factors for HCV infection are present, or the patient is unwilling to discuss the subject. The data entry screen complements delivery of clinical care by generating documentation for the clinical note as data entry is completed. Automated roll-up of these data nationally are available for three federal fiscal years from October 1998 through September 2001 and are shown in the table. This yields a total of 1,602,334 unique persons served by VA who have extractable documentation of risk assessment for hepatitis C in the VA electronic medical record nationally. Therefore, a combination of passive and active data collection into a computerized system is effective in documenting assessment of patients for risk for hepatitis C infection in the VA nationally.

New Patients with Risk Assessment Completed

Resolution	FY 99	FY 00	FY 01	Totals
1. Declined	150	4,126	17,741	22,017
2. No risk	5,520	113,775	574,473	693,768
3. Previous assessment	5,565	35,849	42,501	83,915
4. Has risk	3,221	37,652	239,031	279,904
5. HCV Ab+	30,359	31,943	23,536	85,838
6. HCV Ab-	95,061	154,358	157,194	406,613
7. HCV infection/ICD-9-CM	6,855	14,420	9,004	30,279
Total	146,731	392,123	1,063,480	1,602,334

Board 105. New York's Experience with Electronic Reporting of Communicable Disease Test Results from a National Laboratory

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Background: An electronic clinical laboratory reporting system (ECLRS) was begun in New York in early March 2001. Laboratory Corporation of America (LabCorp) was the first large national laboratory that used the Health level 7 (HL7) format and Logical Observation Identifier Names and Codes (LOINC) codes as standards to report test results directly to ECLRS starting in the middle of June. Objectives: To examine the usefulness of LOINC in specifying communicable diseases for public health surveillance, and to assess the completeness and timeliness of electronic reporting from a large national laboratory to New York State compared with paper-based reports. **Methods:** Electronic reportable communicable disease laboratory data performed by LabCorp for cases residing in New York State were obtained for specimens collected between July 1 and October 31, 2001. Laboratory tests were coded with LOINC and test results were coded with LOINC and Systemized Nomenclature for Medicine (SNOMED). LOINC codes were reviewed to assess their accuracy in identifying specific communicable diseases. The paper reports of test results from the same laboratory during the same time frame were matched with the electronic reports using the specimen accession number. Reports reported by paper but not reported through electronic reporting were evaluated. The proportion of reports missing gender, birth date or address, and time from specimen collection date to report date were compared between paper and electronic reports. **Results:** There were 10,452 records received electronically from LabCorp for specimens collected between July 1 and October 31, 2001. LOINC codes identifying a specific disease were used for 9,409 (90%) records; 938 (9%) reports had both LOINC and SNOMED codes; and 105 (1%) reports had generic LOINC or missing codes. The proportion of paper reports matched against electronic reports increased from 62% in July to 87% in October. The electronic reports were completed 99% of the time for gender, 96% for birthdate, and 61% in patient's zip-code; where the paper reports were completed 95% for birthdate and 80% for patient's zip-code. The median duration from specimen collection date to report receipt date improved from 13 days for paper reports to 6 days for electronic reports. **Conclusion:** Our data indicated that the use of LOINC codes for one laboratory's test results could identify a specific disease in 90% of the reports, while the use of both LOINC and SNOMED codes improved the identification of reportable conditions to 99%. The more timely reporting seen with electronic reports could facilitate implementation of more rapid disease control measures.

Board 106. Functional Structure of Epizootic Process at Plague

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The existence of the natural plague focus as parasitic system is limited by processes of three types: reservation of Yersinia pestis, periodic magnification its number (accumulation) and distribution on territory. From here all potential participants of epizootic process execute appropriate functional roles, that allows to speak about the carriers, accumulators and distributors of infection. The significance of microbe reservation carriers and vectors carriers is close. The accumulation more effectively happens in mammals organism, however in a quantitative sense infected fleas it happens, as a rule, on the order it and more. The distributors can be only warmblood animals. But just vectors, the first of all the most mass parasites, integrate all potential participants of epizootic process in wohle complex. At such approach the polyfunctionality participating in epizootic process of animals is obvious: specimens of the same kind can be referred to different classification categories, and representatives of different kinds - to one. The functional status of any concrete species herewith it is necessary to consider as a vector of the sum of functional loads of separate specimens, which directedness can vary depending on oscillations of own number, microbe sensitivity, intensity of intraspecific and interspecific contacts, and also their environments. All above-mentioned testifies about to some indeterminacy of the offered concept. However reasons of it are quite objective and conceal in complexity, multi-level of a phenomenon natural plague nudility and probable character epizootic process. Therefore there are basis to consider that Heisenberg's indeterminacy principle which is known for physicists, is apply and to epizootic process. From mathematics point sights epizootic the process is a complicated biological system of an open type, which represents a typical indistinct multitude.

Board 107. Web-Based Outbreak Information Exchange for Southeast Asia: Advancing Outbreak Response Capabilities for the Region

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The United States Naval Medical Research Unit No. 2 (NAMRU-2), based in Jakarta, Indonesia, in cooperation with the Indonesian Ministry of Health, is introducing a new, Web-based information exchange, to be recognized as ASEAN-Net, to facilitate dissemination of regional outbreak information. As a WHO Collaborating Center for Emerging Diseases, ASEAN-Net represents the culmination of an overall NAMRU-2 strategy in promoting outbreak recognition and response activities, throughout Southeast Asia, as part of the Department of Defense's Global Emerging Infections System (GEIS) initiative. Recently adopted by the ASEAN Secretariat for regional implementation, ASEAN-Net will provide respective, host-national institutions with menu driven options for passing sensitive disease information "across borders", training opportunities, regional (and country-specific) centers of diagnostic excellence, new field appropriate, rapid diagnostics, etc. It is hoped that ASEAN-Net will forge greater cooperation and regional stability between ASEAN member countries, through outbreak recognition and response activities.

Board 108. Merlin – The Florida Department of Health's Web-based Communicable Disease Reporting System: The First Year

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Florida's electronic communicable disease reporting system replaced a paper-based reporting system January 1, 2001. Since that time, Merlin has been operating as the Florida Department of Health's electronic disease reporting system and hepatitis registry. Working closely with a contractor, the basic system was designed, developed, and implemented in less than one year. All 67 counties use the system to enter reportable diseases, laboratory results, and submit electronic case report forms for acute viral hepatitis and bacterial meningitis cases. Additional screens for submitting case report forms online will be added in the coming year. The system is well received by the county users and allows them to access their own data for simple analysis and reports, which was not possible with the paper-based reporting system. Merlin has the capacity to manage large amounts of data in multiple formats within the SQL 7 database. The flexibility of the system also allows other bureaus within the Department of Health, like Immunization and the Childhood Lead Program in Environmental Epidemiology to add

data entry screens easily. Merlin is Florida's early warning surveillance system allowing epidemiology staff to monitor the data before it has been reported. Future plans include hospital connection, electronic transfer of laboratory results, and an outbreak module.

Board 109. Mortality Surveillance for Emerging Infection-Related Deaths in the Armed Forces

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Mortality Surveillance for Emerging Infection-Related Deaths in the Armed Forces, Pearse LA, Potter RN. Office of the Armed Forces Medical Examiner, Armed Forces Institute of Pathology (AFIP), Washington, DC. The Office of the Armed Forces Medical Examiner and the Department of Defense Global Emerging Infections Surveillance and Response System recently initiated a mortality surveillance system to obtain baseline mortality data on military members, monitor mortality trends and detect deaths possibly related to emerging infections or bioterrorist attacks. Mortality surveillance through the medical examiner's office has provided advantages over a passive system relying on death certificates. These include improved timeliness of notification and receipt of specific information, leading to more rapid intervention when necessary, improved accuracy of cause of death and access to the legal authority of the medical examiner. That authority, traditionally used for homicide, suicide and aviation accident cases, has been extended to obtain additional specimens and testing for infectious causes and to perform more extensive investigations if indicated. Among young, healthy members of the armed forces, infectious disease deaths are usually sudden and unexpected, and have the potential to be sentinel events. The surveillance system has a component that attempts to rapidly identify confirmed or possible infection-related deaths for immediate evaluation and follow-up. Data are systematically and routinely collected from uniformed service casualty offices and supplemented by direct contact with local pathologists and clinicians. When infectious etiologies are identified or suspected, specimen collection and processing are immediately reviewed and additional specimens are often requested for more thorough evaluation at the Armed Forces Institute of Pathology and elsewhere. Educational initiatives to raise awareness for infectious agents among the pathology community and syndromic protocols to standardize testing for infectious agents are being developed. Reporting is being audited for completeness and accuracy. During January 1-December 15, 2001, 654 cases were evaluated; five were studied extensively. Three are still under study. One case, a P. falciparum-related death, led to the rapid identification of a malaria outbreak and implementation of control measures. Infectious disease deaths are rare in the military. However, this surveillance system is a prudent financial investment in the military public health infrastructure because it is producing useful data not only on infectious disease deaths, but also on vehicular, training injury and all accidental and sudden deaths.

Board 110. Rapid Detection of Nosocomial Infections Using Automated Typing and Data Mining

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Nosocomial infections are responsible for ca. 90,000 deaths annually in the U.S. with an associated medical care cost of ca. 3.5 billion dollars. Despite being the fourth leading cause of death, there has been limited development of rapid, integrated tools for determination of hospital-acquired infections. Nosocomial infections should be largely preventable by health care personnel aided by rapid, precise diagnosis and by better prevention and treatment regimens. Currently, the time to notice a potential outbreak, perform typing and then institute control measures may take days or weeks. Subjective decisions are often required for initiating such control measures, followed by time consuming molecular confirmation. Cellular fatty acid analysis by gas chromatography has been extensively used for bacterial taxonomy and identification of organisms. Standardized protocols have enabled strain tracking and typing capabilities with this methodology, using principal component and dendrogram analyses. Currently these analyses are performed retrospectively. More advanced algorithms were developed to generate immediate multivariate clustering of fatty acid analysis data. A sequential, single-link clustering algorithm was developed to automatically compare a just-analyzed sample with data from previously analyzed samples. Comparisons can be restricted to user defined time intervals (week, month, year). A year's worth of data (2181 samples) acquired from a collaborating hospital was analyzed with this algorithm. Among the clusters generated was a group of suspect resistant *Staphylococcus aureus* strains from a hospital ward. In addition to clustering these strains, the system provided a correct identification of *S. caprae*. Since an estimated 60,000 profiles can be searched in less than one minute, rapid estimation of prior occurrence would have been possible. By the addition of patient information, antibiotic susceptibility profiles, hospital location, etc., common characteristics of isolates can be determined about that cluster. These software algorithms can be integrated into the current Sherlock® Microbial Identification System as a fully automated real-time epidemiology tool. Hospital infection-control personnel will be able to use the output to immediately implement infection control measures, and thus reduce the impact of nosocomial infections. The information can be readily disseminated by electronic means to participating hospitals, state health laboratories and the CDC facilitating global recognition of outbreaks.

Board 111. Evaluation of Active Bacterial Core Surveillance Methodology for Invasive Group A Streptococcus Infection and Effects on Incidence Rates

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Background: A primary goal of CDC's Active Bacterial Core Surveillance (ABCs) is to determine the incidence and epidemiologic characteristics of five invasive bacterial infections based on active, population-based surveillance. The ABCs case definition for Group A Streptococcus (GAS) is more inclusive than for the other four pathogens; in addition to sterile sites isolates, tissue isolates collected during surgical procedures and wound infections accompanied by necrotizing fasciitis or toxic shock are included as cases. We investigated the possible effect of variability in surveillance methods on GAS incidence rates. **Methods:** Distributions of GAS cases by source of bacterial isolate (e.g. blood, joint, surgical specimen) were compared among ABCs areas for 2000 (eight areas) or 2000/2001 (one area began surveillance July 2000). For two of three ABCs areas that conduct GAS surveillance statewide, rates for the main metropolitan area were calculated. Age and race adjusted incidence rates were calculated for GAS cases identified through blood cultures for the eight metropolitan areas. Qualitative assessment of GAS surveillance methods was performed by telephone interviews of ABCs staff in each area. For one area, the distribution of emm types among blood isolates was compared to isolates from other sources. **Results:** Incidence rates of invasive GAS ranged from 1.9 to 8.0 per 100,000 persons among the nine ABCs areas (median=3.4). The proportion of GAS cases isolated from blood ranged from 49% to 89% (median=77%). The ABC's area with the highest GAS rate had the highest proportion of surgical specimen/aspirate isolates; the two areas with the lowest GAS rates had no surgical specimen/aspirate isolates. Age and race adjusted incidence rates of GAS identified through blood cultures among the eight metropolitan surveillance areas ranged from 2.2 to 4.7 per 100,000 (median=2.9). In the area with the highest pro-

portion of non-blood isolates, the distributions of emm types of blood isolates versus all other isolate sources were significantly different (Chi-Square, P=.05). Qualitative assessment of surveillance indicated substantial variability among ABCs areas in the degree to which invasive GAS tissue isolates are actively ascertained; this roughly correlated with the proportions of surgical specimen/aspirate isolates among surveillance areas. **Conclusions:** Although variability in GAS incidence rates among ABCs surveillance areas is multifactorial, differences in surveillance methods appear to be one important factor. Current surveillance for GAS may underestimate the true incidence of invasive infection due to under-ascertainment of invasive tissue infections diagnosed through surgically obtained tissue specimens. ABCs surveillance for GAS should be better standardized to more accurately ascertain the incidence and epidemiology of this important bacterial disease.

Board 112. DALY — Disability Adjusted Life Years as an Effectiveness Indicator in Health and Sanitation

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This study applies Cost-Effectiveness analysis for evaluation of projects in the field of health and sanitation programs. The Cost Effectiveness Analysis is indicated when dealing with projects in which the benefits are difficult to be expressed in monetary units. As main indicator for effectiveness in the Cost-Effectiveness Analysis, we have chosen the DALY: Disability Adjusted Life Years, to study the impact of sewage projects in morbidity caused by fecal-oral diseases in children between 0-4 years old, in the municipality of Volta Redonda of Rio de Janeiro State, in Brazil. DALY is an indicator that measures the burden of diseases, and use the formula: $DALYs(x) = (D)(C\ x\ e^{-b\ x})(e^{r\ (x-a)})$ where: **D** = weights for incapacity levels, from 0 = dead, 1 = healthy, (we assumed here D = 0.5 for the health status associated to children from 0 - 4 years old, with fecal-oral diseases); **C** = 0.16243 (fixed); **r** = discount rate (recomended = 0.03); **b** = 0.04 (fixed); **e** = 2.71 (neperian value); **x** = age; **a** = year that happened the incapacity. We made the calculations for children of 0 - 4 years old with incapacity due to fecal oral diseases followed by total recuperation. See following table 1. Table 1 - DALYs missing by incapacity due fecal - oral diseases, followed by complete recuperation, of 0 - 4 years old children of Volta Redonda, from 1992 to 1998. (D=0.5)

Year	Cases with fecal-oral diseases for bovs of 0 - 4 years old	Cases with fecal-oral diseases for airls of 0 - 4 years old	DALYs estimated for bovs 0 - 4 vears old	DALYs estimated for airls 0 - 4 vears old	DALYs bv bv incapacitv and total recuperation - both sexes
1992	695	596	284.48	243.95	528.43
1993	707	684	289.39	279.97	569.36
1994	634	617	259.51	252.55	512.06
1995	436	406	178.46	166.18	344.65
1996	112	76	45.84	31.11	76.95
1997	58	49	23.74	20.06	43.80
1998	65	58	26.61	23.74	50.35

From: SIH/DATASUS-hospital internation of children of 0-4 years old with fecal-oral diseases, and DALYs estimated. The focus in this study was to apply the technique recomended by the experts of the world bank in this situation, (see Murray J. L. and Lopez D. A. 1996, in The Global Burden of Disease — *A comprehensive assessment of mortality and disability from diseases, injuries, and risk factors in 1990 and projected to 2020*; Washington, D.C. Vol.1 World Health organization, Harvard School of Public Health, World Bank. Library of congress), The results of this study have shown a decrease in the DALYs value for the municipality of Volta Redonda, and we noticed that the population health was improved when the local company of water and sewage had increased the sanitation services, specially in water and sewage treatments.

Board 113. How Laboratory Surveillance is the New Model for Detecting Emerging Infectious Diseases, Thailand, 2000

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Introduction: In the past, there has used the laboratory data in two kinds for specific treatment of individual case and activities summary in the quarter or annual report. Mostly use of quarter or annual report has been for budgeting. But we know this data is very useful for improve medical service and public health awareness. Then we conducted a pilot study in the whole province in the north-east part of Thailand. **Objectives:** To establish the laboratory surveillance for food-water-born diseases (FWBD), to monitor trends of bacterial pathogens and antibiotics susceptibility, to describe epidemiological information of bacterial pathogens and antibiotic-resistant bacterial pathogens and to detect abnormal bacterial pathogens (EIDs) **Methodology:** Research and Development. This system has based on the existing passive case surveillance and conducted the whole province since April 2000. Inclusion criteria for FWBD are admitted diarrhea, watery diarrhea and mucous-bloody diarrhea. **Results:** Ubon Ratchthani has 25 districts which has one community hospital in each district. They have been divided into 4 zones for administration. Then we set 4 zonal hospitals to be sentinel sites of this project. A year of project was during April 1, 2000 - March 31, 2001. There was 26,709 cases of FWBD and 2,659 (9.96 %) collected specimens of culture, male and female ration was 1:1.23. In-patient was 65 % (1,712 cases), out-patient was 22.2 % (590 cases), and community patient was 9 % (238 cases). Median of age was 38 years (1 month - 95 years). The most cases were acute diarrhea (68.4 %). Specimen collection were 71.7 % of RSC, 23.8 % of stool culture and 4.4 % hemo-culture. Bacterial isolation was 7.9 % of pathogens, 82.6 % of non-pathogens and 9.5 % of no growth. Pathogen bacteria was 49 % (102 cases) of *vibrio* parahemolyticus, 26 % (55 cases) of shigella spp., 9 % (19 cases) of *salmonella* spp., 8 % (16 cases) of *vibrio* choleae. VP was the main bacterial pathogen for FWBD, affected to all age group and occurred all the year. 94 % of VP resisted to ampicillin. **Discussion:** We succeeded setting the new laboratory surveillance system in provincial level. It based on the passive case surveillance then it can easily to continue and it can support to detect EIDs. The obstacles were data entry and analysis by laboratory technicians or district epidemiological workers. It spent more time and workload. **Action Taken:** After the pilot project was finished. They commit to 1) continue this project by themselves 2) feedback the analytic information to doctors, nurses, ICN, pharmacists and health care workers in health centers every month 3) If this system is strong, then they plan to expand to others pathogen in other human systems.

Board 114. SentinelCASE: A Customizable Internet Based System for Rapid Epidemiologic Alert

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Background: Communicable disease control needs promotion of rapid and efficient tools for data collection, analyses, and information feed-back. In case of an epidemic outbreak from any origin, the likelihood that the existing local health information system will allow for real-time collection and analysis of data is low. Available tools which may be customized to any epidemic situations are then required. **Methods:** SentinelCASE is based on a 17 yr-experience in France, with the daily participation of general practioners to an electronic system of data transmission currently

available on the Internet 24-hrs a day (http://www.u444.jussieu.fr/sentiweb). The server has been developed on a PC with a Linux OS, an Apache HTML server, Java code, a MySQL relational database. Clients are microcomputers with Internet connection. **Results:** Health professionals are collecting data on SentinelCASE through a securized web interface. After having identified the notifier, the system allows data to be stored into a MySQL relational database. Any authorized persons (or the world wide public if no access restrictions is considered) can consult on a real-time basis all entered data on maps, graphs, and tables. Row data may be downloaded on a spreadsheet for further analyses. The engine of SentinelCASE is currently in use at an international level for the ongoing global surveillance of Influenza (FluNet) or dengue (DengueNet, see on http://oms.u444.jussieu.fr/). It has been chosen by WHO-HQ because of its easyness, flexibility, rapid implementation, and low cost. SentinelCASE may equip within a few weeks any networks of health professionals. Although a good knowledge in Linux and Apache is required for the local implementation and management of the server, no specific computer skills are required for the database management, or for customization of the surveillance system. Through an Internet interface, the system is easily and rapidly customizable. The autorized user defines items to be monitored. SentinelCASE may be used for epidemiologic purpose, but also for entomologic surveillance or for monitoring any environmental indicator. The use of the system is self-understandable. None of the 1270 French sentinel GPs, nor the 110 national influenza centres have been specifically trained for its use. **Conclusion:** Inserm (French Institute of Health and Medical Research) provides a user-friendly tool which allows for a rapid impementation of epidemiologic surveillance in any part of the world.

Board 116. Use of the Web To Enhance Disease Surveillance and Bioterrorism Preparedness

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Background: Timely reporting of notifiable diseases is critical to early detection and response to outbreaks or bioterrorism (BT) attacks. Previous studies indicate some clinicians are unaware of what, when, how or where to report diseases. The Web offers an unprecedented opportunity to provide high quality, accessible information and also a means to report disease and BT related syndromes. **Objectives:** To evaluate accessibility and usefulness of Web-based information on infectious diseases reporting (DR) and BT preparedness, and to suggest areas for improvement. **Methods:** (1) In November 2001, we surveyed 57 jurisdictions that report notifiable diseases to the Centers for Disease Control and Prevention (CDC) through the National Electronic Telecommunication System for Surveillance (NETSS). An E-mail questionnaire asked epidemiologists about availability of reportable diseases lists (RDL) on their Web sites, and plans to use the Web for DR and syndromic surveillance. (2) In December 2001, we used the *Google* search engine to locate online DR information. We used a standardized instrument to collect data on availability of reportable diseases lists and reporting instructions, capability for online disease reporting, and information on six CDC BT Category A agents. **Results:** (1) Fifty-six of the 57 jurisdictions responded by email or subsequent phone interview. Forty-nine (88%) indicated that they have online RDL, and 42 (75%) of those are current. Sixteen (29%) provide means for electronic reporting of notifiable diseases; four provide Web-based reporting. Three have Web-based syndromic surveillance in use; nine plan to start in the next six months. (2) We located 45 (90%) of the 49 Web sites with DR information. Eleven (24%) of the jurisdictions require reporting of all Category A agents while at other sites BT agents are reportable only as "unusual conditions." Thirty-three 33 (73%) provide a telephone number for DR, 18 (40%) provide a fax number, and 14 (31%) had an online DR card. Forty-five (90%) indicate the required time frame for reporting different diseases, and 36 (80%) explained the basis for reporting. **Conclusions:** The Web is being used to promote DR but its potential for facilitating timely reporting of diseases and syndromes has not been fully realized. Up-to-date DRL, telephone and fax numbers for reporting, on online DR cards and instructions could readily be provided on jurisdictions' Web sites. Some states already have recognized the benefits of Web-based systems. The Web offers a cost-efficient way to enhance surveillance and BT preparedness.

Board 117. Time Series Modeling and Space-Time Clustering of DoD-GEIS Data For Early Outbreak Detection

H. S. Burkom[1], J. Lombardo[1], F. Mostashari[2], Y. Elbert[3], J. Pavlin[3], P. Kelley[3]

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The objective of this effort is the capability for early indication of the spatial location and extent of an outbreak of disease. The exigency of responding to recent terrorist activity and advances in database technologies are increasing the timely availability of surveillance data while presenting the problem of how to analyze the growing volume of data for prompt outbreak recognition.

The U.S. Department of Defense Global Emerging Infections System (DoD-GEIS) has developed the Electronic Surveillance System for Early Notification of Community-based Epidemics (ESSENCE) to enable outbreak alerting using syndromic surveillance. This system reduces the surveillance of outpatient visits to the inspection of counts in a manageable number of syndromes, defined as logical groupings of ICD9 codes. Researchers at DoD-GEIS and the Johns Hopkins Applied Physics Laboratory have calculated time series predictions for background levels of daily visits expected in each monitored region for the various syndromes. Autoregressive modeling and other time series methods have yielded predictions that account for temporal patterns of consumer behavior. Small spatial resolution is needed for early alerting so that increases in visits at the neighborhood level are not masked by normal variability at the state or county level. We have used the patient-residence zipcodes provided by the ESSENCE system to perform spatial-temporal cluster analysis of the variations of daily data from the levels predicted by the models. The resulting clusters indicate approximate regions of outbreak for further investigation by human expertise or by other automated means. To seek potential clusters, we employ Kulldorff's space-time scan statistic because it gives a p-value for each cluster along with the component zipcodes and avoids selection bias as well as the zipcode resolution allows. Applications have located unlikely clusters of syndrome visits using model-based expectations. We have also clustered visits for single ICD9 codes based on the representation of each zipcode in the ESSENCE system. The resulting clusters may be inspected using GIS plots. Simulations have been used to assess the utility of this approach for early detection of a point-source outbreak. We used the Sartwell lognormal model to estimate the epidemic curve for diseases regarded as biowarfare threats, and we estimated the spatial case dispersion to inject cases into authentic background data. Simulations are parametrized by the total infected to determine how severe an outbreak may be detected according to time after exposure.

14 ICEID 2002 Keynote Session

Sunday, March 24, 5:00 p.m.
Centennial Ballroom

15 Meet-the-Experts I

Monday, March 25, 7:30 a.m.
Regency Ballroom VI/VII

16 Plenary Session I

Monday, March 25, 8:30 a.m.
Centennial Ballroom I/II

17 Plenary Session II

Monday, March 25, 8:30 a.m.
Centennial Ballroom III/IV

20 Antimicrobial Resistance I

Monday, March 25, 10:00 a.m.
Grand Hall East

Board 1. Mutational Analysis of Position Arg164 in TEM-1 and SHV-1: Two Highly Similar ß-Lactamases

F. K. Majiduddin, T. G. Palzkill

Baylor College of Medicine, Houston, TX

Resistance to ß-lactam antibiotics is a serious threat to the effective treatment of infectious disease. Several mechanisms are involved in resistance, the most prevalent being the production of ß-lactamases. The TEM-1 and SHV-1 ß-lactamases are important contributors to resistance to ß-lactam antibiotics in Gram-negative bacteria. These enzymes share 68 % amino acid sequence identity and their atomic structures are nearly superimposable. Extended spectrum cephalosporins were introduced, in part, to avoid the action of TEM -1 and SHV-1 ß-lactamase. However, the widespread use of these antibiotics has lead to the evolution of variant TEM and SHV enzymes that can hydrolyze extended spectrum antibiotics. Interestingly, despite being highly similar in structure, the TEM and SHV enzymes have evolved somewhat differently in response to the selective pressure. Examples of this are at residues Arg164 and Asp179, two positions that form a salt bridge at the base of an omega-loop structure. Among TEM variants substitutions are only found at position 164 while substitutions are only found at position 179 among SHV variants. To explain this observation, we examined the effects of mutations at position 164 in both TEM-1 and SHV-1 on antibiotic resistance and catalytic efficiency. In addition, competition experiments were carried out between mutants to understand why certain substitutions preferentially evolve due to the selective pressure of antibiotic therapy. Based on these competition assays, the SHV Arg164Ser variant is more fit than wild-type SHV-1, but is unable to compete effectively versus the SHV Asp179Gly variant. Among the TEM variants, the Asp179Gly variant is more fit than strains expressing the parental TEM-1 enzyme, but this mutant is unable to compete effectively against its Arg164Ser counterpart. This explains why only mutants at position Asp179 exist in SHV enzymes and Arg164 mutants in TEM enzymes in the clinical setting. Subtle unseen differences in the structures of TEM-1 and SHV-1 may account for the divergent evolutionary paths these two enzymes are undertaking.

Board 2. Synthetic Peptide Antibiotics: Solutions for the New Millenium

D. Wade

Helsinki University, Helsinki, FINLAND

The current public health problems of antibiotic resistant microorganisms, and bioterrorism, necessitate the development of new antibiotic strategies and therapeutics. During the past two decades, a new category of antibiotics has been discovered, the gene-encoded peptide antibiotics of the animal, plant, and bacterial kingdoms. Research interest in these peptide antibiotics has grown exponentially, and there is a hope that they may provide a partial solution to the problems mentioned above. Several hundred new, naturally occurring, peptide antibiotics have been isolated, and one of the most prolific sources of these new antibiotics has been the skin of frogs and toads (anurans). One group of these antibiotics, the temporins and temporin-like peptides, are composed of 31 different peptides from 8 species of frogs. Surprisingly, there are an additional 8 peptides with very similar structures to the frog peptides that have been isolated from the venoms of wasps. One of the frog skin peptides, temporin A (TA), has been shown to have antibacterial activities against antibiotic resistant bacteria. Synthetic manipulations of the structure of TA has shown that it is possible to improve its antibiotic properties and reduce its toxicity, and they have provided information about the structural features of TA that endow it with antibiotic properties. It is expected that further work with the temporins, and the other members of the new class of gene encoded peptide antibiotics, will eventually provide at least a partial solution to the problem of antibiotic resistant microorganisms.

Board 3. Growth Inhibition by Cisplatin in Group-I Intron Containing Pathogens: A Study in *Candida albicans*

K. Chandrasekhar, R. Malathi

Dr.ALM Post Graduate Institute of basic Medical Sciences, University of Madras, Taramani Campus, Chennai, INDIA

We previously reported that antitumor agent cisplatin, which has been clinically used in treatment of wide range of cancer has been found to inhibit group-I intron splicing *invitro* from Tetrahymena thermophila[1]. Interestingly this has been found to arrest the growth of *C.albicans*, an opportunistic human fungal pathogen that has become a major cause of morbidity and mortality in immunocompromised as well as cancer and HIV patients[2,3]. This gains lot of significance from clinical point of view since *C.albicans* is known to possess this group-I intron in 25s rRNA and their absence in human will pave way for an alternative target site, in addition to the well known cell-membrane therapeutic agents which are gaining resistance in present conditions. Recently we have carried out an *invitro*-screening assay using ATCC and 4 clinical strains and the parameters include disk diffusion method, growth curve analysis, RNA isolation and a fluorescence microscopic study using a new staining method "Ethidium Bromide" in order to analyse the morphological features. The above experiments were carried out with normal as well as with drug treated

C.albicans strain. The results have indicated that, in growth curve, cis-DDP at 60µg concentration shows a remarkable inhibition of multiplication of *C.albicans* cells with respect to control after 10 hour incubation period while analyzing O.D values at 600nm range. On the other hand low molecular weight RNA [25s, 18s rRNA] from the culture was isolated, analysed using agarose gel electrophoresis and the results suggest that cis-DDP might have completely abolished the 25s rRNA with high efficiency. While the microscopic study has clearly shown that the cis-DDP treated cells at 60µg concentration shows inhibition of hyphae growth as well as enlargement of ovoid cell irrespective of the control whose ovoid cells are smaller and the hyphae with many branches/budding visualized under 40X and 100X of Nikon Fluorescence Microscope and the same experiment was also carried out to compare with EtBr stain using normal *C.albicans* stain, the results were similar. These findings suggest that cis-DDP if properly oriented /targeted with epitope/liposome delivery, could possess antifungal property besides their antitumor activity especially in cancer patients. Moreover as pathogens continue to evade therapeutic targets search of novel agents with new target site is becoming a serious problem in persistence of human life, not only for fungal pathogens but also for other pathogenic organism. Reference: 1.Malathi R. and Chandrasekar K. *Journal of Biosciences*. 1999 suppl.11, 96. 2.Chandrasekar.K, Shyla J., and Malathi,R. *Journal of Clinical Microbiology*. 2000 vol.10 (38). 3.Leibowitz M.J., *Antimicrobial Agents and Chemotherapy*. 2000, Vol.44, No.4, 958-966.

Board 4. Hemolytic and Non-Hemolytic Vancomycin-Resistant *Enterococcus faecalis* from Imported Beef in Malaysia

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Twenty-two strains of vancomycin resistant Enterococcus faecalis were isolated from 9 (6%) of 150 imported beef samples. 12 strains (54.5%) were b-hemolytic and all strains harbored vanA gene. Hundred percent of the strains tested were resistant to 10 of the antibiotics including vancomycin and teicoplanin. Strains were 95.4% resistant to trimethoprim-sulfamethoxazole, 68.8% resistant to chloramphenicol and 41% resistant to ampicillin and penicillin. Small sized plasmids ranging from 1.5 to 5.8 Kb were detected in 8 (36.4%) strains. The twenty-two isolates were differentiated into twenty RAPD-types. It was concluded that vancomycin-resistant Enterococcus faecalis with different clones is widespread among isolates from imported beef in Malaysia.

Board 5. Phenotypic Typing and Molecular Fingerprinting of Fluoroquinolone-Resistant *Campylobacter* Species Isolated from a Treated Broiler Flock

H. A. Wadda[1], G. Domingue[2], D. J. Griggs[3], M. Siccardi[2], M. Johnson[3], J. A. Frost[1], T. Humphrey[4], L. J. Piddock[3]

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Aim: To investigate the incidence, types and mechanisms of resistance in *Campylobacter spp*. during therapeutic treatment of a poultry flock. **Background:** Antimicrobial resistance in *campylobacter* isolated from human infections has increased over the years. Monitoring this increase is important for those severe infections where antimicrobial therapy is essential. It is known that resistance can be spread from one ecosystem to another ie. transfer of resistant strains from farm animals to humans, humans to environment, environment to animal and vice versa. Poultry meat consumption is thought to be one of the main routes of transmission to humans. **Methods:** Samples were taken from one poultry flock before, during and at 1 and 2 weeks after fluoroquinolone treatment. A total of 66 chickens tested positive for *Campylobacter spp.* and 3 picks were isolated from each bird. These isolates were speciated and characterised using serotyping, phagetyping and biotyping methods at the *Campylobacter* Reference Unit. Drug resistance screening using 12 antibiotics was performed using the method developed as part of the NCCLS working party on *Campylobacter* susceptibility testing. Pulsed Field Gel Electrophoresis (PFGE) and Amplified Fragment Length Polymorphisms (AFLP) were used for more detailed strain characterisation. Mutations in *gyrA* and *gyrB* was determined with DHPLC. **Results:** Both *Campylobacter jejuni* and *Campylobacter coli* were isolated in all three of the treatment phases. Resistant *C.jejuni* were isolated mostly pre-treatment and during treatment, whilst resistant *C.coli* were seen in the post-treatment phase (no resistant *C.coli* were isolated in pre-treatment). Results indicated that 17.4% of the positive chickens at the pre-treatment phase were fluoroquinolone-resistant, 100% during the treatment phase and 82.8% at the post-treatment phase. Phenotypic analysis of the resistant strains showed *C. jejuni* HS27/PT67 to be the predominate strain at the pre-treatment stage, but this was not seen in the other two phases. *C.jejuni* HS31/PT1 was the predominant resistant strain during treatment but less commonly detected at the post-treatment phase. More *C.coli* strains were seen in the post-treatment phase where *C.coli* HS56/PT44 was the predominant strain. Isolates examined to date all had a substitution of Thr86 in *gyrA*. **Conclusion:** An increased proportion of resistant strains were seen during treatment, these persisted post treatment. Changes in species and subtype prevalence also occurred during the course of this study. The resistant mechanism observed so far is the substitution of Thr86 in *gyrA*.

Board 6. Enhanced Surveillance for Antimicrobial Resistance Among Enteric Bacteria: NARMS Retail Food Study

J. E. Stevenson[1], D. G. White[2], D. J. Torpey, III[3], A. S. Craig[4], K. E. Smith[5], M. M. Park[6], M. A. Pascucilla[7], A. D. Anderson[1], . and the NARMS Working Group[1]

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Background: The food supply, including meat and poultry, is an important source of enteric bacteria, including *Campylobacter*, *E. coli*, *Salmonella* and possibly enterococci. Antimicrobial resistance among these foodborne bacteria is not uncommon and often is associated with the use of antimicrobial agents in food animals. Retail food represents the point of exposure that is closest to the consumer and, when combined with data from slaughter plants and on-farm studies, provides a more representative picture of the prevalence of resistance in foodborne pathogens. To focus efforts to mitigate antimicrobial resistance and to better understand the contribution of the food supply to antimicrobial resistance among enteric bacteria, the National Antimicrobial Resistance Monitoring System (NARMS) for Enteric Bacteria is extending surveillance of antimicrobial resistance to bacteria isolated from food. **Program Description:** The NARMS Retail Food Study is a collaborative effort between the Centers for Disease Control and Prevention (CDC), five FoodNet sites (Connecticut, Georgia, Maryland, Minnesota and Tennessee) and the U.S. Food and Drug Administration (FDA). The NARMS Retail Food Study has adopted a standard method to monitor the prevalence of antimicrobial resistance among *Campylobacter*, *E. coli*, *Salmonella* and enterococci isolated from a convenience sample of meat and poultry from selected grocery stores in the United States. Data collection will begin January 1, 2002. Each site will

visit at least one grocery store per month, not returning to the same store for at least two months, and purchase packages of meat or poultry including 10 packages of chicken breasts, 10 packages of pork chops, 10 packages of ground turkey and 10 packages of ground beef. Isolation procedures have been adapted from the FDA's Bacteriological Analytical Manual. Each site will culture the rinse from each sample for the presence of *Salmonella* and *Campylobacter*. In addition, Georgia, Maryland and Tennessee will culture the rinse for *E. coli* and enterococci. Isolates will be forwarded to FDA for antimicrobial susceptibility testing. **Conclusion:** This collaborative surveillance project will provide data and isolates useful for focusing efforts to mitigate antimicrobial resistance in enteric bacteria. Enhanced efforts are needed to mitigate the increasing prevalence of antimicrobial resistance among foodborne bacteria. By examining the prevalence of antimicrobial-resistant enteric bacteria we will better understand the extent of antimicrobial resistance in the food supply and will be better equipped to implement mitigation strategies.

Board 7. Multidrug Resistance Among Human Non-Typhoidal *Salmonella* Isolates in the United States: NARMS 1999-2000

S. Rossiter, K. Joyce, J. E. Stevenson, T. Barrett, A. D. Anderson, and the NARMS Working Group;

Centers for Disease Control and Prevention, Atlanta, GA

Background: An estimated 1.4 million *Salmonella* infections occur in the United States annually. Emerging antimicrobial resistance, including multidrug resistance, contributes to the human health burden of *Salmonella* and threatens the utility of antimicrobial agents, including third generation cephalosporins (e.g., ceftriaxone). The National Antimicrobial Resistance Monitoring System (NARMS) for Enteric Bacteria was established in 1996 as a collaborative effort among the Centers for Disease Control and Prevention (CDC), participating state and local health departments, the U.S. Food and Drug Administration (FDA), and the U.S. Department of Agriculture (USDA). NARMS data are helpful in directing applied research and mitigation efforts.

Methods: In 1999 and 2000, 17 participating public health laboratories forwarded every tenth non-typhoidal *Salmonella* isolate to CDC. *Salmonella* isolates received at CDC were tested by broth microdilution (Sensititre®) for minimum inhibitory concentrations (MIC) to 15 antimicrobial agents including ampicillin (A), chloramphenicol (C), kanamycin (K), streptomycin (S), sulfonamides (Su), and tetracycline (T), using NCCLS interpretive standards. Isolates with decreased susceptibility to ceftriaxone (MIC ≥ 16 µg/ml) were tested by E-test (AB Biodisk).

Results: Of the 2876 human *Salmonella* isolates tested in 1999-2000, 26% (743) were resistant to ≥ 1 agent; 21% (601) were multidrug-resistant (resistant to ≥ 2 agents). Three multidrug-resistant strains, *S.* Typhimurium R-type ACSSuT, *S.* Typhimurium R-type AKSSuT, and *S.* Newport R-type ACSSuT accounted for 10% (278/2876) of non-typhoidal *Salmonella* isolates, 37% (278/743) of the resistant isolates, and 46% (278/601) of multidrug-resistant isolates. *S.* Typhimurium R-type ACSSuT was present in all sites, ranging from 12% of *Salmonella* from Washington to 5% of *Salmonella* from California. *S.* Typhimurium R-type AKSSuT was present in 16 of the 17 sites; it was most prevalent in Washington where it was 9% of *Salmonella*. S. Newport R-type ACSSuT was present in all sites, ranging from 8% of *Salmonella* in Kansas to <1% of *Salmonella* in New York State. Among human *Salmonella* isolates, ceftriaxone resistance was present in 2% (3/170) of *S.* Typhimurium R-type ACSSuT isolates, 3% (2/63) of *S.* Typhimurium R-type AKSSuT isolates, 71% (32/45) of *S.* Newport R-type ACSSuT isolates, and <1% (16/2764) of other *Salmonella* isolates.

Conclusion: Three multidrug-resistant strains account for nearly half of multidrug resistance among human *Salmonella* isolates; ceftriaxone resistance also is common among multidrug-resistant *Salmonella* Newport and present in some multidrug-resistant *Salmonella* Typhimurium. Further studies are needed to determine sources for these multidrug-resistant strains and support prevention efforts.

Board 8. Expanded-Spectrum Beta-Lactam Resistance among Human Clinical Enterobacteriaceae in the United States: Results and Characterization of 2000 NARMS Surveillance

J. M. Whichard[1], K. Joyce[1], P. D. Fey[2], J. McClellan[1], F. J. Angulo[1], T. Barrett[1], and the NARMS Working Group[1]

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Background: Third-generation cephalosporins are useful for the treatment of invasive salmonellosis and other severe pediatric infections. The National Antimicrobial Resistance Monitoring System (NARMS) for Enteric Bacteria has identified increased cephalosporin resistance in human bacterial enteric pathogens; in 1999 1.5% of isolates tested exhibited intermediate or resistant minimum inhibitory concentrations to expanded-spectrum cephalosporins. Preliminary molecular characterization of resistance determinants in the 2000 NARMS collection is presented. **Methods:** As NARMS participants, the 17 state and local public health laboratories submitted every 10th non-typhoidal *Salmonella*, every 10th *Shigella* and every 5th *E. coli* O157:H7 received in 2000 to the Centers for Disease Control and Prevention for antimicrobial susceptibility testing. Minimum inhibitory concentrations (MIC) were determined for 17 antimicrobials using broth microdilution (Sensititre®). Isolates were chosen for further study based on an intermediate or resistant MIC for the expanded-spectrum cephalosporins: cefoxitin (≥16 µg/ml), ceftiofur (≥4 µg/ml) or ceftriaxone (≥16 µg/ml). ß-lactamases were characterized using isoelectric focusing and pcr for bla_{CMY-2}. **Results:** Of the 2236 isolates tested in 2000, 57 (2%) met the MIC criteria and were selected for further study. These 57 isolates comprised 3% (46/1378) of the non-typhoidal *Salmonella* isolates tested, 2% (7/451) of *Shigella*, and 1% (4/407) of *E. coli* O157:H7. Overall, 52 (91%) of the 57 isolates produced a ß-lactamase with a pI≥8.4, consistent with an ampC-type ß-lactamase. Forty-four (77%) were pcr-positive for a bla_{CMY} gene. All 4 *E. coli* O157:H7 isolates tested produced an enzyme with a pI≥8.4 and were also pcr-positive for a bla_{CMY} gene. All 7 *Shigella* isolates tested were *S. sonnei* and produced an enzyme with a pI≥8.4, but were negative by pcr for bla_{CMY}. Forty of the 46 *Salmonella* isolates tested produced an enzyme with a pI≥8.4 and were pcr-positive for a bla_{CMY} gene. Notably, 24 of the 40 bla_{CMY} positive *Salmonella* were serotype Newport. Seven of the 57 isolates (12%) produced additional ß-lactamases, including 4 *Salmonella* and 3 *Shigella sonnei*. One isolate (*Salmonella* serotype Nienstedten) produced enzymes of pI 5.4 and 8.0. **Conclusion:** The presence of isolates exhibiting intermediate or resistant MIC to expanded-spectrum cephalosporins increased in 2000. The major determinant in the 2000 NARMS collection appears to be a bla_{CMY}-type ß-lactamase. *S.* Newport is the predominant organism among the 2000 NARMS isolates exhibiting this resistance. Additional ß-lactamases are expressed in over 10% of the isolates as well. Because of the pervasive ß-lactam resistance phenotype conferred by the ampC-type enzymes, these additional enzymes would not have been identified by susceptibility testing alone.

Board 9. Irrigation Water and Associated Sediments as a Source of Integron Bearing Enteric Bacteria

E. Vega, M. T. Roe, S. D. Pillai

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Use of antibiotics in humans and animal feed is thought to be responsible for the increased prevalence of antibiotic resistant bacteria in the environment. The Texas-Mexico border region is significantly impacted by anthropogenic activities. The Rio Grande River serves as the primary source of irrigation water in this region.

Considering the numbers and types of possible sources of fecal contamination of irrigation water, we hypothesized that irrigation water and agricultural fields harbor a large number of integron-bearing enteric bacteria. Antibiotic resistance in Gram-negative bacteria is primarily thought to be mediated by gene cassettes within the integron gene sequence. *E. coli* was isolated from sediment and water at 11 sampling sites along the Texas-Mexico border. Antibiotic resistant profiles were determined using the agar dilution method for *E. coli*. Out of 326 *E.coli* isolates, only 31 isolates (9.5%) were determined to be resistant to more than one antibiotic. The isolates were characterized using PCR primers specific for the variable region of the class I integron gene sequences. Of the 31 *E. coli* multiple drug resistant isolates, only 5 isolates (16.1%) indicated the presence of the class I integron sequence. Sequencing *E.coli* cassettes verified the presence of the *aadA* gene in three isolates and *dhfr XII* gene and *aadA* genes in one isolate. The results indicate that agricultural fields harbor low numbers of integron-bearing *E.coli*. It is, however, critical to understand whether integron elements are involved in horizontal gene transfer of antibiotic resistant genes on fresh produce especially those that are consumed raw or minimally processed.

Board 10. Infections Caused by Rapidly Growing Mycobacteria: Experience of Infectious Diseases Consultants

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Background: Because non-tuberculous mycobacterial infections are seldom reportable, their epidemiology remains poorly understood. Although the National Jewish Medical and Research Center has appreciated an increase in the number of infections due to rapidly growing mycobacteria (RGM); it is not known whether this experience reflects that of the nation. To examine this question, we surveyed members of the Infectious Diseases Society of America Emerging Infections Network (EIN) about their recent experiences with RGM. **Methods:** In October 2001, a questionnaire was distributed to all 797 infectious diseases consultants participating in the EIN. **Results:** Overall, 374 (47%) of the 797 members responded. Of the respondents, 183 (49%) had encountered 559 cases of RGM during 2000-2001. Moreover, 17% had noted more cases in recent years. EIN members from all nine regions of the US (especially the South Atlantic, Pacific and Mid-Atlantic) reported seeing increased numbers of cases. Respondents noted a wide spectrum of RGM disease, including pulmonary, cutaneous, and, to a lesser extent, disseminated and lymphatic. By region, 23 to 54% of EIN members reported seeing M. chelonae cases, 14 to 44% M. abscessus cases, and 23 to 54% M. fortutium cases. Fifty-six (31%) of respondents described environmental exposures associated with infection: medical procedures (45%), soil or water (21%) and trauma (29%). Predisposing host conditions included immunocompromise (steroids, HIV, and malignancy) and chronic lung diseases (emphysema and cystic fibrosis). Some EIN members expressed concern about distinguishing colonization from infection and establishing the need for treatment. Most respondents (79%) use in vitro susceptibility testing to guide therapy. EIN members indicated that a diverse array of facilities, including several national reference laboratories, perform RGM identification and susceptibility testing. **Conclusions:** RGM infections are frequently seen by infectious diseases consultants in all regions of the country. They appear to be increasing in some areas, especially in coastal states. Clinical features of member cases suggest that RGM are opportunistic pathogens, frequently acquired from environmental sources. Since numerous laboratories isolate RGM, consistent methods for identification and susceptibility testing will help define the epidemiology and proper therapy of these emerging pathogens.

Board 11. Outbreak of Community-Acquired Methicillin-Resistant *Staphylococcus aureus* (MRSA) Skin Infections Among Alaska Natives, 2000

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Background: Reports of MRSA-infected patients without hospital exposure indicate that MRSA infection is now acquired in both healthcare and community settings. In August 2000, an MRSA skin infection outbreak among patients without hospital exposure was reported in southwestern Alaska. We investigated these community-acquired MRSA infections and potential risk factors for disease. **Methods:** Using ICD9 codes, we determined the percentage of clinic visits for skin infection to the regional hospital from January 1998-July 2000. We reviewed charts of all patients with a positive *S. aureus* culture from May-July 2000. Community-acquired MRSA was defined as culture-confirmed illness in someone without hospitalization, surgery, dialysis, admission to a long-term care facility, or presence of an indwelling catheter in the prior year. In one village, we conducted a case-control study using 34 case-patients with MRSA skin infections and 94 controls with no history of skin infection. MRSA nasal carriage was assessed for case-patients, controls and their household members. We conducted an environmental assessment of traditional saunas, which have been linked to skin infections in prior outbreaks. Pulsed-field gel electrophoresis (PFGE) was performed on available clinical, carriage, and environmental MRSA isolates. **Results:** During March 1999 through July 2000, the number of MRSA skin infections at the regional hospital increased from 5 to 56 per month ($p<0.01$), and visits for skin infections increased from 1% to 3% of outpatient visits ($p<0.01$). In the peak three months of the outbreak (May-July 2000), 85% (142/168) of *S. aureus* skin infections were MRSA and 75% (107/142) of these were community-acquired. In the case-control study village, 5.1% (39/760) of residents had confirmed *S. aureus* skin infections during a 5-month period, and all *S. aureus* isolates from that village were MRSA. Case-patients used more antibiotics than controls in the year before the outbreak (median 4.0 vs. 2.0 courses, $p=0.01$). Sauna use was reported by 85% of case-patients and was not more common than among controls (89%). However, MRSA was cultured from 8 (17%) of 47 saunas, and 44% of case-patients and 13% of controls used MRSA-positive saunas (OR=5.6, $p<0.01$). MRSA in biofilms were identified in sauna wood. A single PFGE pattern was seen in 71 (89%) of 80 MRSA isolates from clinical, carriage, and environmental sources; an additional 7 (9%) isolates differed by only 2 bands. **Conclusions:** A large outbreak of community-acquired MRSA skin infections occurred among Alaska Natives in southwestern Alaska. Illness was associated with antibiotic and sauna use. Response has included judicious antibiotic use education and a sauna disinfection efficacy study.

Board 12. National and Regional Susceptibility Patterns of *Staphylococcus aureus* and Methicillin-Sensitive and Methicillin-Resistant Staphylococci: Results of the Antimicrobial Resistance Management (ARM) Program

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Background: The ongoing ARM program was developed to document susceptibility patterns, including for *S aureus*, methicillin-sensitive *S aureus* (MSSA) and methicillin-resistant *S aureus* (MRSA) in inpatient and outpatient isolates. Since 1987, more than 10 million isolates have been collected on 19 organisms and 46 antibiotics from 105 US hospitals in 5 regions (Northeast, North Central, Southeast, South Central, Southwest). **Methods:** Antibiograms and sensitivity reports of *S aureus*, MSSA, and

MRSA isolates were reviewed for susceptibility to fluoroquinolone (ciprofloxacin, levofloxacin, ofloxacin, trovafloxacin) and other antibiotics (vancomycin, clindamycin, erythromycin, and nafcillin/oxacillin). **Results:** Total number of isolates and percentage of isolates susceptible to each antibiotic were determined both nationally and regionally. Nationally, *S aureus* isolates were as susceptible to ciprofloxacin (62.3%, n=194,937) as to levofloxacin (62.2%, n=78925), with a greater sensitivity to ciprofloxacin seen in North Central (60.9% vs 58.7%), Southeast (62.7% vs 62.2%), and Northeast (60.7% vs 52.8%). These data suggest cross-resistance between ciprofloxacin and levofloxacin. Susceptibility to levofloxacin was greater than to ciprofloxacin in South Central (82.9% vs 72.4%) and Southwest (80.4% vs 54.3%). *S aureus* isolate susceptibility to erythromycin nationally was 32.5% (n=272,184), accounted for primarily in Southeast (22.9%); it was higher in all other regions: North Central (53.4%), Northeast (54.3%), South Central (61.1%), Southwest (67.1%). Compared with erythromycin, *S aureus* isolates had a much greater susceptibility to clindamycin (75.9%, n=33180). This difference was seen in every region, with the smallest comparative difference noted in South Central (61.5% vs 70.3%). Susceptibility to nafcillin/oxacillin nationally was 64.9% (n=256,121); this ranged from 63.2% in North Central to 78.0% in South Central. The majority of change in susceptibility to nafcillin/oxacillin and ciprofloxacin nationally over the past decade has occurred in the last 3 years (1998 to 2000), with ciprofloxacin sensitivity declining with increasing levels of MRSA; however, there is a lack of correlation regionally. For example, in Southeast, *S aureus* susceptibility to ciprofloxacin declined 15.8%, while MSSA declined 0.5%. Nationally and regionally, percentages of *S aureus* and MRSA isolates susceptible to vancomycin were similar (*S aureus*, range 99.6% to 99.9%; MRSA, range 99.4% to 100%). **Conclusions:** Nationally and regionally, the majority of *S aureus* and MRSA isolates remain sensitive to vancomycin. For *S aureus*, nafcillin/oxacillin, ciprofloxacin, and levofloxacin show similar rates of susceptibility; however, as sensitivity to ciprofloxacin has decreased, MRSA levels have increased nationally.

Board 13. The Association Between Individual Treatment with Oxytetracycline and Antibiotic Resistance and Virulence Factors in Commensal *E. coli* in Cattle

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Commensal enteric bacteria may undergo selection pressure and represent a reservoir of resistance or virulence genes for potentially pathogenic bacteria. We examined the effect of individual antibiotic treatment on the prevalence of resistance to antibiotics in commensal fecal *E. coli* isolates from cattle. The *E. coli* were also tested for the presence of verotoxin (VT) genes and two accessory virulence factors: intimin (*eae*) and enterohemolysin (*hlyA*). Fecal samples were collected between October and December 1998 from bulls treated with injectable oxytetracycline for respiratory disease. For each treated bull, samples were collected from 2 untreated pen mates. From 26th December 1998, for 16 days, all bulls received in-feed chlortetracycline. Final post-treatment samples were collected in February 1999. Five *E. coli* were isolated from each sample and tested for resistance to 19 antibiotics. Fecal samples were tested by a generic polymerase chain reaction (PCR) capable of detecting all *vt* genes; when positive the 5 *E. coli* were further subtyped for the presence of *vt1*, *vt2*, *eae* and *hlyA* genes. The unit of observation and analysis were the isolate and the bull respectively. Wilcoxon's rank test compared the distribution of the ranked prevalence of resistance between individually treated and untreated bulls. To determine the effect of time of sampling on the prevalence of VT an exact test for the binomial distribution of the discordant pairs was used, the null hypothesis being p = 0.5. Discordant pairs refer to bulls initially positive (Oct to Dec) then negative at the second test (Feb) or visa versa. This tests the concept that if time of sampling was unrelated to becoming positive, then an equal number of bulls should change from positive to negative for VT as change from negative to positive. Fishers exact test for comparison of multiple proportions examined the effect of individual treatment on the distribution of the counts of the paired outcomes for each virulence gene. From 83-paired samples 39 were individually treated and 44 were untreated. Individual treatment was associated ($p<0.05$) with increased prevalence of resistance to chloramphenicol and sulfisoxazole. 23 bulls were positive for VT at both samplings. The point estimate and 95% confidence interval for the binomial distribution of the discordant pairs tested for VT was 0.64, 0.46-0.80 ($p=0.12$). Among these 23 bulls, individual treatment was not associated with increased prevalence of virulence genes. Therefore, individual animal treatment appears to be associated with a change in the prevalence of select antibiotics but unassociated with the prevalence of genes. We also noted an effect of timing of sampling on the prevalence of VT and resistance. Two factors that varied between sampling times were mixing of the cattle and the addition of chlortetracycline. The individual effects of these cannot be differentiated given the study design.

Board 14. Analysis of the Aminolgycoside 6'-N-Acetyltransferase Type Ib [AAC(6')-Ib] AcetylCoA Putative Binding Site

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Aminoglycoside antibiotic use is threatened by inactivating enzymes that eliminate the antibiotic's biological activity. The pJHCMW1 plasmid, isolated from a clinical *Klebsiella pneumoniae* strain, carries the transposon Tn*1331*, which confers resistance to a wide variety of aminoglycosides as well as beta-lactam antibiotics. The resistance to several aminoglycosides such as amikacin, kanamycin, tobramycin, sisomicin, and netilmicin is due to the 6'-N-acetyltransferase type Ib [AAC(6')-Ib] which belongs to the GCN5-related acetyltransferase superfamily. These proteins include 4 conserved regions (motifs A - D). We performed a study on amino acids present in motif A, a region that has been implicated in binding the donor acetylCoA molecule. Site-directed mutagenesis was used to substitute the highly conserved Gly129, and Gly131 amino acids of this motif. Substitutions of Gly131 for Tyr, Ile, Lys, Val, Thr, Ala, or Gln and substitutions of Gly129 for Ile, Leu, Pro, Phe, or Asn resulted in proteins with dramatically diminished ability to confer resistance to kanamycin or amikacin. Only the Asn129 derivative was able to confer reduced but substantial resistance to both antibiotics. These results suggest that the Gly residues at this position play important roles in the enzymatic activity of AAC(6')-Ib. Hybrid fold recognition methods have been used to generate a 3-D model of the AAC(6')-Ib which includes motifs C, D, and A. This model is considered to have the correct fold at the 99% confidence level. Our mutations occur in a proposed helix loop region flanking the acetylCoA binding site. Altered activity profiles may be explained by putative conformational changes that would result from modified acetylCoA binding to accomodate mutated side chains.

Board 15. Integron Gene Sequences on Retail Chicken Products

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Integron gene sequences have been shown to provide a mechanism for the lateral gene transfer of antibiotic resistance genes between bacteria. Previous work done in our lab has shown that integron gene sequences were present on chicken products

throughout all stages of poultry production. From this we hypothesized that the integron gene sequence would be further present on retail chicken products. In this study we examined the prevalence of two classes of the integron gene sequence within the microflora of retail chicken. A total of 15 chicken products (legs, breasts, and thighs) were purchased from 5 retail markets and examined for total heterotrophic bacterial loads, and the presence and characteristics of integron sequences. Total microbial community DNA was extracted and tested for the presence of the class 1 and class 2 integron gene sequence by PCR. All samples showed as expected high levels of total heterotrophic bacteria (> 1x 105 CFU/ml). Further, all samples 15 out of 15 (100%) showed the presence of the class 1 integron gene sequence and 8 out of 15 (53.3%) samples showed the presence of the class 2 integron gene sequence. A number of the class 1 integron variable regions were amplified and further characterized by sequencing. Results indicate that the integron gene sequence is prevalent within on-shelf poultry and serve as a reservoir for antibiotic resistance gene cassettes. Studies to elucidate the potential for these gene cassettes to participate in gene transfer events on chicken products are needed.

Board 16. Community-Onset and Healthcare-Associated Methicillin Resistant *Staphylococcus aureus* in Minnesota, 2000

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Background: Community-onset (CO) methicillin resistant *Staphylococcus aureus* (MRSA) is increasingly recognized among patients outside the hospital setting who lack traditional MRSA risk factors. To assess and characterize MRSA in MN, we initiated prospective surveillance in 2000. The object was to compare CO and healthcare-associated (HA) MRSA patient and isolate characteristics. **Methods:** 12 sentinel MN hospital laboratories were selected to represent different geographic regions. Sentinel sites reported all cases of MRSA. Case information was collected; MRSA isolates were obtained. Antimicrobial susceptibility testing and pulsed-field gel electrophoresis (PFGE) subtyping was done on all CO-MRSA isolates and 25% of HA-MRSA isolates. CO-MRSA cases were patients with a positive MRSA culture obtained within 48 hours of admission and no permanent indwelling catheters or percutaneous devices, no history of hospitalization, surgery, long-term care residence or dialysis in the prior year, and no history of MRSA infection or colonization. Patients that met the CO-MRSA case definition by chart review were interviewed to verify their medical history. **Results:** 4612 patients with positive *S. aureus* cultures were identified; 25% (1164/4612) were MRSA (range 9-50%). Of all MRSA cases, 85% (991/1164) were HA-MRSA, 11% (133/1164) were CO-MRSA, and 3% (37/1164) could not be classified. After interview, 13% of presumed CO-MRSA cases were reclassified as HA-MRSA. CO-MRSA patients were younger than HA-MRSA patients (median age 23 yrs vs. 68 yrs). CO-MRSA patients were more likely to have MRSA isolated from skin compared to HA-MRSA patients (74% vs. 40%; p <0.001). Among all MRSA isolates, 119 distinct PFGE patterns and 5 clonal groups containing 3 or more isolates were identified. CO-MRSA isolates (71%) were more likely than HA-MRSA isolates (18%) to be clonal group A (OR 10.9; CI 6.3-18.9). CO-MRSA isolates were more likely than HA-MRSA isolates to be susceptible to all of the following: ciprofloxacin, clindamycin, TMP-SMX, and gentamicin (OR=17.6; 95% CI 9.4, 33.0). Of CO-MRSA patients for whom information was available, 63% (67/107) received a beta-lactam antibiotic as initial therapy. **Conclusions:** Differences in age, site of infection, antimicrobial susceptibilities, and PFGE patterns were observed between CO-MRSA and HA-MRSA cases. CO-MRSA strains have distinct features that may have led to their emergence in the general population and may require new approaches for prevention and control. CO-MRSA has important clinical consequences, since isolates are resistant to beta-lactam agents, the most common empiric therapy for outpatient infections. Studies are needed to determine risk factors for CO-MRSA infection. Continued surveillance will further define the epidemiology of CO-MRSA and shape guidelines for prevention and control.

Board 17. Antimicrobial Resistance Pattern of Isolated Bacterial Pathogens Obtained from Diarrheic Patients in Indonesia

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Antimicrobial resistance of emerging and reemerging pathogens is of increasing concern to health care physicians. The use of antibiotics has a well documented risk factor for infection or colonization with resistant bacterial pathogens. The antimicrobial susceptibility pattern for 1892 bacterial pathogens isolated from diarrheal patients admitted to hospitals and community health centers located in the cities of Jakarta, Padang, Medan, Denpasar, Pontianak, Makassar and Batam, Indonesia, were analyzed by the disk diffusion method from 1995 to 1999, to determine their changing trends in response to 9 antibiotics. Using routine culture methods, *Vibrio cholerae* O1 (46.7%) was the pathogen most frequently detected, followed by *Shigella* spp. (17.8%), *Salmonella* spp. (14.5%), *Vibrio parahaemolyticus* (8.2%), *Salmonella typhi* (4.9%), *Campylobacter jejuni* (3.4%), *Vibrio non* O1 (2.8%), and *Salmonella paratyphi* A (1.0%). Of the 339 *Shigella* spp. isolated, found were: *Shigella flexneri* (84%), *Shigella sonnei* (12%) and *Shigella dysenteriae* (4%). The reemergence of *Shigella dysenteriae* was noted in 1998 after an absence of 15 years. All *V. cholerae* O1 were resistant to colistin. *Shigella* spp. were resistant to ampicillin, trimethoprim/sulfamethoxazole, chloramphenicol and tetracycline. *Salmonella typhi* was susceptible to all antibiotics tested, while *Salmonella* spp. showed various resistance patterns according to the species grouping. *Campylobacter jejuni* showed increasing multiple resistance to ceftriaxon, norfloxacin and ciprofloxacin. All bacterial isolates were susceptible to ciprofloxacin and norfloxacin, with the exception of *Campylobacter* spp. and *Salmonella* group C. *Campylobacter jejuni* was susceptible to erythromycin. This study shows the emergence of resistant bacterial pathogens to quinolones in Indonesia.

Board 18. Prevalence of Aminoglycoside Resistance Among Enterococci Isolated from Poultry and Swine

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In this study, the prevalence of resistance to three aminoglycosides (gentamicin, kanamycin, and streptomycin) in enterococci isolated from poultry and swine was examined. One hundred and sixty-two enterococci from poultry and 444 enterococci from swine were isolated and speciated. The predominant species identified were *Enterococcus faecium* (n=105), followed by *Enterococcus faecalis* (n=40), and *Enterococcus durans* (n=8) from poultry and *Enterococcus durans* (n=175), followed by *Enterococcus faecalis* (n=120), and *Enterococcus faecium* (n=106) from swine. Approximately 74% of the poultry enterococci and 60% of the swine enterococci were resistant to at least one aminoglycoside. Using PCR, the isolates were also examined for the presence of 12 aminoglycoside resistance genes (*ant(6)-Ia, ant(6)-Ib, ant(9)-Ia, ant(9)-Ib, ant(4')-Ia, ant(3')-Ia, aph(3')-IIIa, aph(2')-Ib, aph(2')-Ic, aph(2')-Id, aac(6')-Ie-aph(2')-Ia,* and *aac(6')-Ii*). Eight of these resistance genes were identified in the isolates, most frequently *aac(6')-Ii* and *ant(6)-Ia* from *E. faecium* from both poultry and swine samples. *E. faecium* also contained the highest combination of resistance genes for both poultry and

swine. Thirty-seven percent of *E. faecium* from poultry contained *aac(6')-Ii-ant(6)-Ia-aph(2')-Ic* while 21% from swine contained *aac(6')-Ii-ant(6)-Ia-aph(3')-IIIa*. Seven isolates exhibiting high-level resistance to all three antimicrobials (MIC ≥ 1024 µg/ml) were negative for all genes tested. These data suggest that enterococci from animal sources contain diverse and potentially unidentified aminoglycoside resistance genes.

Board 19. The Gene *bolA* Ensures Survival by Linking Cell Wall Metabolism with Cell Division: Implications or ß-Lactam Resistance

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The gene *bolA* has been shown to trigger the formation of osmotically-stable round cells when overexpressed in stationary phase. Our results show that in poor growth conditions *bolA* is essential for normal cell morphology in stationary-phase and in response to sudden carbon starvation. We also show an unprecedented *bolA*-related phenotype in exponentially-growing cells based on transmission electron microscopy results. In exponential growth *bolA* promotes round morphology through a mechanism which is exclusively dependent on the two main *E. coli* D,D-carboxypeptidases PBP 5 and PBP 6. We show that somehow *bolA* controls the levels of transcription of *dacA* (PBP 5), *dacC* (PBP 6), and *ampC* (AmpC), a class C ß -lactamase, thus connecting for the first time PBPs and ß -lactamases at the level of gene regulation. Furthermore, PBP 5 and PBP 6 are shown to be regulated and to have distinct effects on the the peptidoglycan layer. Presented evidence demonstrates that *bolA* can confer resistance to ß -lactams by two different pathways: a stress-mediated mechanism and a stress-independent route, which involves aquired tolerance to these antibiotics. *bolA* seems to be a regulator of cell-wall biosynthetic enzymes with different roles in cell morphology and cell division.

Board 20. Detection of Antibiotic-Resistant Enteric Bacteria in Groundwater in the Vicinity of Swine Farms in Eastern North Carolina

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About half of the antibiotics produced globally flow into the agricultural industry. Antibiotics are used heavily by the United States commercial swine industry for growth promotion and disease treatment. This use of antibiotics has led to high proportions of multiply antibiotic-resistant enteric bacteria being fecally shed by swine and other agricultural animals, and growing concerns about the spread of these bacteria into environmental media. A study was conducted to determine enteric bacterial occurrence and extent of release of antibiotic-resistant bacteria from swine farms into groundwater. Four study sites with known groundwater flow paths were screened for enteric bacteria and coliphages. These sites include two swine farms with lagoons and land application of the swine waste, one farm with land application of swine wastes but no swine present, and a farm with only crops and no land application of swine wastes or swine present. Of a total of 48 study wells, 25% were positive for enterococci, 17% were positive for *Escherichia coli* and only one well (~2%) was positive for both somatic and male-specific coliphages. Of the total of 115 enterococci isolates, 34% were *Enterococcus faecium*, and 5% were *E. faecalis*, both of which are species associated with fecal contamination, and can be pathogenic. Of 45 presumptive *E. coli* isolates, 89% were confirmed by biochemical testing. The bacterial isolates were tested for antibiotic resistance using a panel of 17 drugs that are typical of human and veterinary use. The enterococci isolates were predominantly resistant to four or fewer antimicrobials, including streptomycin, gentamicin, neomycin and clindamycin; a few were pan-resistant and the predominant resistance patterns of the isolates differ among study sites. For example, one swine farm isolate was resistant to ten antimicrobials: vancomycin, chlortetracycline, tetracycline, trimethoprim, chloramphenicol, erythromycin, ampicillin, florfenicol, tylosin base, and clindamycin. The majority of the *E. coli* isolates were resistant to three or more antimicrobials (e.g., tetracycline, tylosin base and clindamycin), with a few also showing pan-resistance to eight or nine drugs and differences in antimicrobial resistance among the study sites. For example, one swine farm isolate was resistant to nine antimicrobials: chlortetracycline, tetracycline, trimethoprim, chloramphenicol, gentamicin, ampicillin, florfenicol, tylosin base, and clindamycin. The results of this study demonstrate that antibiotic-resistant enteric bacteria are present in groundwaters of swine farms that have the lagoon and land application system for waste management. The extent to which such contamination of groundwater with multiple antibiotic-resistant enteric bacteria poses risks to human health is uncertain and deserves further investigation.

Board 21. Risk Factors for Emerging Antimicrobial Resistance in *Helicobacter pylori* Infection in the United States

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Introduction: *Helicobacter pylori* (HP) infection is the principal cause of primary gastritis, peptic ulcer disease, and is strongly associated with gastric adenocarcinoma. Therapy entails complicated multi-antimicrobial dosing regimens administered for at least two weeks. Widespread use of antimicrobials for various illnesses may induce antimicrobial resistance among HP isolates. The *Helicobacter pylori* Antimicrobial Resistance Monitoring Project (HARP) is the only prospective, multi-center U.S. network tracking regional and national prevalence rates of HP resistance. **Methods:** Beginning in 1998, 11 U.S. medical centers submitted HP isolates obtained at diagnostic upper endoscopy to CDC for antimicrobial resistance testing. Each isolate is linked to a case report form with clinical and epidemiologic patient data. Susceptibility testing was performed using agar dilution methodology, with validated quality controls strains and standardized break points according to NCCLS guidelines. Univariate analysis was performed with SAS version 8.2. **Results:** From December 1998 until May 2001, 352 HP isolates were submitted by participating sites. Susceptibility testing was performed on 325 isolates; 99 isolates (30.5%) were resistant to 1 antimicrobial, and 15 (4.6%) were resistant to 2 antimicrobials. Among 325 isolates, 73 (22.5%) were resistant to metronidazole (MET), 24 (7.4%) to clarithromycin (CLA), and 2 (0.6%) to amoxicillin (AMOX). Of 15 isolates resistant to 2 antimicrobials, 1 (6.6%) was resistant to CLA and AMOX and 14 (93.3%) were resistant to CLA and MET. One-hundred ninety-four patients (63.0%) were male and 114 (37.0%) were female, the median age was 58 range, (3-94), 122 (40.3%) were white, 165 (54.5%) were black, and 10 (3.3%) were Asian. In univariate analysis, factors associated with infection by resistant HP were: antacid use in 12 months preceding endoscopy (OR=1.8, 95% CI, 1.1-3.1); use of Zantac^{R} or Tums^{R} in 30 days preceding endoscopy (OR=2.7, 95% CI, 1.2-6.1 and OR=3.3, 95% CI, 1.3-8.8, respectively); non-white race (OR=1.7, 95% CI, >1.0-2.7); earnings > $30,000/yr; (OR=1.8, 95% CI, 1.1-3.2); and residence in rural or farm area (OR=3.5, 95% CI, 1.2-10.8). **Conclusions:** HP antimicrobial resistance to CLA, AMOX, and MET is prevalent among endoscopy patients at HARP project sites and is associated with preceding antacid use. Association of demographic and socicoecomonic factors with resistance requires further evaluation, and has potential future implications for screening and treatment strategies. Expanding HARP to increase project population representativness will enhance monitoring HP resistance on a regional and national level, and help clarify its risk factors in the U.S.

Board 22. The Epidemiology of Community-Onset Methicillin-Resistant *Staphylococcus aureus* (MRSA) Infection/ Colonization in the Atlanta Metropolitan Area, 2001

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Background: Methicillin resistance in *Staphylococcus aureus* is becoming a public health concern because of its emergence in the community setting. Most reports have been hospital-based and limited to medical record review. **Objectives:** To determine the epidemiology of community-onset (CO) MRSA infections/colonizations in the 8 county Atlanta metropolitan area, population approximately 3.1 million. **Methods:** Prospective review of laboratory reports of MRSA isolates from hospital laboratories and reference laboratories serving 32 hospitals and many outpatient settings. A case of MRSA is considered healthcare (HC)-associated (HCA) if ANY of the following criteria are present: hospitalized > 48 hrs prior to MRSA culture; previous MRSA isolation; dialysis, surgery, or hospitalization in the past year; or a percutaneous or indwelling device in place at the time of culture. Cases are initially screened by consulting hospital personnel and reviewing medical records. If no HCA criteria are documented, the case is interviewed to identify previously unrecognized HC associations. If no HCA criteria are present, it is considered a CO case. **Results:** Data for January 1 through June 30, 2001 identified 2041 incident cases of MRSA. On initial screen, 141 (6.9%) of the cases met no documented HCA criteria and required a telephone interview. 42 of the 141 have been interviewed; 29/42 (69%) were confirmed as CO. 21 of the 29 (72.4%) had clinically relevant infections: skin infection (10), sinusitis (3), soft tissue infection (2); and one each of osteomyelitis with secondary bacteremia, endocarditis, primary bacteremia, conjunctivitis, diverticulitis, and bronchitis. 1 (3.5%) was considered a contaminant; 7 (24.1%) were of indeterminate relevance. The median age for CO cases was 39.5 yrs compared with 69 yrs for HCA cases ($p<0.01$). 69% of the CO cases were male compared with 48% for HCA cases ($p=0.02$). At the time of interview, HC exposures were identified that fell outside of the HCA criteria in 18 (62%) of the 29 CO cases: 15 cases received antibiotics and 3 were employed in the HC sector in the previous year; 9 had been hospitalized in the prior 2-5 years. **Conclusion:** Preliminary results indicate that CO MRSA represents < 7% of all MRSA in Atlanta. CO cases were more common in younger males and involved skin and soft tissue infections in more than half of the clinically relevant cases. Healthcare exposures were identified during the interview that may provide insight into the acquisition of MRSA in the community.

Board 23. Transmission of the *bla*$_{CMY-2}$ gene from *Salmonella enterica* Serotype Newport in the Dairy Farm Environment

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Background: The incidence of multiple drug resistant strains of *Salmonella enterica* serotype Newport isolated from farm animals in Pennsylvania has increased in the past 12 months. Isolates are most frequently bovine in origin and primarily come from dairy facilities. The organism is resistant to cephalosporin antibiotics due to the presence of the *bla*$_{CMY-2}$ gene on a large plasmid. The predominant 140kb resistance plasmid has been shown to be non-conjugative, but it can be mobilized. This study was designed to determine whether transfer of the resistance plasmid, and thus the *bla*$_{CMY-2}$ gene, occurred readily between organisms from a dairy farm environment. **Methods:** In September 2001 the Field Investigation Group were invited to visit a 350 cow dairy farm that had recently suffered calf and cow mortalities due to *Salmonella* Newport infection. Prior to serotype identification, animals on this farm were being treated for diarrheal disease with ceftiofur. Thirty-five samples were obtained from a variety of sources that included individual cows and calves, feed, drinking water, pooled fecal samples from the calf and cow pens, bird feces, cat feces and a variety of additional environmental samples. All samples were held at 4ºC overnight and delivered to the *Salmonella* Reference Center for processing. Following pre-enrichment in buffered peptone water, samples were sub-cultured to MacConkey agar (MAC), deoxycholate citrate agar, sodium selenite broth and Rappaport Vassiliadis broth. Four colonies that were classified as non-*salmonella* by visual identification were sub-cultured from the initial MAC plates to a fresh MAC plate. A ceftiofur disk (30µg) was added to identify resistant organisms. All resistant organisms were identified using Sensititre AP80 Gram negative identification plates and tested for the presence of the *bla*$_{CMY-2}$ gene by PCR. **Results:** Twelve of the 35 samples (34%) were positive for *Salmonella* Newport. Of 140 non-*salmonella*-like colonies tested 29 (21%) were resistant to ceftiofur. One isolate was positive by PCR for the presence of the *bla*$_{CMY-2}$ gene and this isolate was subsequently found to be *Salmonella* Newport. Other genera identified included *Enterobacter, Citrobacter, Providencia, Proteus,* and *Pseudomonas*. The alternate mechanism(s) of cephalosporin resitance are under further investigation. **Conclusions:** Multiple drug resistant *Salmonella* Newport was isolated from sick cows and environmental samples from a Pennsylvania dairy farm. Cephalosporin resistance was observed in other genera but, in this instance, there was no evidence to support transfer of the *bla*$_{CMY-2}$ gene from *Salmonella* Newport to other organisms in the environment.

Board 24. Susceptibility Testing Practices for *Streptococcus pneumoniae*, 2000:Are Laboratories Prepared To Monitor Antibiotic Resistance?

I. Chuang[1], N. L. Barrett[2], D. R. Feikin[3], A. Reingold[4], K. Gershman[5], K. McCombs[6], L. H. Harrison[7], S. Johnson[8], J. R. Hibbs[9], P. R. Cieslak[10], A. Craig[11], J. Jorgensen[12], C. G. Whitney[13]

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Background: Pneumococcus causes 63,000 invasive infections and 6,100 deaths per year in the US. A high proportion of pneumococci have become resistant to antibiotics. Because antibiotic susceptibility results are increasingly important for guiding therapy decisions and for monitoring emerging resistance patterns, we conducted a survey to assess laboratory practices for susceptibility testing in 2000. **Methods:** The survey was sent to clinical laboratories located in the nine Active Bacterial Core surveillance (ABCs) areas in 2000. Survey questions addressed the susceptibility testing methods used for invasive isolates, compliance with current National Committee for Clinical Laboratory Standards (NCCLS) guidelines, selection of antibiotics for routine testing, and methods for reporting susceptibility results. **Results:** Of 659 laboratories surveyed, 547 (83%) responded. Three hundred and fifty-three (65%) laboratories reported doing at least some suscep-

tibility testing of pneumococcal isolates in-house. More than half (n = 188, 53%) of the laboratories performed oxacillin disk screening before doing confirmatory minimum inhibitory concentrations (MICs) testing for invasive isolates, a practice discouraged by NCCLS because it delays reporting of the MIC results. Nearly all (n = 351, 99%) of the laboratories performed MIC either in house or at a reference laboratory. Of the 250 laboratories performing in-house MIC testing, the majority (n = 222, 88%) of laboratories used appropriate MIC methods for penicillin susceptibility testing. Most laboratories (n = 190, 76%) performed susceptibility testing for penicillin, cefotaxime or ceftriaxone, and vancomycin on isolates from patients with life-threatening infections as recommended by NCCLS. Only 39% (n = 98) of laboratories performed susceptibility testing against fluoroquinolones, a first-line agent for community-acquired pneumonia. Some laboratories reported either the exact MIC values (n = 35, 14%) or the interpretations (i.e., susceptible [S], intermediate [I] or resistant [R]; n=66, 26%), rather than reporting both (n = 137, 55%) as recommended. **Conclusions:** Although the majority of clinical laboratories were using appropriate methods for pneumococcal susceptibility testing, there were some inconsistencies with NCCLS guidelines. Because of the recent increase in fluoroquinolone use, both to treat pneumonia and in response to the recent anthrax attack, more laboratories should consider testing isolates for fluoroquinolone resistance.

21 Syndromes and Diagnosis I

Monday, March 25, 10:00 a.m.
Grand Hall East

Board 25. Brucellosis among Persons at High-Risk Occupation

A. M. Abou-Eisha

Suez Canal University, Ismailia, EGYPT

Brucellosis is considered one of the most important zoonotic diseases constituting a public health problem throughout the world, particularly in the developed countries. This study was to determine the prevalence of brucella infections among persons at high- risk occupation. A total of 1316 persons (886 at high-risk and 430 of city dwellers), from Ismailia and Port Said provinces, Egypt, was first screened for brucella antibodies by Rose Bengal test (RBT) to measure the exposed rate. Reactive sera were further analyzed by the standard tube agglutination test (STAT). The prevalence of brucella infections among the examined persons was 5.1% (67 out of 1316 human sera). The highest infection rates were recorded among veterinary assistants (44.4%) followed by veterinarians (23.5%) then abattoir workers (11.6%), farmers and their families (3.1%), and lastly the city dwellers (1.6%) that were not in contact with the farm animals. The seroprevalence among farmers and city dwellers was not influenced by sex. All isolates were identified and biotyped as *Brucella melitensis* biovar3 (4 isolates) that isolated from human blood of four seropositive persons at high-risk occupation had STA-antibody titers of ≥1:1280. The current study found a very high risk associated with assisting in animal parturition and contact with the blood of infected animals but no significant risk associated with other direct animal contact. Such findings could be used as means to locate cases of human brucellosis and design measures to control brucellosis in man and animals.

22 Bioterrorism II

Monday, March 25, 10:00 a.m.
Grand Hall East

Board 26. Bioterrorism-Related Anthrax: CDC's International Response

C. S. Polyak, J. T. Macy, M. Irizarry-De La Cruz, J. E. Lai, J. McAuliffe, T. Popovic, E. D. Mintz, and the EOC International Team

Centers for Disease Control and Prevention, Atlanta, GA

Immediately following reports of the intentional release of *Bacillus anthracis* in the United States, epidemiologists, microbiologists and clinicians around the world were called upon to respond to widespread political and public concerns. Specific threats, hoaxes and incidents in other countries directly affected citizens and expatriate U.S. government employees, businessmen, journalists and travelers. The Centers for Disease Control and Prevention (CDC) established an international team in the Emergency Operations Center to respond to inquiries for assistance from other countries regarding anthrax and bioterrorism.

During 12 October - 12 December, CDC's international team received 128 requests from 68 countries and 2 territories. An average of 3.3 requests per day (peak 9 requests on October 19) were received by email (56.3%) and phone (43.8%). Of the 128 requests, 52 (40.6%) were laboratory related; 51 (39.8%) were general requests for bioterrorism information; 14 (10.9%) were for environmental or occupational health guidelines; and 11 (8.6%) were about developing bioterrorism preparedness plans. Ninety-one (71.1%) of the requests were from persons or agencies affiliated with Ministries of Health; 15 (11.7%) were from other public health or medical professionals; 13 (10.1%) were from private citizens; and 9 (7.0%) were from international organizations. Europe and Central/South America each accounted for 25% of the total requests; followed by Asia (17.2%) and Africa (11.7%).

Of the 68 countries and 2 territories, 55 (78.6%) countries received phone and/or email consultation regarding issues concerning bioterrorism events and/or preparedness. The remaining 15 (21.4%) countries received a high level of support including CDC testing of specimens (n=10). CDC confirmed three isolates from outside of the U.S. as *B. anthracis*. Two of these isolates were recovered from State Department mail pouches sent to the U.S. embassy in Peru. The other isolate was obtained from Chile in a letter sent to a private physician; this isolate was a different subtype from the strain isolated in the U.S.

The team disseminated documents on anthrax and bioterrorism preparedness to 130 CDC employees stationed in 41 countries and to epidemiologists and microbiologists in 111 countries through the Training Programs in Epidemiology and Public Health Interventions Network (TEPHINET) and World Health Organization (WHO) Global Salm-Surv listservs. The team collaborated with the WHO and the CDC International Emerging Infections Program in Thailand to develop and support a training course in anthrax management held in Bangkok and attended by representatives from 14 countries.

The information and technical support provided by CDC's international team helped allay fears, prevent unnecessary antibiotic treatment and enhance laboratory-based surveillance for bioterrorism events worldwide.

Board 27. Emergency Department and Walk-in Center Surveillance for Bioterrorism: Utility for Influenza Surveillance

N. M. Bennett, J. Konecki

University of Rochester School of Medicine & Dentistry, Rochester, NY

Emergency departments (ED's) and ambulatory care settings often identify unusual occurrences of communicable disease. Immediately following the identification of the first case of anthrax, the New York State Department of Health asked local health units to establish ED-based surveillance. The Monroe County Department of Health established ED and walk-in center surveillance that included tracking of influenza-like illness (ILI), as well as total numbers of visits and unusual illness or clusters.

Methods: The Health Director convened a meeting of the directors of all the local ED's to discuss the need and rationale for BT surveillance and to request that they institute the system within one week. A form was developed, for submission by fax or e-mail, which included number of total and ILI visits per 24-hour period, as well as information regarding any unusual illnesses. The form also included phone and pager numbers for consultation with public health physicians. The surveillance covered the five acute care hospitals that serve a population of approximately 1.25 million people in the Rochester, NY region. In addition, several geographically separated walk-in clinics reported respiratory vs. non-respiratory disease visits. Patterns of ED and clinic use are compared to laboratory reporting of influenza cultures and results of sentinel site surveillance and absenteeism.

Results: All ED's and the walk-in clinics instituted surveillance on the requested date (10/8/01). Two ED's reported by e-mail and three by fax or phone by noon each day. Compliance has required occasional reminders, but data are complete. ED's without electronic triage data have developed systems to identify ILI. ED visits to all hospitals averaged 4435 (SD=227) per week with an average of 8% (SD=1%) for ILI at baseline. Clinic visits averaged 173 (SD=16) for respiratory illness and 282 (SD=32) for non-respiratory illness. The sensitivity and specificity of the system for identifying influenza will be studied during the winter of 2002.

Conclusion: Baseline use of ED's and walk-in clinics is remarkably consistent suggesting the usefulness of these data for tracking unusual communicable disease activity, including influenza, in the community. In addition to improving ED and LHU communication to assure the early identification of a BT event, this system has been useful to track influenza and thus, to manage care in a community with insufficient ED and hospital capacity.

Board 28. PHLS Response to the Threat of Bioterrorism in England & Wales

N. Asgari-Jirhandeh, N. Lightfoot, J. Kramer, D. Cooper, S. Gregor, E. Collins, A. Nicoll, On behalf of PHLS Deliberate Release Response Teams

Public Health Laboratory Service, Various Locations, UNITED KINGDOM

The Public Health Laboratory Services (PHLS) is a national network organisation set up in 1939 initially to provide defence against biological warfare during World War Two. It delivers general and specialist microbiological services, surveillance and public health support for communicable disease control and health protection. Its two main centres are the Communicable Disease Surveillance Centre and the Central Public Health Laboratory are in London but the network extends throughout England & Wales. The PHLS has been preparing for bioterrorism for a number of years and accelerated its work since September 11th and the deliberate releases of anthrax in the USA. The PHLS has been both proactive and reactive in its management of the situation. Its work supporting the UK's national response to bioterrorism have been in the following categories:

- Assessing, identifying and strengthening appropriate reference labs for specific diseases
- Preparing detailed peer- reviewed guidelines for clinicians and health professionals
- Rapidly establishing laboratories with additional testing capacity
- Technical information on deliberate release on a single web-site platform at www.phls.co.uk/facts/deliberate_releases.htm
- Devising alert and surveillance mechanisms for hospitals to detect potential cases of key infections
- Testing the potential of a pre-existing primary care telephone system ('NHS Direct') to detect large scale events
- Identifying and tracking any potentially exposed people from abroad who may come to UK
- Supporting other agencies to provide cohesive plans in the event a deliberate release of unknown substances
- Providing expert advice to the Department of Health and the Cabinet Office
- Acting as a point of information for healthcare providers
- Auditing current organisational procedures in order to improve their effectiveness

In the six weeks following the first anthrax case in the USA, the volume of phone calls by concerned health care professionals and public to CDSC increased by over 600% with a peak in October, while the number of press enquiries to PHLS jumped by 400%. In response to the needs of the health professionals, by the third week of October, the number of original postings at the PHLS website had increased by over 600% compared to before October 2001.

During this period, PHLS has been working with other organisations to arrange appropriate levels of laboratory support and division of labour for various biological agents. This was useful particularly during follow up of exposed people where serological confirmation was essential. Furthermore, during an epidemic of 'white powder incidents' in UK, PHLS in conjunction with police and other government organisations was able to increase the national anthrax-testing laboratory capacity and respond to the needs of the emergency services.

Board 29. Urgent Prophilaxis in an Epidemic Focus

V. P. Batmanov, V. I. Ilyukhin

Volgograd Plague Control Research Institute, RUSSIAN FEDERATION

Urgent prophylaxis (preventive treatment) constitutes a complex of medical measures to prevent the development of the disease in humans in case of suspicion of contagion with dangerous infection agents. Urgent prophylaxis should be conducted immediately after establishing a fact of bacterial or viral infection, or appearance of dangerous infectious disease cases among population, and also in case of massive infectious diseases of unidentified etiology, and it assures prompt protection of infected persons.

Urgent prophylaxis is divided into general and special. General urgent prophylaxis should be conducted before identification of the type of agent. After the final diagnosis, special urgent prophylaxis should be conducted (vaccines, sera, bacteriophages, immunoglobulins). We believe that as means of general urgent prophylaxis it is reasonable to use easily available antibiotics with diverse mechanism of action, active against the majority of known dangerous infectious diseases. Duration of the course of general urgent prophylaxis is governed by probable incubation period and the time necessary for identification of the etiological agent and determination of its susceptibility to antibiotics, and averages 2 - 5 days.

Efficiency of the measures of urgent prophylaxis largely depends on the right selection of drug combinations and their timely use. Urgent prophylaxis should be conducted virtually for all the exposed or infected population, taking into account the usual counterindications. If urgent prophylaxis for the public is required in case of unidentified agent, one of the following combinations can be recommended:

1. Doxicycline + rifampicin
2. Ciprofloxacin (or ofloxacin, or pefloxacin) + rifampicin
3. Co-trimoxazole + rifampicin

These preparations should be prescribed in maximal allowable daily doses recommended by the manufacturers.

These preparations, with diverse mechanisms of antibacterial action, inhibit formation of resistance and act on the strains which probably have resistance to one of these preparations. The above combinations can be efficacious against the following diseases: plague, tularemia, anthrax, brucellosis, pseudotuberculosis, legionellosis, cholera, glanders, and melioidosis.

Board 30. Clinical Validation Study of the EMS 911 Syndromic Surveillance System for Bioterrorism or Pandemic Influenza in New York City

J. A. Greenko, F. Mostashari, A. Fine, M. Layton

New York City Department of Health, New York, NY

Introduction: Since March 1998, New York City has used citywide Emergency Medical Services (EMS) ambulance dispatch data to monitor for a community-wide rise in influenza-like illness (ILI), which could be an early marker of a large outbreak caused by bioterrorism (e.g. inhalational anthrax) or influenza. This syndromic surveillance system analyzes data from seven of 52 call-types, which were selected because they were markers for respiratory and/or viral symptoms thought to have the highest sensitivity for detecting increases in ILI. This study sought to clinically validate this novel surveillance system.

Methods: A retrospective review of all visits to six selected high-volume emergency departments (EDs) was conducted for a 24-hour period on January 19, 1999. The objectives were to validate whether or not these call types accurately capture patients with ILI, and to compare ILI patients arriving by ambulance to those presenting to the ED by other means. These cross-sectional surveys were conducted using standardized data extraction forms and a standard case definition of ILI consisting of fever AND cough or sore throat.

Results: A total of 2294 ED visits were reviewed, with 522 patients (23%) meeting the case definition for ILI, 64 (12%) of whom came by ambulance. The combination of selected call types had a sensitivity of 72% for clinical ILI, and a Predictive Value Positive (PVP) of 24%. When compared to individuals not brought in by ambulance, those who utilized the EMS system were older, more likely to complain of chest pain and shortness of breath, have abnormal lung sounds, receive a chest X-ray, be diagnosed with pneumonia, and be admitted to the hospital ($p<0.05$ for all comparisons). A third of those brought in by ambulance had been sick for one day or less. However, the median time since onset of symptoms was similar for the two groups (48 hours).

Conclusion: This ambulance dispatch data-based syndromic surveillance system is sensitive for early detection of ILI. Individuals with symptoms that might occur during the prodromal phase of inhalational anthrax (chest pain, shortness of breath) were more likely to utilize the EMS system, and usually did so early in the course of illness. This population-based surveillance system has the potential to assist in the early detection of a bioterrorist attack or a significant respiratory event and would facilitate prompt public health intervention.

Board 31. Enhanced Passive Surveillance for Anthrax, New York City, 2001

S. Balter[1], A. Fine[1], D. Weiss[1], M. Phillips[1,2], K. Bornschlegel[1], C. Van Beneden[3], M. Fischer[2], D. Feikin[2], B. Nivin[1], P. Thomas[1], M. Layton[1], The NYCDOH-CDC Anthrax Surveillance Team[1,2]

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Background: Following the terrorist attacks on the World Trade Center on Sept. 11th 2001, and the subsequent announcement of a case of inhalational anthrax in Florida on Oct 4th, 2001, the New York City Department of Health (NYCDOH) initiated enhanced passive surveillance for a biologic agent attack including anthrax in New York City. **Methods:** On Sept. 12, the NYCDOH began sending broadcast fax alerts promoting bioterrorism awareness to all New York City Hospitals. On October 4th, all hospital Emergency Departments, Infection Control Departments and laboratories in New York City were called to alert them to the Florida case and request immediate reporting of suspect cases. Laboratories were instructed to call and submit any isolate that was a non-motile, non-hemolytic gram-positive bacilli. A broadcast fax alert on clinical recognition, diagnosis and reporting of anthrax was sent to Emergency Departments, laboratories, Infection Control Directors, Infectious Disease Directors, Radiology Departments and intensive care units via broadcast fax and e-mail. Broadcast alerts were faxed and e-mailed 1-2 times/week to update providers and posted on the NYCDOH website. An anthrax hotline for medical providers was staffed 24 hours a day. Hotline numbers were publicized in the weekly alerts and on the web. Providers reporting suspect cases were transferred to a 24-hour on-call communicable disease physician. Dermatology consultation was arranged at two academic dermatology clinics so cutaneous cases could be quickly assessed. Suspect cases were triaged over the phone as a)highly suspect b)additional evaluation needed by provider, c)not likely to be a case. Highly suspect cases were actively managed by NYCDOH personnel including: physical examination and/or digital photographic examination, interview, chart review, and submission of specimens to the NYC Public Health Laboratory and CDC. Frequent follow-up occurred to monitor clinical status and to relay laboratory results. **Results:** Seventeen broadcast alerts were sent in Oct. and Nov.; the communicable disease hot-line received > 600 calls reporting suspected cases of anthrax. Ninety-four cases were highly suspect. Seven cases of cutaneous anthrax and 1 case of inhalational anthrax were identified: 3 were reported by infectious disease physicians (including the inhalational case), 1 by a dermatologist, 1 by a public health doctor, 1 by an emergency physician and 2 patients self-reported. **Conclusion:** This outbreak highlighted the need for public health agencies to develop protocols for rapid implementation of enhanced surveillance in response to terrorism attacks including several modalities--broadcast fax, hotlines, websites, e-mail-- to facilitate communication with healthcare providers to rapidly identify new cases.

Board 32. Response to Anthrax Terror Attacks in the Winter Season

A. Flahault, F. Carrat, C. Viboud, T. Hanslik, A. Valleron

Inserm, Paris, FRANCE

The fear to suffer from anthrax rather than influenza even after having detected influenza outbreak in the area may lead to panic attitudes. We recommend that all potentially exposed persons should be preventively vaccinated against influenza, such as health professional, municipal employees, postmen and postwomen and other people who may be involved at any stage in the control process of bioterrorism.

An appropriate search for risk factors of anthrax exposure may be practiced in all influenza-immunized persons consulting with ILI and in all non previously immunized persons with ILI (i.e. having received or handled a suspicious mail, or having been in a place of known exposure to Anthrax as determined by public health authorities). These two simple measures (influenza vaccination in risk groups and individual search for risk factor to anthrax exposure), may avoid antibiotics supplies to shorten, desorganization to occur, and true victims of anthrax not to receive appropriate care. These attitude may also dissuade the temptation for such a confusion by the terrorists. Even if ILI due to other natural viral origins may occur in a vaccinated person (field efficacy of the vaccine

against ILI has been estimated to be around 66% IC95% [52%-79%], ranging from 16% and 83% depending on the age, influenza vaccination may limit extensive usage of antibiotics in viral diseases and may also help people to decrease their acute perception of risk of a bioterrorist consequence on their health in this highly sensitive period of the year. It may also help preparedness plan for the next months. As an example, in a large urbanized city with about 10 million people, it may be expected that between 170,000 and 1 million inhabitants will suffer from ILI in the absence of influenza vaccination and consult their GP for that reason during winter in Northern hemisphere. If a bioterrorist attack was to occur at that time, mass influenza vaccination coverage would allow to reduce by 60% people consulting with ILI next winter and then the undue utilization of antibiotics.

Board 33. Syndromic Surveillance for Bioterrorism – New York City, Oct-Dec 2001

A. Karpati[1,2], F. Mostashari[1,3], R. Heffernan[1], J. Leng[1], P. Thomas[1], D. Weiss[1], J. Ackelsberg[1], S. Balter[1], D. Das[1], S. Young[1], K. Bornschlegel[1], B. Cherry[1], A. Fine[1], M. Layton[1]

[1]New York City Department of Health, New York, NY, [2]Centers for Disease Control and Prevention, Atlanta, GA, [3]OutbreakDetect, Inc., New York, NY

Background: Syndromic surveillance for bioterrorism is aimed at identification of population-level outbreaks in their early stages, when patients might present to the health-care system with mild, non-specific illness. Early detection of a bioterrorist event would allow public health authorities to expedite public health interventions (e.g, mass prophylaxis) to help lessen morbidity and mortality. The recent World Trade Center disaster and anthrax attacks have heightened the need for such systems.

Methods: In October 2001, the NYCDOH instituted a syndromic surveillance system using hospital emergency department (ED) data. Each morning, 7 days per week, hospitals electronically transfer a line list of all patients seen in the ED in the previous 24 hours. Each dataset includes the patients' chief complaints, home zip codes, and ages. The data are compiled and the chief complaints are computer-coded, using key words, into distinct clinical syndromes (e.g., respiratory illness, non-specific febrile illness, gastrointestinal illness) corresponding to likely prodromal manifestations of illness caused by potential bioterrorism agents. Using a modified, temporal-spatial "scan" statistic, proportions of all visits due to the syndromes of interest are compared to the previous 14-days' values, and a quantitative measure of geographic and/or temporal clustering is obtained. Unusually elevated rates, or "alarms", defined statistically as clustering in time or space with probability due to chance of <0.01-0.05, prompt an immediate epidemiologic and/or clinical investigation by the Department of Health. **Results:** The NYCDOH receives daily reports from 29 hospitals in all five NYC boroughs (approximately 5000-6000 records per day) via e-mail or file-transfer protocol (FTP). From November 1 - December 4, 2001, statistical "alarms" that prompted further investigation occurred 16 times on 10 separate days (including alarms for respiratory, non-specific febrile, and gastrointestinal illness at each geographic level: citywide, hospital, and zip code). Responses to these alarms have included reviews of the current-day ED logs to verify whether the previous day's increase had been sustained, outreach to hospital emergency departments and infection-control departments for intensified surveillance and diagnostic activities, and chart reviews and telephone contact of patients in the clusters. One citywide outbreak of viral gastrointestinal illness has been detected. **Conclusions:** Electronic reporting of chief complaint data from emergency departments is a viable, though labor-intensive, method for conducting syndromic surveillance in a large urban area. Key optimization issues for the future include balancing sensitivity with specificity in statistical thresholds for response, and in developing sustainable protocols for rapid investigation of elevated rates.

Board 34. Towards a Theoretical (and Practical) Framework for Prodromic Surveillance

F. Mostashari[1,2]

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When syndromic surveillance seeks to detect an increase in mild symptoms that presages an outbreak of potentially fatal illness, this can be termed "prodromic surveillance" and has particular applicability to the timely detection of new and emerging infectious diseases, whether naturally occurring or intentional. Based on our experience with developing, implementing, and evaluating prodromic surveillance for biologic terrorism over the last 3 years, the authors conclude that:

1. Prodromic Surveillance is only one component of bioterrorism surveillance

- Prodromic surveillance aims to identify population-level increases in mild illness, not one or several cases of unusual severe illness. It is unknown, and perhaps unknowable, whether the first detectable signal from a large-scale bioterrorist attack will come through prodromic surveillance or reporting from the astute clinician.
- If the bioterrorist attack is first detected through diagnosis of a single individual with severe illness, prodromic surveillance still can provide critical information on the magnitude of the outbreak, location and timing of release, and case finding.

2. Data sources must be carefully considered. Many possibilities have been examined (e.g., pharmaceutical sales, school and work absenteeism, nurse's hotline calls, ambulance dispatches, emergency department visits). Ideal characteristics include:

- Routinely collected for other purposes, imposing no additional burden on data collectors.
- Computerized.
- "Syndromic"— can be categorized into illness categories (e.g. respiratory, non-specific febrile, gastrointestinal)
- Includes geographic information (e.g., zip code).
- Secure and timely electronic transmission possible

3. Outbreak detection algorithms are needed that are epidemiologically informed and statistically sound, such that:

- We move away from "the eyeball".
- Algorithms detect clustering in space as well as time.
- Different analytic approaches are used, depending on potential confounders and the availability of baseline data.
- Once an algorithm is developed, alarm thresholds are set according to how many alarms the epidemiologists are willing and able to investigate.

4. Prodromic surveillance must be complemented by a rapid epidemiologic response capability:

- Health departments must be able to support investigations 365 days per year.
- An important first step is distinguishing natural variability from an illness outbreak. Has the increase been sustained in the last 12 hours, or returned to baseline?
- The key goal of the investigation is to quickly move from the syndromic "signal" to specific diagnosis. This requires enhancing surveillance for severe illness as well as enhanced diagnostics among individuals with mild illness-clinical tests in individuals who would not normally receive them.

Board 35. Public Health, Bioweapons and the Canadian-American Border: Present Problems and Future Policies

D. H. Avery, II

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This paper will examine the connection between immigration, infectious diseases and bioweapons within a historical and contemporary framework. Or, more specifically, it will examine the question of why immigrants coming from Canada are now per-

ceived, by many American government officials and members of Congress, as representing a serious health and security threat to the United States. While these concerns have been evident during the past five years, the events of September 11 greatly intensified fears about the capabilities of terrorist organizations to move across the 49th parallel, possibly armed with bioweapons.

In many ways this is a timely topic because of the on-going attempts by Washington to convince Canadian authorities to adopt more stringent health and security measures in the new Immigration Act, and thereby establishing conformity with American screening standards. At the same time that these talks are proceeding, there is increased cooperation between public health officials in the two countries. This was evident during the November meetings in Ottawa between Tommy Thompson, US Health and Human Services Minister, and Allan Rock, the Minister of Health Canada, to discuss the possibilities of collaboration in the large scale development of smallpox vaccines. In addition, the long and extensive inter-action between bioweapons specialists of the Canadian Armed Forces, and their counterparts in the United States Army Medical Research Institute of Infectious Diseases, has also been greatly expanded.

The goal of this study is to provide an analytical framework for the on-going discussion of how Canada and the United States can deal with the threat of bioterrorism, and the spread of infectious diseases while at the same time maintaining the relatively 'open' border. Although some reference will be made to earlier border controversies, including the 1962 smallpox incident involving a Canadian visitor, most of the emphasis will be placed on developments since 1995 when the threat of bioterrorism has become a matter of grave concern for both counties. Indeed, the Canadian government has recently demonstrated that it appreciates the grim warnings of the United States Commission on National Security in the 21st Century that "the most serious threat to our security may consist of unannounced attacks on American cities by sub-national groups using genetically engineered pathogens."

In this project I will utilize a wide range of sources within a comparative framework. I have written extensively about contemporary attempts to reconcile Canadian and American immigration policies, as well as how the two countries have cooperated in the field of bioweapons defensive research, and civil defense coordination. As well, I am involved in a multi-disciplinary study on Canada's broader international role in dealing with public health issues associated with bioterrorism.

23 Vectorborne Diseases I

Monday, March 25, 10:00 a.m.
Grand Hall East

Board 40. The Isolation of Yellow Fever Virus of *Haemagogus leucocelaenus* Mosquitoes Lots Obtained Near the Argentina Border at Rio Grande do Sul State, Brazil, 2001

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Following monkey's (*Alouatta fusca*) death in the municipalities of Garruchos and Santo Antonio das Missões, in Rio Grande do Sul state, Brazil, near Uruguay river in the Argentina border, two strains of yellow fever virus (YFV) were isolated into suckling mice from lots of *Haemagogus leucocelaenus* mosquitoes. The minimal infection rate obtained of the infected species was 8.7%. YFV in this species was only reported in two prior occasions: in the 30's years in Brazil in the same region (Shanon et al., 1938), and 40's in the Amazon region of Colombia (Bugher et al., 1941). No human cases were reported, but YFV antigen was detected by immunohistochemistry in a monkey liver fragment of a death animal. The YFV isolation, and the absence in the area of *Haemagogus janthinomys*, the most important YFV vector in Brazil, suggest that *Haemagogus leucocelaenus*, considered unimportant secondary YFV vector in Brazil, play an important role in the disease epidemiology in the Southern Cone, perhaps being the main vector.

This work was supported by IEC/FUNASA, Secretaria de Saúde do Rio Grande do Sul, and CNPq (process 521294/97-5

Board 41. Characterization of the Major Antigenic Protein 2 of *Ehrlichia canis* and *E. chaffeensis* and Its Application for the Serodiagnosis of Ehrlichiosis

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Ehrlichioses have been identified globally as important emerging tick-transmitted diseases. Canine ehrlichiosis (CE), caused by *Ehrlichia canis*, may result in extensive morbidity and mortality. Clinical and hematologic abnormalities are often non-specific during *E. canis* infections. Co-infections with other tick-transmitted agents, such as *E. chaffeensis*, the causative agent of human ehrlichiosis, may be common. Thus a definitive diagnosis may be difficult to reach. Currently, the indirect fluorescence antibody (IFA) assay is the method most widely used to diagnose *E. canis* or *E. chaffeensis* infections. It is considered the "gold standard", however results are often subjective and non-specificity is observed due to cross-reacting epitopes between species. Although currently not available, a rapid, in-house method for serological diagnosis, using the recombinant antigens of *E. canis* and *E. chaffeensis*, would be a useful tool for clinical diagnoses and epidemiological studies. Previously, we cloned and expressed the Major Antigenic Protein 2 (MAP2) of *E. chaffeensis* and *E. canis*. We developed two indirect ELISAs using the rMAP2 from both species. No cross-reactivity was observed with eight other important canine-infecting microorganisms in the *E. canis* rMAP2 ELISA. However, cross-reactivity between *E. canis* rMAP2 and *E. chaffeensis*-positive serum has not been tested. Results of the present study show that the *E. chaffeensis* rMAP2 ELISA failed to differentiate between *E. canis* and *E. chaffeensis* infections. In addition, we further characterized the MAP2 by determining if the *map2* gene is conserved among various geographic isolates of *E. canis* and *E. chaffeensis*, and if a single copy gene encodes the MAP2. Sequences of the *map2* gene of four geographically different isolates of *E. chaffeensis* (Arkansas, Wakulla, Osceola, and Liberty) and five isolates of *E. canis* (Oklahoma, Florida, Israel, DJ, and Jellybean) were compared. The sequences of the *map2* gene were found to be highly conserved among the various isolates of each respective bacterial species. Genomic Southern blot analysis with a DIG-labeled species-specific *map2* gene probe suggested that the *map2* is a single copy gene. Thus, sequence conservation between isolates, the absence of multiple copies of the gene, as well as previous results obtained with the rMAP2 ELISA suggests that the MAP2 of *E. chaffeensis* and *E. canis* is a potential antigen for the serodiagnosis of Ehrlichiosis. However, because significant differences in the MAP2 amino acid composition between *E. canis* and *E. chaffeensis* were observed, we believe that monoclonal antibodies against a specific epitope of the rMAP2 of *E. canis* or *E. chaffeensis* could be used to develop a competitive ELISA, thus improving the specificity of the tests.

Board 43. Fifty-five Years of Tularemia in Alaska, 1946-2001

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The first documented human case of tularemia in Alaska occurred in 1946; eight more cases occurred in the next two decades. Since 1972, Alaska has recorded approximately one case each year. Although the disease occurs infrequently, health care providers must remain alert for the clinical presentation of tularemia as wildlife and environmental reservoirs for the bacteria persist.

Tularemia results following the introduction of *Francisella tularensis* into the body through the bite of certain arthropods (e.g., ticks or deer flies); exposure of pre-existing or new wounds to contaminated water or carcasses; inhalation of dust from contaminated hay or soil; or consumption of inadequately cooked infected meat. Three to five days later, six presentations of tularemia - ulceroglandular, glandular, oropharyngeal, typhoidal, pneumonic or oculoglandular - may develop depending upon several factors, including the portal of entry or the virulence of the infecting strain. Most cases respond well to appropriate antibiotic therapy; less than 4% of cases are fatal.

From 1946 to 2001, Alaska recorded 33 cases of tularemia. Complete data for all cases were not available. Males accounted for 76% (19 of 25) of case-patients. Eighty-six percent (25 of 29) of case-patients were white, and 14% (4 of 29) were Alaska Native. The median age was 36 years (range 18-54 years, data available for 24 persons). Onset dates for the majority of cases (63% or 15 of 24) were in June-August. Sixty-seven percent (22 of 33) of case-patients resided in centraleastern Alaska; 24% (n=8) in the greater Anchorage area; 6% (n=2) in north-western and 3% (n=1) in south-eastern Alaska.

No Alaska cases of tularemia were fatal. Ulceroglandular presentations were most common (84% or 16 of 19) with two typhoidal cases and a single pneumonic tularemia case also reported. Of case-patients with detailed exposure histories (n=19), 17 (89%) had direct contact with animals - 16 with a known wildlife reservoir, e.g., snowshoe hare or muskrat, and one received a cat bite. Among Alaska wildlife, *F. tularensis* has been directly cultured from ticks; and detected indirectly through serologic testing of various animals, e.g., bears and hares.

Cases of tularemia are reportable in Alaska to public health authorities by laboratories and health care providers. Tularemia is enzootic in Alaska so that sporadic human cases are expected, especially among persons who skin hare or muskrat. Impervious gloves worn while skinning animals are an effective means of disease prevention. Case reports receive immediate attention from the Alaska Section of Epidemiology to ensure that appropriate antibiotics are prescribed, laboratory personnel performing tests are kept safe, and information is funneled in a timely manner to bioterrorism surveillance personnel due to the concern that *F. tularensis* could be weaponized.

Board 44. Arbovirus Activity and Surveillance in Australia – Changes and Challenges

R. C. Russell

University of Sydney, Westmead, AUSTRALIA

More than 75 arboviruses are recorded for Australia with 13 implicated in human disease. The most common (>5000 cases p.a.) is the alphavirus Ross River, widely endemic with frequent outbreaks of polyarthritis. Most severe is the flavivirus Murray Valley encephalitis with a few cases almost annually in the endemic north and rare epidemics in the south. In recent years other local and exotic viruses have 'emerged': the alphavirus Barmah Forest has frequent widespread activity and local epidemics; the flavivirus Kunjin (a West Nile subtype) has occasional widespread low level activity in northern and southern regions; Dengue viruses are frequently introduced and locally transmitted with risks for endemicity and haemorrhagic fever; Japanese encephalitis virus established in the northeast may spread southwards through extensive feral pig populations and a competent local vector. Also, the establishment of an exotic vector of Japanese encephalitis across northern Australia, a Dengue vector being repeatedly imported, and a potential vector of West Nile gradually moving northwards, have caused further concern.

Arbovirus surveillance is undertaken variously in most States. Monitoring includes mosquito populations for abundance/virus isolation, sentinel animals for seroconversion, weather data, and reports of human cases. Data are reported directly to state health authorities who contact local operatives for action. Surveillance programs are detecting increased urban activity of Ross River, increased activity of other flaviviruses such as Edge Hill and Stratford, and changing status among vectors. There is no national funding and no national uniformity in surveillance, but a state arbovirus website (http://www.arbovirus.health.nsw.gov.au/) is being expanded to serve as a national site for data coordination/dissemination and a national government expert advisory committee was recently formed.

There are a number of surveillance and control issues being addressed, such as problems of remote locations, selection of appropriate animal sentinels, relative importance of mosquito monitoring and sentinel chickens, and significance of wetlands and irrigation practices in maintaining reservoir and vector habitat. Predicted climate change is likely to enhance virus transmission in some areas, and there are substantial and poorly understood community costs associated with the infections. The potential for increased incidence reinforces the need for efficient surveillance and control but, with no therapeutics or vaccines for the indigenous viruses, vector management is critical to disease management. Mosquito control is not well organised in many risk areas and there are serious concerns for control of widespread epidemics. There is an urgent need for commitments by state and local authorities for funding and organization of mosquito control to reduce disease risks.

Board 45. Survey for *Rickettsia*, *Ehrlichia*, and *Borrelia* Organisms in Ticks from Mississippi

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Objective: Objective of this study was to search for three disease agents in ticks from Mississippi -spotted fever group rickettsiae, *Ehrlichia chaffeensis*, and *Borrelia*-like spirochetes. **Methods:** From Nov 1999 to Oct 2000, ticks were collected for analysis from vegetation as well as deer, dogs, and humans. Ticks were cut longitudinally to make smears on three microscope slides. Remaining tick pieces were frozen at -65°C for additional testing. Tick smears were stained by direct immunofluorescence assays (FA) for *Rickettsia* and *Borrelia*, while indirect FA (IFA) was used for *Ehrlichia*. The tests for each pathogen group are not specific for a single species. The corresponding tick for each positive smear by FA/IFA was removed from the freezer and sent to the CDC for PCR analysis. **Results:** A total of 149 adult ticks (four species) were collected from eleven collection sites from southwestern to northern Mississippi. *Amblyomma americanum* was most commonly collected (n=68), followed by *Ixodes scapularis* (n=53). The bird tick, *Ixodes brunneus*, (usually rare) was the third most commonly collected tick (n=17). Eleven *Dermacentor variabilis* were also collected. FA test results on the 149 ticks were sometimes ambiguous due to non-specific staining of tick tissues and other bacterial contaminants. None of the 149 ticks tested were FA positive for *Borrelia*-like organisms. However, smears of 30 (20%) and 32 (22%) ticks reacted with anti-*E. chaffeensis* sera and anti-*R. rickettsii* sera, respectively. None of the ticks staining with the

IFA for *Ehrlichia* revealed DNA of E. chaffeensis by using PCR; however, 23 (72%) of 32 FA-positive ticks for SFG rickettsiae yielded amplicons of the appropriate size when tested by using a PCR assay for SFG rickettsiae, corresponding to an overall infection rate among the collected ticks of 15%. Incidentally, smears of 12 (71%) of 17 *I. brunneus* revealed abundant bacilliform bacteria. PCR amplification of DNA from a single *I. brunneus* that contained bacilliform bacteria was performed using universal primers for the 16S rRNA gene as well as *Borrelia*-specific primers. PCR using the Borrelia-specific primers was negative. The predominant sequence obtained using the universal primers did not match any known sequence in GenBank, but showed 91% identity with an endosymbiont of Acanthoamoeba. **Conclusions:** *Borrelia*-like spirochetes were not detected in Mississippi. SFG rickettsiae are commonly associated with Mississippi ticks-especially *A. americanum*. An as-yet-unidentified bacterium apparently infects a large portion of *I. brunneus* ticks. Further study will be needed to identify this species.

Board 46. Detection of *Yersinia pestis* and a Novel *Bartonella* Genotype in Prairie Dogs and Their Fleas Using Multiplex PCR

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We developed a multiplex polymerase chain reaction (PCR) assay that simultaneously detects three types of flea-associated microorganisms. The targets for the assay were sequences encoding from the *gltA*, 17 kDa antigen, and *pla* genes of *Bartonella* spp., Rickettsia spp., and *Yersinia pestis*, respectively. A total of 260 flea samples containing blood meal remnants were analyzed from fleas collected from abandoned burrows at the site of an active plague epizootic in Bear Creek Lake Park, Jefferson County, Colorado. Results indicated that 34 (13.6%) fleas were positive for *Bartonella* spp., 0 (0%) were positive for *Rickettsia* spp., and 120 (46.1%) were positive for *Y. pestis*. Twenty-three (8.8%) fleas were coinfected with *Bartonella* spp. and *Y. pestis*. A second group of 295 blood meal-containing fleas were analyzed from abandoned burrows at Red Lion Wildlife Area, Logan County, Colorado where an epizootic had occurred 2-4 months before the time of sampling. Of these 295 fleas, 7 (2.3%) were positive for *Bartonella* spp., 0 (0%) were positive for *Rickettsia* spp., and 46 (15.6%) were positive for *Y. pestis*. Coinfections were not observed in fleas from the older (Logan County) epizootic site. No positives were identified among the 100 unfed fleas examined from each site. The multiplex PCR also was used successfully to identify *Y. pestis* and *Bartonella* in the tissues of prairie dogs. Although plague is routinely identified in prairie dogs and prairie dog fleas, this report represents the first identification of *Bartonella* from these animals and their fleas. In order to further characterize these agents, selected *Bartonella* PCR amplicons from prairie dogs and prairie dog fleas were sequenced. Phylogenetic analyses indicate that the sequences of these prairie dog and prairie dog flea bartonellae cluster tightly within a clade that is distinct from those containing other known *Bartonella* genotypes. The ability of the multiplex PCR to simultaneously test flea samples and rodent tissues for multiple pathogens should save time and sample material, serve as an efficient screening technique, and provide more ecological information on the presence of coinfections or other topics.

Board 47. Molecular Identification of Crimean-Congo Hemorrhagic Fever Virus in Human Clinical Cases in Southern Russia

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Crimean hemorrhagic fever (CHF) was diagnosed in the Russian Federation since 1944. 334 human cases were registered in the Rostov region from 1963 to 1971 years, 51 cases (15%) were fatal [1]. CHF outbreaks have been reported also in the Republics of Kalmykya and Dagestan, the Stavropol, Astrakhan and Krasnodar regions of the Southern Russia. After the period of relative composure the CHF epidemic situation has become worse last years. In 2000-2001 more than 80 CHF cases with 10 deaths were serologically confirmed in Russia [2]. Both old endemic regions and new region (Volgograd) were affected. In the latter region there were 15 CHF cases in 2000 and 9 cases in 2001; the Crimean-Congo hemorrhagic fever virus (CCHFV) antigen was found in the ticks.

The Central Research Institute of Epidemiology has developed the specific RT-PCR-based assay for prompt diagnosis of CHF. To date 15 CHF clinical cases, occurred in the South Russian regions, were confirmed by this assay. Nine isolates were characterized by direct sequencing of the gene fragment (215 nucleotides) locating in RNA small (S) segment and coding nucleoprotein. These data (AF432115-AF432121) were compared with other CCHFV sequences available in GenBank. Pairwise nucleotide p-distance ranged from 0 to 0.038 within recent Southern Russian isolates, whereas the p-distance between Russian isolates and the isolates from Africa, China, and Kazakhstan was greater than 0.11. Russian variant of CCHFV appeared to be rather stable, because the difference between recent isolates and strain Drosdov, isolated in 1967 in Astrakhan, varied from 0.024 to 0.033. Interestingly, the strains isolated in 2001 in Kosovo belonged also to Russian or, possibly, "European" genovariant. Although the number of observations was low, there were probably Stavropol and Volgograd topovariants within Russian CCHFV isolates; in Rostov region, which located in between Stavropol and Volgograd, both topovariants were presented. Most nucleotide substitutions within Russian CCHFV isolates did not result in the amino acid change. One of the isolates from Rostov-2001 had one amino acid substitution and Drosdov strain had two substitutions.

1. Aristova VA, Kolobukhina LV, Schelkanov MI, Lvov DK. Vopr Virusol 2001, 46(4): 7-15.

2. www.depart.drugreg.ru. Russian Ministry of Public Health.

24 Waterborne Infections II

Monday, March 25, 10:00 a.m.
Grand Hall East

Board 48. Waterborne Diseases: A Global View

W. Pasini

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The WHO estimates that at the beginning of the 21 century about 1.1 billion people haven't got access to safe and clean drinking water (Bartram and Hueb,2000). Waterborne disease transmission occurs by drinking contaminated water. This has taken place in many dramatic outbreaks of faecal-oral diseases such as cholera and typhoid fever. Outbreaks of waterborne disease continue to occur across the developed and developing world. Water-washed disease occurs when there is a lack of sufficient quantities of water for washing and personal hygiene. Diarrhea is the most important public health problem affected by water and sanitation and can be both waterborne and water-washed. Approximately 4 billion cases of diarrhea each year cause 2.2 million death, mostly among children under the age of five. Intestinal worms infect about 10% of the population of the developing world. 200 million people in the world are infected with schistosomiasis of whom 20 million suffer severe consequences. Diarrhea is by far the commonest cause of illness in travellers. It affects an estimated 20-50% of all the travelers. It may cause anything from embarrassment and inconvenience to disruption of travel and business plans. For vulnerable people it may even be fatal, if not promptly and effectively treated. Waterborne and foodborne diseases are transmitted by consumption of contaminated drinks and food. Dehydration is the clinical effect of diarrhea and it can be serious, expecially in children. Dehydration may also be caused by a inadequate intake of water. A book on Hydration and Health has been written in late 2001 and will be distributed to the medical community in 2002 in many countries, including Europe, North and Latin America. The books covers all the benefits of a proper hydration, the risks of dehydration, the waterborne diseases and chemical pollutants, water and children, water and seniors and many other aspects. Outbreaks of diseases associated with recreational water are reported from all parts of the world. Surface water including rivers, lakes and oceans, swimming pools and hit pools put health risks to humans through microbial pollution (Hunter 1997). Pesticides and nitrates in drinking water and recreational water constitute a serious problem worldwide. Freshwater can contain hazardous concentration of lead, arsenic, fluoride and radioactivity (WHO 2001). Adequate quantities of safe water and good sanitation are necessary conditions for healthy living, but their impact will depend upon how they are used.

Board 49. Outbreak of Legionellosis in Stavanger, Norway

H. H. Blystad[1], M. Holm[2], O. Natas[3], E. Bjorlow[4,1], P. Aavitsland[1]

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Background: Indigenous legionellosis is a rare disease in Norway with only a handful of sporadic cases diagnosed every year. Prior to this outbreak, no clusters or outbreaks have been documented in Norway. Several studies, however, have shown the presence of various *Legionella (L)* species in cooling towers at hospitals and hotels. We report here an outbreak of legionellosis in the city of Stavanger (population 100,000) on the west coast of Norway. **Methods:** For the descriptive study, a case was defined as a person staying in the city of Stavanger within two years prior to September 2001 with a clinical or radiographic diagnosis of pneumonia and a confirmed laboratory diagnosis of *L pneumophila* serogroup 1 (*Lp*S1) confirmed by culture, by a fourfold or greater rise in specific serum antibody titre seroconversion by indirect immunofluorescent antibody test or by microagglutination or a single high titre, using reagents to *Lp*S1 or other *L* species and serogroups, or by antigen detection of specific *L* antigen in urine. Patients, relatives or the patients' doctor were interviewed. Based on these interviews, 81 water samples were taken from suspected sources. Isolates from patients were compared with environmental isolates by genotyping using the AFLP method. **Results:** From 18 July to 7 September 2001, 26 cases were reported to NIPH. All cases had been staying in Stavanger within a ten days period prior to the onset of symptoms. The case fatality ratio was 23% (6/26). The age range was from 16 to 94 years (median 54). The median age of fatal cases was 84 years. The sex ratio (M/F) was 3.3 (20/6). One case was a British tourist identified through the reporting system of the European Working Group for Legionella Infections (EWGLI). All cases had been in a limited area in the city center within a 500m radius within ten days prior to the onset of symptoms. Three of the patients had been staying in a hotel in the same area. Water samples taken from the cooling tower of this hotel subsequently showed presence of *Lp*S1. The air outlet of the cooling tower was situated five metres above ground level, close to a bus terminal. The onset of symptoms of the last reported case occurred nine days after the cooling tower in the hotel was taken out of service and disinfected on 29 August. Nine isolates from patients and five isolates from the cooling tower were genetically compared and showed similarities, and were different from other known Norwegian *L* isolates. Discussion: Close cooperation between local health authorities, the local microbiological laboratory, and NIPH was essential in this investigation of a classic outbreak of Legionnaires' disease. To prevent further outbreaks, an information programme aimed at hotels, engineering consultants, and health professionals will be implemented. Current Norwegian prevention guidelines will be updated in accordance with the forthcoming European prevention guidelines produced by members of EWGLI.

25 Emerging Opportunistic Infections

Monday, March 25, 10:00 a.m.
Grand Hall East

Board 50. An Outbreak of Blastomycosis in Minnesota

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Background: Blastomycosis outbreaks are infrequently identified and thus opportunities for epidemiologic investigation are limited. In August 2000, a cluster of blastomycosis cases was reported from a small town in northern Minnesota. This report summarizes the investigation of a large outbreak, risk factors for cases, and climatic/environmental conditions contributing to the outbreak. **Methods:** Active surveillance for human cases was done by contacting hospitals and laboratories in the area and encouraging submission of clinical specimens from suspect cases. Active surveillance for cases in dogs was done by contacting veterinarians. A human case was defined as one in which *Blastomyces dermatitidis* was cultured or visualized from sputum or bronchial lavage. Serum

samples were collected from humans and tested for *B. dermatitidis* A antigen by immunodiffusion and complement fixation. A case control study examining risk factors for disease was conducted comparing cases to healthy neighborhood controls. A case in a dog was identified as one in which *B. dermatitidis* was cultured or visualized from sputum, skin lesion, or bronchial lavage; a suspect case had either a chronic cough or unresolving skin lesion and lived in the affected neighborhood. Soil samples from the area were tested by mouse assay. Available human and dog isolates were examined by RAPD PCR and sequencing the ITSI region. Historical precipitation, humidity, and temperature data were reviewed. **Results:** Eighteen human cases were identified. All cases lived in a single neighborhood of approximately 200 households. The median age was 38 years (range, 7 to 70). Thirteen (72%) cases were female. Ten (56%) were hospitalized 1 to 22 days. Onset of illness ranged from 7/11/00 to 9/7/00. Serologic testing did not identify additional cases. Only 2 patients developed an antibody response. Cases were younger (p= 0.08), had a history of a chronic medical condition (OR=2.6, p=0.08), reported other family members ill (OR=6.8, p<0.01), and lived closer to a recent excavation site than controls (p<0.05). Nineteen confirmed and 4 suspect canine cases lived in the same neighborhood with onsets ranging from 8/23/00 to 10/23/00. All soil testing was negative for *B. dermatitidis*. All of the outbreak isolates (human and dog) were the same genotype. The preceding months had above average precipitation (p<0.05), humidity (p<0.01), and temperature (p<0.01). **Conclusions:** Weather conditions and recent disruption of vegetation and soil contributed to this outbreak. Improved diagnostics are needed for blastomycosis as evidenced by the lack of serologic response in culture confirmed cases. RAPD PCR was useful in linking outbreak related cases.

Board 51. The Emerging Diarrhoeal Pathogen: *Cyclospora cayetanensis* and HIV Seropositive Individuals in Lagos, Nigeria

E. G. Alakpa

Nigerian Institute of Medical Research, Lagos, NIGERIA

The advent of the Human Immunodeficiency Virus (HIV) infection and detection has spontaneously changed the spectral of infectious disease management and has lead to the reclassification of some once accepted non infectious agent as pathogenic agent with the subsequent increase in the number of supposed newer pathogen. One of these 'newer' agents is the emerging diarrhoeal protozon, *Cyclospora cayetanensis* whose involvment as an emerging diarrhoeal pathogen has been globaly reported. We report the first documented isolation of this pathogen form HIV individuals from the first ever study conducted in Nigeria and the West coast of Africa. Stool and blood samples were obtained from 182 confirmed HIV seropositive individuals from some government accredited HIV screening centers in Lagos. Stool samples were screened parasiologically. Seven (3.8%) stools were confirmed positive for the presence of the pathogens' oocyst and all positive stools were form diarrhoeal patients. Confirmation of oocyst was done at the SMP Reference Laboratory, Glasgow, UK. Bacteriology was negative in these positive stools. The result was significant ($p < 0.05$), and of interest as patients whose stools were positive, have been diarrhoeic for over 3 weeks despite having been on antidiarrhoeal drugs. Also, majority of the health workers and physicians in the State and country were completely ignorant of the existence of this pathogen. The need for more studies and education of health practitioners can not be over emphases as this study has shown the existence of this pathogen in this state and country. Key words: *Cyclospora cayetanensis* HIV, diarrhoea, Lagos, Nigeria

Board 52. Prevalence of Virulence Factors in *Aeromonas hydrophila* and *Aeromonas caviae* Isolates from Groundwater and Human Stool Samples

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The US Environmental Protection Agency has added *Aeromonas hydrophila* to the contaminant candidate list for drinking water, because of its suspected pathogenic importance and ubiquitous occurrence in water. One study estimated aeromonads to cause 13% of the reported gastroenteritis cases in the US. *A. hydrophila* was identified as the causative agent in 36% of diarrheal patients at a long-term care facility with ingestion of contaminated food or water as the potential source. The pathogenicity of *A. hydrophila* and *A. caviae* is related to production of adherence factors, enterotoxins, and toxin activators (serine proteases). A previous report compared *Aeromonas* spp. isolates from diarrheal patients and their drinking water for relatedness by DNA fingerprinting. One could hypothesize that DNA fingerprints would be similar between the clinical and groundwater isolates if water was the source of infection, but no relatedness among these isolates were found. To determine if the linkage between pathogenicity and disease potential might be better understood by comparing virulence factors in these samples, we screened the 17 human clinical (fecal) and 78 groundwater isolates for the toxin and toxin activating genes. These virulence factors were detected using PCR with consensus sequence primers derived from multiple DNA sequences for hemolysin and cytolytic enterotoxin genes from *A. hydrophila* and *A. caviae* (GenBank), aligned using Clustal W. The PCR product is a 224 bp amplicon. Since no serine protease sequence has been published for *A. caviae*, the three reported activator sequences from *A. hydrophila* were used to develop primers with a 175 bp amplicon. Of the 10 fecal and 46 water isolates identified as *A. hydrophila*, none of the clinical and 29 (63%) of the water isolates contained enterotoxin genes. Of the remaining isolates, 1 clinical and 10 water isolates also had at least one virulence gene. To date, 6/17 A. caviae from water origin are positive. The prevalence of hemolysin/cytolytic enterotoxin genes was 5.9% (1/17) and 50% (39/78) for fecal and environmental isolates, respectively. Our findings support the previous work suggesting little relatedness among clinical and water isolates as determined by virulence factor occurrence. Our data suggest that 94.1% of *Aeromonas* from these clinical sources do not have the hemolysin/cytolytic enterotoxins reported in the literature. Other enteropathogenic microbes including *Salmonella*, *Campylobacter*, and *Cryptosporidium*, were found in 5/17 clinical isolates. Our findings suggest either *Aeromonas* was not the caustive agent, the enterotoxin traits were on a plasmid that had been deleted, or a LPS-toxin that dissolves the lipid bilayer of cells, not tested for, may be responsible. The mechanism of pathogenicity is an important to resolve, since 50% of water isolates possessed enterotoxin genes suggesting potential pathogenicity.

Board 53. *Bordetella pertussis* Infection in US Military Recruit Populations

J. C. Sammons, C. Le, J. M. Fuller, S. Poddar, M. K. Ryan, K. L. Russell

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Background: Pertussis (whooping cough) is a highly contagious respiratory disease caused by infection with *Bordetella pertussis*. Some epidemiological evidence suggests that the prevalence of pertussis infection is on the rise among adolescents and adults, potentially due to waning vaccine-acquired immunity. Confined populations, including those in daycare centers, nursing homes, and military camps, are particularly at risk. The extent to which *B. pertussis* infection contributes to acute respiratory disease among military trainees has not been extensively studied. Therefore, surveillance was established at 4 basic training sites throughout the US

in 1999. **Objective:** Measure the proportion of prolonged-cough illness attributable to *B. pertussis* infection among US military trainees. **Methods:** Recruits at four military training sites meeting the case definition of seven or more days of cough were eligible to participate. One nasopharyngeal swab (NP), one throat swab, and 15 cc each of acute and convalescent sera were collected. The NP specimens were cultured on Regan-Lowe with cephalexin and Bordet-Gengou without cephalexin. The NP and throat specimens underwent PCR assay for a 153-bp region with primers for a *B. pertussis* repeated genome sequence. Serologic assays were performed using the MarDx PT/FHA EIA kit. This kit tests collectively for IgG, IgM and IgA specific antibodies against pertussis toxin (PT) and filamentous hemagglutanin (FHA). An individual was considered a positive *B. pertussis* case if they were culture positive, PCR positive, or sero-converted from negative to positive in their paired sera. **Results:** Of 130 specimens tested by all three methods, 10% (13) were identified as *B. pertussis* positive. One (0.78%) individual was positive by culture and PCR, 9 (7%) were PCR positive from NP and/or throat specimens, and 3 (2%) were positive by sero-conversion. **Conclusions:** This study demonstrates that pertussis infection is potentially an important pathogen among military recruits, accounting for 10% of prolonged-cough illness. If acellar pertussis vaccine becomes available to young adults in the US, immunization with this product may be warranted in this population. Additional surveillance may address the value of such a practice in the future.

26 Emerging Aspects of HIV and STDs

Monday, March 25, 10:00 a.m.
Grand Hall East

Board 54. Etiology of Leucorrhoea in HIV Seropositive and HIV Seronegative Women with Special Reference to Bacterial Vaginosis

V. A. Palan, III

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200 HIV seropositive female patients with multiple sex partners and 100 seronegative female patients with single sex partners presenting with chief complaint of leucorrhoea were studied over a period of 2 years.Multiple STD'S were seen more commonly in former group with significant P=0.0176 when compared between two groups.Common multiple STD was Candida albicans with Trichomoniasis. Bacterial vaginosis was also found more commonly in HIV seropositive patients.Prevotella - Porphyromonas group was associated in 93.2% of patients with bacterial vaginosis.Among the Amsel's and Nugent's criteria used for diagnosing bacterial vaginosis, χ^2=0.0043; Df=1; P=0.9476{NS} Amsel's Criteria v/s Nugent's Criteria: Kappa Agreement Test=0.0618 (kappa < 0.60 indicates moderate agreement). There was increase in incidence of non albicans Candida particularly C.glabrata among HIV seropositive patients.

Board 55. HIV Infection in Northwestern Russia: An Epidemic Unfolding

E. Bjørløw[1], A. Chernev[2], A. Gavrilov[3], A. Tulisov[4], P. Aavitsland[5]

[1]European Programme for Intervention Epidemiology Training, Oslo, NORWAY, [2]Regional State Sanitary and Epidemiological Control Center, Murmansk, RUSSIAN FEDERATION, [3]Republican AIDS Centre, Petrozavodsk, Republic of Karelia, RUSSIAN FEDERATION, [4]State Sanitary and Epidemiological Control Center, Archangel, RUSSIAN FEDERATION, [5]Norwegian Institute of Public Health, Oslo, NORWAY

Background: In the mid nineties an explosive spread of HIV infection was noted in the Russian county of Kaliningrad on the Baltic coast. From 1999, a similar explosive increase has been observed in the city of St. Petersburg and surrounding Leningrad County and in other parts of the central Russian Federation. The epidemic has been driven by unsafe injecting practices among injecting drug users (IDU). Norway borders to Murmansk county (1.0 million inhabitants) and has also close links with the two other Russian counties in the Barents region, Archangel (1.5 million) and the republic of Karelia (0.8 million). Our objective was to assess the spread of HIV in these parts of the Russian Federation. **Methods:** In the Russian Federation, newly diagnosed cases of HIV infection is reportable by name on a specific form to the State Sanitary and Epidemiological Control Centre in the county. Cases diagnosed after anonymous testing are not reported. We reviewed cases reported up to October 31 2001. **Results:** In Murmansk, a cumulative total of 173 cases had been reported up to 2001. During the first ten months of 2001, 387 cases (37 per 100,000) were reported compared to only 70 cases for the whole of year 2000. 92% of the cases in 2001 were reported to have been infected by injecting drug use. In Archangel, 37 cases (2.5 per 100,000) inhabitants were reported in by October 31 2001 compared to 11 for the whole of year 2000. 17 of the cases were infected by injecting drug use. In the Republic of Karelia, 58 cases (7.5 per 100,000) were reported by October 31 2001 compared to 51 for the whole year of 2000. Discussion: The Russian HIV epidemic is driven by injecting drug use and has unfolded during 2001 in the far northern county of Murmansk and may be starting in neighbouring Archangel and Karelia in 2002. The rate of spread in Murmansk is comparable to the rate metropolitan St. Petersburg (50 per 100,000). In neighbouring Norway, the annual rate of newly diagnosed HIV infection is 3 per 100,000, possibly making the Norwegian-Russian border the international border with the highest HIV rate gradient in the world. The epidemic may currently constitute the biggest threat to public health in Murmansk. In the future, the epidemic may spread by sex to the larger heterosexual population and vertically to newborns. Preventive measures are urgently needed to save young Russians from this grave infection.

Board 56. Genetic Analysis of Perinatal Transmission of HIV-1 Subtype C Isolates from India

S. R. Das[1], S. Sehgal[2], S. Gopalan[2], N. Ahmad[3], S. Jameel[1]

[1]ICGEB, New Delhi, INDIA, [2]PGIMER, Chandigarh, INDIA, [3]University of Arizona College of Medicine, Tucson, AZ

The HIV epidemic in India is at critical levels with an estimated 3.5 million Indians presently infected. It is known that HIV-1 subtype C is responsible for majority of infection in India. The dynamics of perinatal transmission and the viral factors responsible for it have not been worked out in this situation. The actual mechanisms of perinatal transmission are unknown but theoretically it occurs at three stages: prepartum (transplacental passage), intrapartum (exposure of infants skin and mucus membrane to maternal blood and vaginal secretion) and postpartum (breast feeding). To date, there are no clearly defined factors, viral or host, associated with maternal transmission of HIV-1. Host factors like low CD4+ lymphocyte counts, maternal immune response, high viral load or disease progression may contribute to transmission. Some studies on HIV-1 subtype B have shown that only minor variants found in the genetically heterogeneous population of viruses in the mother are transmitted to the infants. Whether it is cell free or cell-associated HIV-1 that is transmitted, the envelope glycoprotein(s) will play an important role on account of its interaction with CD4 receptor and one of the co-receptors. Mutations in the envelope V3 region could potentially affect mother-infant transmission of HIV-1, since this region is an important determinant for cellular tropism and virus neutralization. To study the relationship between transmission and genetic diversity, we are analyzing the HIV-1 envelope sequences in perinatally infected mother-child pairs by

examining the proviral sequences. After PCR amplification the C2 through V5 region of ~650 bp, it was cloned in pGemT Easy vector. For each pair, 20 clones from the mother and 20 clones from the child were sequenced. After alignment of the sequences and phylogenetic analysis we have observed that the predominant variant from the mother is not the dominant one in the child. Rather, a minor variant from the mother was dominant in the child. Thus, perinatal transmission for subtype C Indian isolates appears to follow a pattern similar to HIV-1 subtype B, where the minor variants are transmitted to the child. The data from multiple mother-child pairs, its analysis and implications will be presented.

Board 57. Addressing Emerging Sexually Transmitted Diseases (STDs) in the US Military

V. H. MacIntosh[1], S. L. Ludwig[2], K. T. McKee, Jr.[3], P. O. Renzullo[4], W. B. Calvert, III[5], C. E. Bader[6], M. Malakooti[7], J. C. Gaydos[8,4]

[1]Air Force Medical Operations Agency, Washington, DC, [2]Office of the US Coast Guard Commandant, Washington, DC, [3]US Army Medical Research Institute of Infectious Diseases, Ft. Detrick, MD, [4]Henry M. Jackson Foundation, Rockville, MD, [5]Naval Environmental Health Center, Norfolk, VA, [6]J4 Medical Readiness Division, JCS, Pentagon, Washington, DC, [7]Navy Environmental Health Center, Norfolk, VA, [8]Department of Defense Global Emerging Infections Surveillance and Response System, Silver Spring, MD

Background: Sexually transmitted diseases (STDs) remain significant problems for the military services. Department of Defense (DoD) study panels and civilian consultants have identified inadequate reporting, complacency and inconsistent clinical practices as possible contributing factors to persistence of these problems. Additionally little attention has been given to the viral STDs, human papillomavirus (HPV) and herpes simplex virus (HSV) infections. **Methods:** Surveillance data from service (Army, Navy, Marine Corps, Coast Guard and Air Force) reportable events systems, as well as data from available peer-reviewed publications were reviewed. Surveillance systems were assessed using published guidance for evaluating surveillance systems. **Results:** Service surveillance systems were uniformly passive. Although based upon identical reportable disease lists, data reported by the different service systems were not standardized. Laboratory test results and tests used were often unknown. Herpes simplex virus (HSV) and human papillomavirus (HPV) were not reported. No studies of reporting completeness and validity of STD diagnoses were available. Disease rates/100,000 persons (or person-years) ranged from 73-340 for *N. gonorrhea* (GC), 54-1127 for *C. trachomatis* (CT), and 2-9 for syphilis. Only 1 installation reported antibiotic resistance data for GC. Peer reviewed studies, conducted on selected populations, tended to yield more uniform data. Limited prevalence data were available for GC (0-3%) and syphilis (0.02%). Among basic trainees, CT prevalences of 9-11% in Army and Marine females, and 5% in Army males, were found. Among military members who had completed basic training, CT prevalences ranged from 3-7% in Navy women, 7-12% in Army women, and 3-5% in male Marines. *Trichomonas vaginalis* prevalences had been reported only for female Marine recruits (2%) and an Army female clinic population (6%). HPV had been studied only among Army women seeking care (45-51% prevalence). No reports on HSV were found. Large population-based studies of incidence were lacking. **Conclusions:** Surveillance data on STDs in the military are inconsistent and inadequate. Wide variations in STD rates exist among services and within individual services over time. Reasons for variations could not be determined, but lack of standardization and reporting deficiencies probably contributed. Attention must be given to validating completeness and accuracy of data submitted to the surveillance systems. All recruits should have STD screening and periodic exams mandated for high-risk service members. Steps must be taken to capture data on antibiotic resistance and viral STDs.

Board 58. Prevalence of the Ist/Aids in the Laboratory of the Health Center King Baudouin of Guediawaye in Senegal

I. Nidr

Health Center King Baudouin Of Guediawaye, Dakar, SENEGAL

Objectives: The prevalence of the IST/AIDS at patients that present themselves to the laboratory for the tracking of an ist/aids.

Methodology: A retrospective survey based on the exam of patient files that is presented themselves to the laboratory during the year 1999 for the tracking of an IST/AIDS.

Results: * Vaginal prelevement: the IST find out on 857 taking is : - Vaginose bacterienne : 383 (44,7%); - Vaginal candidose: 316 (36,8%); - Vaginal trichomonose : 86 (10%); - Vonococcie : 02 (0,2%).

*Verologie chlamydienne : on 388 patients,175 patient have a serology positive (45%) . The indications most frequent clinics are - The pelvic pains (28,5%); - The secondary barrenness (27,4%); - The primary barrenness (17,7%). *Recherche of mycoplasmes patient : surs 263 ,198 have a positive research (75%). Indications the most frequent clinics are : - The secondary barrenness (26,3%); - The primary barrenness (22%); - The pelvic pains (21,7%). * Syphilitic serology : on 2164 patient ,47 had a RPR positif and confirmed by a spécific serology (TPHA) either 2% . Most of patients came for a prenatal balance. * Retroviral serology: on 215 patient presenting themselves to the laboratory for a retroviral serology, 56 had a positive serology : HIV 1 (44 patients), HIV2 (4 patients), HIV1+2 (8 patients). The mean of age is 26 years. It is about of patient symtomatiquess or having greatly journey either of partners of people living with the VIH.

Conclusion: Seen the prevalencess of the IST/AIDS as in the Center of Health King Baudouin of Guediawaye, we put in œuvre of struggle modes to master the fast development of the IST/AIDS as to know : IEC, the adapted management of the cases diagnostiques, the systematic depistage of the syphilis at the pregnant woman and proposition of the test VIH at the pregnant woman.

Board 59. A Large Military Chlamydia Testing Program Demonstrates the Need for Increased Screening

L. C. Canas, A. T. McComb, C. Otremba, V. R. Carpenter, L. Bock, B. Delgado, Jr.

Brooks Air Force Base, San Antonio, TX

Chlamydia trachomatis continues to be the most common bacterial sexually transmitted disease (STD) in the United States. The burden of this infectious disease to the US military has great impact both in terms of health care dollars and lost training/work time. Following the recommendations of the Centers for Disease Control and Prevention (CDC) concerning guidelines for cost effective screening programs, the Armed Forces Epidemiological Board (AFEB) has recommended routine chlamydia screening for new female recruits within the first year of service, all female military service members under the age of 25 during each recommended routine Papanicolaou Smear, and male military personnel with identifiable risk factors or symptoms. Screening is also considered to be the standard of care for obstetrics patients. Many chlamydia infections are asymptomatic and are particularly problematic in females often leading to pelvic inflammatory disease, infertility, ectopic pregnancy, and neonatal transmission. The Brooks Air Force Base (BAFB) virology laboratory in San Antonio routinely conducts diagnostic chlamydia testing for those military medical treatment facilities (MTF) that choose to send the test out rather than do it on site. Reasons for this decision are mainly due to a shortage of trained personnel or too few requests to make on site testing cost effective. The BAFB laboratory now averages >8,000 clinical specimens/month and performs testing using the ligase chain reaction test (Abbott Laboratories, Chicago, IL). This nucleic acid amplification test is approved for both female and male genital and urine specimens. During the month of July 2001,

8100 patient samples from 69 MTFs around the world were processed and results were reported. Of those, 84.5% (6844/8100) were females and 5.9% (401/6844) of those results were positive for *C. trachomatis*. Urine samples accounted for only 2.2% (180/8100) of the female specimens but made up 3.5% (14/401) of the female positive results. By contrast, only 15.5% (1219/8100) of the specimens were from males, but 22% (273/1219) of those were positive. Urine samples accounted for 20% (242/1219) of the male samples of which 8.7% (21/242) of those urines were reported to be positive. The military has recognized the value of chlamydia screening programs to detect disease presence and prevent asymptomatic transmission.

27 Emerging Zoonoses II

Monday, March 25, 10:00 a.m.
Grand Hall East

Board 60. The Selectiv Extraction Method of *B. anthracis* Capsul Antigen

B. M. Suleimenov, Sr.[1], I. S. Arakelyan, Sr.[2], E. E. Li, Sr.[2], E. E. Li, Sr.[2]

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The *B. anthracis* capsule antigen detects at 36° C and it's the most perspective antigen for creating of diagnostic preparations as compared with O- antigen or lipopolysaccharide of the cell wall. We were detected 4 preparations which are in different intensity of minor concentration selectively extracts with *B. anthacis* capsule antigen. On the based was devised the technique of capsule antigen selective extraction with the most peculiar and sensitive production of capsule antigen by Zenkovsky's vaccine strain. Peculiarity and sensitivity of antigen were tested in indirect hemagglutination and erythrocytic immunoglobulin diagnosticum in the reaction of immuno-fluorenscenses. The devised technique has no lacks of E. Baker's (1952) technique with using the high concentration of sulfate ammonium and is no complicated on the fulfillment and is perspective for production of native *B. anthracis* capsule antigen.

Board 61. Detection and Characterization of Swine Hepatitis E Virus from Herds in Costa Rica

J. A. Kase[1], M. T. Correa[2], C. Luna[3], M. D. Sobsey[1]

[1]University of North Carolina, Chapel Hill, NC, [2]North Carolina State University, Raleigh, NC, [3]National University of Costa Rica, Heredia, COSTA RICA

Recent findings, including the discovery of almost genetically indistinguishable swine and human Hepatitis E virus (HEV) strains, have suggested a potential role of swine in the transmission of HEV. Routes of human exposure to swine HEV are uncertain but may include direct and indirect animal contact and exposure to swine fecal matter. Serological evidence indicates that HEV is enzoonotic in swine regardless of the status of human HEV endemicity. Although swine HEV isolates from North America, Europe, and Asia have been genetically characterized, little is known about the strain presumed to be circulating in swine from South and Central America. The virus is known to circulate among the population in Costa Rica as shown by a seroprevalence study conducted in 2000. In addition, the extent to which HEV may be present in fecal waste generated from intensive swine operations found globally, is largely unknown. In this study, four commercial swine production sites served by the Veterinary School in Costa Rica were surveyed for fecal HEV in freshly passed swine feces collected from individual barns. A questionnaire was presented in Spanish to all farm managers to elicit information on swine demographics and waste management strategies. Methods for concentration and purification of HEV from stool suspensions consisted of clarification, solvent extraction of sedimented solids, and polyethylene glycol precipitation. Because HEV cannot be cultivated, viral genomic RNA was extracted and RT-PCR, with primers located in ORF2, was utilized for the detection of viral RNA. Of the samples analyzed, 7/21 produced a product of the expected size following two rounds of (i.e. semi-nested) amplification. Five of the seven positive samples were from swine between the ages of 1-1/2 to 3 months of age. Notably, samples from swine aged 1 month and 4 months were negative. Our data corroborate the previous finding of seroconversion, based upon the detection of anti-HEV antibodies, occurring in piglets approximately three months of age. The identity of all RT-PCR products was confirmed by nucleic acid sequencing and all isolates were found to be genetically similar. Based upon GenBank sequence comparisons with characterized swine and human HEV strains and phylogenetic analysis of nucleic acid regions amplified by ORF2 primers, our isolates closely resembled and clustered with the US swine and human strains (nucleic acid identity >90%). The majority of the nucleotide changes resulted in no differences at the amino acid level. Our data provide further insight into the natural ecology of HEV in swine and raise further public health concerns about occupational as well as off-farm exposures, such as via fecally contaminated surface water or food and xenotransplantation.

Board 62. Laboratory Diagnosis and Antibiotic Sensitivity Testing of *Brucella* Species in Egyptian Patients

T. Ismail[1], M. Wasfy[1], F. G. Youssef[1], M. Abdel-Maksoud[1], K. C. Earhart[1], M. Rakha[2], F. Mahoney[1,3]

[1]U.S. Naval Medical Research Unit No. 3, Cairo, EGYPT, [2]Central Public Health Lab, Ministry of Health, Cairo, EGYPT, [3]Centers for Disease Control and Prevention, Atlanta, GA

Introduction: Brucellosis is a zoonotic infection that represents an important health problem in Egypt. In a surveillance study on acute febrile illness (AFI) in Egypt, a blood culture system was established in 12 fever hospitals throughout the country and *Brucella* isolates were received for quality control purposes. The objective of this study was to test the in vitro antibiotic activity of 80 *Brucella* strains against 6 antibiotics commonly used to treat brucellosis. **Methods:** *Brucella* strains were characterized by PCR using *B. melitensis* specific primers. Antimicrobial sensitivity was obtained using Kirby-Bauer disk diffusion and E-test methods. **Results:** All isolates were confirmed as *Brucella melitensis* by standard microbiological methods and a Polymerase Chain Reaction (PCR) technique. The average Minimum Inhibitory Concentration (MIC's) obtained by the E-test [MIC100] were tetracycline (TCN) (0.125 mic/ml), doxycycline (0.19 mic/ml), trimethoprim-sulfamethoxazole (SXT) (0.25 mic/ml), gentamicin (Gn) (1.5 mic/ml), rifampicin (R) (2.0 mic/ml) and streptomycin (SM) (2.0 mic/ml). Zone diameters obtained by Kirby-Bauer techniques showed a high reverse correlation with the MIC's of TCN, R, SXT, Gn and ceftriaxone. The 'r' values were -0.98, -0.98, -0.93, -0.92 and -0.97, respectively. **Conclusion:** *Brucella melitensis* is the major cause of Brucellosis in Egypt. Our in vitro findings support the current empirical regimen for the treatment of brucellosis with either doxycycline and streptomycin or septra and tetracycline. Sensitivity results supports a treatment role for all six antibiotics. The close correlation between inhibition zone size with the MIC suggests the Kirby-Bauer method could be standardized for Brucella. Further study and standardization of antibiotic susceptibility of Brucella species may prove particularly important in situations such as relapse or treatment failure.

Board 63. The Development of an In vitro Replication System for Nipah Virus

K. Halpin, B. Harcourt, W. J. Bellini, P. A. Rota; CDC, Atlanta, GA.

A new member of the family Paramyxoviridae emerged in Malaysia in late 1998. Nipah virus (NV) was responsible for the deaths of over 100 people, and also caused a respiratory disease in pigs, which devastated the country's pig farming industry. Initial characterization of NV showed that it is very closely related Hendra virus (HV). NV and HV represent a new genus within the Paramyxoviridae, which has some unique genetic properties. However, the biocontainment classification of NV (BSL-4) restricts the type and frequency of work conducted on this virus. Therefore, alternatives to the use of live virus for further characterization experiments are highly desirable. Here we report the establishment of a system to study NV replication that does not require the use of infectious virus. A minigenome was constructed to encode an NV genome-sense RNA analogue containing the gene for chloramphenicol acyltransferase (CAT) under the control of the putative NV transcription motifs and flanked by faithful copies of the NV genomic termini. Transfection of plasmids encoding the NV minigenome, nucleocapsid protein (N), phosphoprotein (P) and the polymerase protein (L), each under the control of T7 promoter, into CV1 cells infected with a vaccinia virus recombinant expressing the T7 RNA polymerase gave rise to detectable CAT activity. The levels of CAT expressed by the NV mini-genome replication system were equivalent to those expressed by a well-characterized, measles mini-genome system. This replication system will now be used to study transcription and replication of NV and to investigate the functional significance of the unique genetic properties of NV.

Board 64. Functional Properties of the Fusion and Attachment Glycoproteins of Hendra and Nipah Viruses

A. Tamin, B. Harcourt, P. E. Rollin, T. G. Ksiazek, W. J. Bellini, P. A. Rota

CDC, Atlanta, GA

Hendra virus (HV) and Nipah virus (NV) are recently emergent, related viruses that are capable of causing severe disease in humans and animals. The goal of this study was to examine the immunogenic and functional properties of the fusion (F) and attachment (G) glycoproteins of NV and HV. Vaccination of mice with recombinant vaccinia viruses (rVV) expressing either the F (rVV/NV-F) or the G (rVV/NV-G) proteins of NV induced neutralizing antibody responses to NV, with higher titers produced after vaccination with rVV/NV-G. Co-infection of Vero cells with rVV/NV-F and rVV/NV-G produced multi-nucleated giant cells, which were not visible in cells infected with either of the rVVs individually, and cell fusion was inhibited by antibodies to either NV-G or NV-F. When the homologous pairs of G and F proteins from either HV or NV were co-expressed in a transient expression system, extensive syncytia formation was observed within 24 hours. An equivalent amount of syncytia formation was observed when the heterologous pairs of F and G proteins from HV and NV were co-expressed. Therefore membrane glycoproteins of HV and NV, like the membrane proteins of other paramyxoviruses, are able to induce a neutralizing antibody response, and both proteins are necessary for cell fusion.

Board 65. The Laboratory Diagnostics of Plague Patients in Kazakhstan

B. M. Suleimenov, Sr.[1], B. B. Atshabar, Sr.[2]

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In the natural plague foci of Kazakhstan mainly are registered bubonic and bubonic-septic forms of plague. In single cases are dermal, anginouse-bubonic and pneumonic forms. The complex of plague laboratory diagnostics consists of three stages: the express-method with native material; accelerated methods (the crop of material on nutritious mediums, the infection of white mice and research after 10-15-24 hours); developed method (bacteriological and biological). Mandatory for the research, are blood, material from tonsil, the type of another material depends on disease forms. 10 ml of blood take in two tubes - 3-4 ml for the serum deriving, remaining with 20-30 unite heparin for other methods. From contents vesicle and pustule make washing by a syringe with a physiological solution. There is investigate differentiate the cortex from dermal ulcer, separated ulcers, punctate of an edge of an ulcer. Separately - right and left the tonsile, patch on tonsil and purulent tap. At the first 24-72 hours is investigate punctate of the center of central inflammation of bubon. In 72 hours after melting of tissue study punctate of an edge of the center. Differentially take contents fluctuating of the center and separated bubon of availability of a fistula. From the phlegm - traces of blood, pus. The feces of septic and anginouse forms. At meningitis syndrome is investigate the liquor. At a corpse - besides from parenchymatous organs, marrow (if necessary), surface lymphatic gland, is necessary mesenteritic lymphatic gland. For increase of possibility of isolation microbe from material to make crop of 4-6 samples of the same material. For the serological research to Fга 1 to use at once three variants of sample - are native and in titers 1:10, 1:100. These methods used in practice during many tens years. The last cases of people's plague in Kazakhstan were registered on station Saksaulsk (Kyzylorda oblast, August, 2001). At first in this region two patients at the ages of 13 and 41after great number of fleas bites was registered with bubonic-septic forms of plague with thigh localization of bubo. One of them is died (late hospitalization). After 24 hours in blood and bubo punctate was observed continuous growth. The Fra 1 from bubo punctate is 1:81920, from blood is 1: 320. The white mice died from plague in 2-3 days. The microbe was isolated from lymphatic gland and lungs (2 colonies). The Fra 1 was founded only in lymphatic gland - 1:5120. During medical treatment of second patient were founded the antibodies to Fra1 after 8 days - 1:320, 10 days -1:2560. In 1999 the rare anginouse-bubonic form of plague was registered. Y.pestis was isolated only from right tonsil with marked center of inflammation and from faces. The titer of antibodies is 1:320 on the 7th and 1:80000 on the 15th days. The devised scheme of plague laboratory diagnostic is simple in execution, effective and adapt to local conditions.

Board 66. Efficiency Improved Enterotoxic Antigen Erithrocyte Immunoreagents in Cholera Diagnostics

B. M. Suleimenov, Sr.[1], I. S. Arakelyan, Sr.[2], E. E. Li, Sr.[2], I. B. Utepova, Sr.[2], R. S. Mussagalieva, Sr.[2], T. Khamzin, Sr.[3]

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The registration of specific antibodies to enterotoxic - choleragen with allowance of regional features of cholera epidemiology, represents not only diagnostic, but also preventive value. The regular research of serums of patients blood with acute intestinal infections, in regions with often cholera diseases of people, it is rationally for information maintenance of preventive measures. Therefore it is necessary the availability of a highly sensitive and specific preparation for registration of antibodies to choleragen. The most active is commercial enterotoxic antigen erythrocyte preparation, registers maximum titer of antibodies in patients blood in cultivation of serum 1:10 000. We advance the method of production choleragen by following parameters: there is constructed the new selective medium for production choleragen and the optimum conditions are developed for production of deriving erythrocyte preparation. It was produced the choleragen V. cholerae

569B of type Inaba, V. cholerae 680 of type Ogava, V. cholerae O-139, V. cholerae 505 non 01. All these strains, except V. cholerae 569B we were isolated from the patients. All antigen erythrocyte preparation obtained on the bases of choleragen from different strains have the high specificity and sensitivity. All of them gave negative results in Reaction of Indirect Hemagglutination (RIHA) with commercial agglutinative serums О, Ogava and Inaba. The liquid variants antigen preparation till to lyophilization, registered specific antibodies in serum of cholera patients (О-139) for 20 day of disease in the range of 1:500 000-1:1000 000. After the lyophilization were registered the positive results of reactions in the range of this serum of 1:125 000-1:500 000. In 2001 (September) was investigated about 300 serums of patients infected by cholera Eltor type of Inaba in Aktau, Mangyshlak oblast. The range of positive reactions of RIHA from the patients in critical period of process changed from 1:20 to 1:160000. In control reactions with commercial preparations the titer of positive reactions did not exceed 1:10 000 Obtained preparations are perspective in cholera diagnostics and in realization of prophylaxis measures.

Board 67. Case of Hantavirus Pulmonary Syndrome in Europe

P. Caramello[1], F. Lipani[1], R. Balbiano[1], F. Canta[1], L. Bonino[2], C. Moiraghi[2], F. Navone[2], V. Gay[2]

[1]Malattie Infettive A, Osp. Amedeo di Savoia, Torino, ITALY, [2]Medicina d'urgenza, Ospedale Molinette, Torino, ITALY

Abstract Withdrawn

Board 68. West Nile Virus Activity in Israel In 2001: Human and Mosquito Infections

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Background and Objectives: Following an outbreak of West Nile (WN) fever in 2000 the virus activity was closely monitored in humans and mosquitoes in 2001. We present laboratory results of the human and mosquito testing. **Methods:** The case definition for laboratory diagnosis in 2001 included only meningitis and encephalitis cases. Human infections were monitored by testing for IgM antibodies primarily in adults age 18 y and above. RT-PCR was attempted on CSF and pre-seroconversion sera. Between April 24 and November 14, mosquitoes were collected in high-risk areas. 534 mosquito pools were tested for presence of WN virus genome by real-time RT-PCR, TaqMan., identifying the ENV and NS5 regions. Virus isolates were compared to the year 2000 isolates. **Results:** In 2001, 44 out of 1358 patients were positive (3.2%) and 3 patients died (case fatality rates: 6.8%). The fatal cases were confirmed by positive TaqMan results. In 2000, 439 out of 1600 patients (27%) were positive and 29 died (case fatality rate: 6.6%). 20 out of 534 mosquito pools (3.7%), containing 899 out of 19499 (4.6%) of Culex pipiens and Culex perexigus species had WNV sequences. Virus was isolated from 8 pools, and molecular analysis of the PrM/M/ENV genes revealed 2 lineages. Similar to 2000 findings, one most closely related to the 1999 New-York isolates, and the other to the 1997 Romanian isolate. These lineages were reported by others in Israel in birds and horses since 1998 as well. The geographic distribution of the clinical cases and the positive mosquito pools was partially overlapping. Two main geographic foci of WN fever in 2000 were not affected in 2001. **Conclusions:** Given the narrow case definition for WN laboratory testing in 2001, and the high activity of Echo4 causing aseptic meningitis during the same months as the WNV activity, we have not yet enough evidence to determine if the 2001 activity represents an outbreak or normal endemic situation. However, the presence of the same WN genomic lineages in birds, humans and mosquitoes for more than 3 years is suggestive of endemic activity.

Board 69. Environmental Risk Factors and *Campylobacter* infection – An Ecological Approach Using a Geographical Information System

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Campylobacter spp is the most common cause of acute bacterial gastroenteritis in Sweden. Case-control studies to identify risk factors have been conducted in several countries during the 90s, but still many cases remain unexplained. The geographic distribution of *Campylobacter* infections varies substantially, and there are many environmental factors that may influence the observed pattern, but few studies have investigated the influence

of these factors. Geographical Information Systems (GIS) offers an opportunity to use routinely available surveillance date in ecological studies in order to investigate the association betweens variables showing a geographic pattern and disease incidence. This method can complement traditional approaches to the investigation of risk factors for *Campylobacter* infections, both in outbreak situations and for sporadic cases. We conducted an ecological study on the association between environmental variables related to water and livestock and *Campylobacter* incidence in Sweden 1998 - 2000. Information on cases and environmental factors were collated and plotted using GIS. Pearson correlation coefficients and multiple Poisson regression were used to estimate the strength of the associations. Positive ecological associations were found between *Campylobacter* incidence and average water-pipe length per person, with ruminant density, and a negative association with percentage of people having public water supply. This indicates that drinking water and contamination from livestock may be important factors in explaining part of the sporadic human *Campylobacter* cases.

Board 70. Induction of Cellular Angiogenic Factors in Macrophages by *Bartonella henselae*

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Bartonella henselae is a bacterial human pathogen whose natural reservoir is the domestic cat. The emerging zoonotic syndromes associated with *B. henselae* are cat-scratch disease (CSD) and bacillary angiomatosis (BA). CSD is the primary manifestation of *B. henselae* infection in the immunocompetent individual and the most common cause of chronic, benign adenopathy in children. However, in the immunocompromised individual, infection tends to be systemic and includes fever with bacteremia. In addition, *B. henselae*-induced angiogenesis or BA is the primary manifestation of infection in HIV-positive, immunosuppressed individuals, and chronic alcoholics. The mechanism by which BA developes remains unclear. We hypothesize that *B. henselae*-infected macrophages may induce the production of cellular angiogenic factors that may in turn cause endothelial cell (EC) proliferation. The induction of angiogenic factors in differentiated human promonocytic THP-1 cells upon infection with live or killed *B. henselae* was evaluated. Supernatants analyzed by ELISA demonstrated that both, vascular endothelial growth factor (VEGF), a direct positive regulator of angiogenesis, and interleukin-1 beta (IL-1ß), a potentiator of VEGF, were induced in THP-1 upon infection with live or UV-killed bacteria. Similar results were observed when macrophages were pre-treated with cytochalasin D, a phagocytosis inhibitor, suggesting that bacteria-cell attachment is sufficient for VEGF and IL-1ß induction. Neither VEGF nor IL-1ß was produced when heat-killed (70º or 100º C) bacteria were used. In addition, conditioned medium from infected macrophages induced the proliferation of human microvascular endothelial cells (HMEC-1) thus demonstrating angiogenic activity. The data suggests that VEGF and IL-1ß are linked to a paracrine angiogenic loop promoting the development of bacillary angiomatosis during *B. henselae* infection.

Board 71. A Case of Fatal Autochthonous Acquired *Angiostrongylus cantonensis* Infection in Jamaica

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Human infection with *Angiostrongylus cantonensis* can be serious and life threatening. Once thought to occur only in Southeast Asia and Pacific islands, infection in both man and rats, the normal definitive host, appears to be spreading. Infected rats have been reported from Egypt and the Caribbean. Recently, human infection has been recognized in the United States (Louisiana), Australia, Africa and Jamaica. We report the occurrence of a fatal infection with *A. cantonensis* in a 14-mo-old male Jamaican child who, until the time of his illness was developing normally. Initial complaints were itching and restlessness progressing to poor appetite, abdominal distention, and fever. The child was admitted to hospital, where his condition progressively deteriorated, marked by respiratory stridor, poor head control, weakness of limbs, and decreasing consciousness. Differential diagnosis included encephalitis, Guillian-Barre syndrome, and meningitis. Treatment with antibiotics and dexamethasone was started but death occurred on day 35 post-admission. Examination of stained sections of the brain and lungs revealed intense inflammation, eosinophilic meningo-encephalitis and numerous sections of worms identified as *A. cantonensis*. The child had not traveled outside of Jamaica. This is the first case of fatal *A. cantonensis* infection recognized in Jamaica. The case in conjunction with a recent outbreak in a group of travelers to Jamaica and the finding of the parasite in rats and snails on the island indicate that A. cantonensis is well established in Jamaica and poses risk of infection to both residents and travelers alike.

Board 72. The Incursion of West Nile Virus into Canada in 2001

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West Nile (WN) virus was first detected in the Western Hemisphere during a 1999 outbreak of viral associated illness and death among humans, animals, and birds in New York state. As of December 14th, 2001 the virus had spread to 26 additional states, the District of Columbia, the Cayman Islands and Canada (this report). To undertake surveillance for the possible incursion of WN virus into Canada, an avian surveillance system was put into place the spring of 2001. Kidney and brain tissues from dead birds (Corvid species) collected at various sites in Saskatchewan, Manitoba, Ontario, Quebec, and the Atlantic Provinces were homogenized in tissue culture medium and RNA isolations performed. Purified RNA was screened for the presence of WN virus genome by TaqMan and one-step reverse transcriptase (RT)-PCR diagnostics. Confirmation of WN virus infection within bird tissues was carried out by viral isolation and immunohistochemical (IHC) procedures using WN virus specific antisera. To date a total of 2828 Canadian birds have been analysed for WN virus infection in a variety of tissue types. PCR based diagnostics revealed the presence of viral genome in a crow collected in Windsor, Ontario on August 8/ 2001. Virus isolation, IHC analysis, and amplicon sequencing confirmed that this bird was infected with the North American strain of WN virus that was responsible for the 1999/2000 outbreaks in north eastern United States. From mid-August onward, WN virus has been detected in a total of 127 birds (106 crows, 21 blue jays) from 12 different health units in southern Ontario. The latest date documented for finding a WN virus infected bird was October 29. Dead bird submissions from other Canadian provinces have thus far shown no evidence of infection. In addition to dead bird surveillance a study was undertaken to determine the occurence of WN virus in various mosquito species collected at distinct sites in southern Ontario during the months of

August and September. A total of 1092 pools of mosquitoes (5852 individuals) were screened for the presence of WN virus genome by RT-PCR. Three Culex pipiens pools were found to be positive for viral RNA. Sequencing of capsid and membrane protein encoding regions of a number of Canadian WN virus isolates showed nucleotide sequence changes when compared to various genotypes currently circulating in the US. Further genetic characterization is ongoing to determine the extent of sequence divergence that presently exists among Canadian and American isolates.

Board 73. Intestinal Heterophyidiasis: An Emerging Parasitic Zoonosis In Southern Philippines

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Heterophyidiasis is an infection of the small bowel caused by heterophyid flukes. In the Philippines, the prevalence of heterophyidiasis has been noted to be low. In in connnection with an outbreak of intestinal capillariasis in Southern Philippines, community surveys showed heterophyid infection rates of 16.7% and 15.7% in 1998 and 1999, respectively. An active case detection was conducted in San Isidro, Monkayo, Compostela Valley in the early part of May 2000 by a team from College of Public Health, University of the Philippines Manila. An interview of patients with a history of bowel disturbance in the past 4 weeks prior to the survey was conducted, and stool specimens from the same patients were examined using Kato-Katz method and/or Formalin ether concentration technique. With Kato-Katz method, heterophyid eggs were counted, and a frequency distribution was prepared using a proposed scheme for classification of intensity. Key informant group interviews were also conducted to help describe practices of food preparation and eating habits that possibly expose local residents to infection. Possible intermediate hosts were also collected from the field and were forwarded to the Institute of Marine Biology of the University of the Philippines for specimen identification and examination of the larval stages of heterophyid fluke and other helminths. A total of 87 patients in Barangay San Isidro, were diagnosed to have heterophyidiasis. Overall infection rate was 36.0%. Infection rates were higher in age groups 5 years old and over, although infection rate in children less than 5 years of age may not be considered insignificant. Males 60 years old and younger had higher infection rates compared with females in the same age groups. To determine efficacy of treatment, stool specimens were collected from patients who were diagnosed to have heterophyids 7 to 14 days after treatment with praziquantel. Cure rate among those with heterophyidiasis was excellent at 97.1%. Collected samples of possible intermediate hosts, which included freshwater fishes and other aquatic animals were examined and found to be infected with various parasites in different life cycle stages. Parasites were found in the scales, gills, muscles, intestines, and caeca. The high incidence of parasites in freshwater fishes may have an important impact on the health of the community as a whole considering that fish is a major source of food in the area. Early diagnosis and treatment of heterophyidiasis are important to ensure prompt resolution of infection, hence, decreased morbidity and decreased chances for complications like heart or brain involvement. This study illustrated the importance of recognition of the possible problem of heterophyidiasis and other food-borne parasitoses, accurate laboratory diagnosis, and recognition of possible intermediate hosts that will be crucial for control and prevention of this health problem.

Board 74. Expansion of WNV Activity in Massachusetts During 2001

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Following the emergence of West Nile Virus (WNV) in New York City in 1999, the Massachusetts Arbovirus Surveillance Program was expanded to track not only Eastern Equine Encephalitis Virus but also WNV. In 2000, the virus was found primarily in birds, especially crows. During the 2001 season, however, virus was associated with three human cases, (ages 70, 72 and 89), including one fatality, with onsets from mid-September through early November. The record breaking warm weather during the fall is thought to have played a role in the extension of this arboviral season. Another striking feature of the reappearance of WNV was an outbreak in horses; 37 clinical cases were laboratory confirmed with onsets between August 28 and October 15. Only one clinical case and a second infection were documented previously in the state. Once again large numbers of dead birds were reported, and 1104 tested positive for WNV by RT-PCR. The total increased over the 849 found positive in 2000, even though the routine collections were suspended in many towns during September and October and not all submissions were tested. Crows and blue jays accounted for 93% of the positives, but 18 additional avian species were also virus positive. Geographically, the virus spread throughout eastern Massachusetts. A total of 25 mosquito pools were WNV positive in cell culture and/or RT-PCR compared to 4 isolates the previous summer. Mosquito trapping will resume in the spring, but human and veterinary surveillance testing continues.

Board 75. Epidemiological Survey of Bacterial Colonization in Poultry Production Workers and a Human Referent Population

J. P. Furuno

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Background: Cases of human disease have been attributed to bacterial infections associated with consumption of poultry products. Few studies have addressed the possible transfer of microorganisms from agricultural production into the human community through other (non-food) pathways. We conducted an epidemiological survey of bacterial colonization in poultry production workers and a human referent population. **Methods:** This was a pilot, cross-sectional study in the Delaware/Maryland/Virginia (Delmarva) region; an area with high-density chicken growing and processing. Poultry industry workers and community residents >18 yrs were enrolled; persons working in health care and those with recent foreign travel were excluded. Exposure assessment was performed using questionnaires administered by trained interviewers in English or Spanish. Additional exposure assessments were conducted by visits to chicken houses in Delmarva. Each participant provided a fresh stool sample. Aliquots of specimens were incubated at 42o C in enrichment broth and transferred to blood agar plates under microaerophilic conditions. *Campylobacter jejuni* were identified biochemically as oxidase and catalase positive colonies that hydrolyzed both hippurate and indoxyl acetate. **Results:** Thirty-four subjects were enrolled in the study, including whites, African Americans, and Hispanics. A high prevalence of *campylobacter* colonization was found: among community residents 100% (9/9) were positive; among workers in contact with live chickens 41% (7/17) were positive; and among workers in poultry processing plants 63% (5/8) were positive for *campylobacter*. **Conclusions:** These results suggest a high prevalence of *campylobacter* exposure among residents in Delmarva living near poultry growing and processing facilities. Furthermore, they suggest that there are likely other pathways of exposure in rural communities in

addition to occupational exposures. These data highlight the importance of studying the prevalence of colonization in communities with a high likelihood of exposure. Research supported by a contract with US FDA, CVM.

Board 76. Reverse Genetics for *Bunyaviridae*: Rescue of Crimean-Congo Hemorrhagic Fever Virus (CCHF) Minigenomes

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In order to manipulate the viral RNA genomes of different members of the family *Bunyaviridae*, we have used an RNA polymerase I expression system based on the approach recently published for Uukuniemi virus (J. Virol. 75: 1643-1655). A cDNA consisting of the CAT- or GFP-ORF in the antisense orientation flanked by the 5` and 3` terminal non-coding sequences (S-segment) of a Crimean-Congo Hemorrhagic Fever (CCHF) virus was inserted between an RNA polymerase I promoter and terminator. Following transfection, the cellular RNA polymerase I generated an artificial vRNA segment (minigenome) without any end modification, e.g. CAP structure, poly(A)-tail. The viral proteins necessary for transcription and replication of this RNA minigenome were provided by CCHF-superinfection, which was performed under biosafety level 4 conditions. Using this approach, CAT activity/GFP fluorescence was observed, demonstrating that the helper virus was able to recognize the pol I transcript as an artificial genome segment. Our data further suggests that the RNA polymerase I expression system can be used for the manipulation of genomes of bunyaviruses with a high efficiency, despite the fact that the replication cycle of these viruses takes place exclusively in the cytoplasm of the cell. Different strategies to optimize the production of recombinant virus will be discussed. This is the first step towards the successful rescue of a human-pathogenic member of the family *Bunyaviridae*. In future we will use the RNA pol I system in combination with expression plasmids encoding the viral proteins which will allow us to rescue infectious CCHF particles without the need of a helper virus. We believe that the continued improvement of this system will facilitate the development of attenuated, recombinant CCHF viruses that can be used for studying the pathogenesis and the host immune response of this important viral pathogen.

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Monday, March 25, 10:00 a.m.
Grand Hall East

Board 77. Surveillance and Genotyping of Norwalk-like Virus (NLV) in Specimens of Viral Gastroenteritis Outbreaks in New York State (NYS) Over a Twenty-Month Period

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NLVs have been recognized as one of the leading causes of viral gastroenteritis with an estimated 23 million cases nationwide per year. Based on trend analysis of 1979-1995, approximately 3,000 adult deaths occurred annually from an estimated 267 million disease episodes. But an etiologic agent could be detected in <10% of these cases due to unavailability of sensitive and specific diagnostic tests. Molecular methods now available enable the detection of NLVs in clinical specimens. Consequently, NLV strains can be identified and linked to outbreaks in multiple locations, tracing them to their sources in contaminated food and water. The endemic disease burden caused by NLVs remains unknown. Furthermore, contributions by other diarrhea-causing viruses like rota, enteric adeno and some enteroviruses have not been thoroughly investigated. In a collaborative study with the CDC and other EIP sites, this investigation was designed to assess the contribution of viruses to gastroenteritis outbreaks in NYS. From January 2000 to August 2001, we tested approximately 180 non-bacterial stool specimens received from 43 gastroenteritis outbreaks throughout the state. Methods used were RT-PCR and nucleotide sequencing for detecting NLVs; ELISA for rota-; and tissue cultures (RhMK, A549, RD) with IFA and neutralization for entero- and enteric (types 31, 40, 41) adenoviruses. Two primer sets and automated nucleotide sequencing analyzed the strains from both genogroups I and II of NLV in these outbreaks. The patients, mostly adults, with the majority female (54% : 43%) exhibited symptoms such as diarrhea, nausea, vomiting, fever, abdominal cramps and headache. NLVs were the sole viral agent detected in 54% (81/150) of all specimens tested from 30 out of 43 outbreaks (70%). Genogroup II NLV strains predominated in >90% of the outbreaks, including Spykenisse and Gwynedd. The outbreaks appeared to be more frequent (69% in 2000, 61% in 2001) in the 6 warm weather months, perhaps relating to increased outdoor activities involving food. Interestingly, two NYS counties experienced multiple outbreaks during 2000 and 2001. In one county, the same genogroup II virus caused more than one outbreak, while in the other, viruses of different genogroups were responsible. Thus, it is evident that NLVs are a predominant pathogen of non-bacterial gastroenteritis in NYS. Furthermore, trends of NLV-infections can now be investigated both among and within regions across the counties in NYS with a focus on connections between genogroups and geographic location. (Supported in part by a CDC/EIP Viral Gastroenteritis Project Grant).

Board 78. Acute and Long-Term Mortality Associated with Foodborne Bacterial Gastrointestinal Infections: A Registry Based Study

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Background: Despite marked improvements in the living conditions and hygienic standards, foodborne bacterial infections have a major impact on the public health and economy of the industrialized countries. We conducted a registry based, matched cohort study to determine the excess mortality associated with infections with *Salmonella*, *Campylobacter*, Yersinia enterocolitica and Shigella spp and to address the issue of interaction with pre-existing illness. **Method:** By using data from the National Registry of Enteric Pathogens and the Danish Civil Registration System, we were able to estimate the long-term effect on survival. Additionally we collected data on admission and discharge diagnoses from The Danish National Patient Registry and the Cancer Registry, thereby allowing us to control for pre-existing illness. By survival analysis (conditional proportional hazards regression) we estimated one-year-mortality among patients compared with a sample of the general population in Denmark, matched by age, gender and county of residence. **Results:** A total of 48,857 patients, distributed over 26,974 *Salmonella*-cases, 16,180 *Campylobacter*, Yersinia 4,045 and Shigella 1,658 were registered in the National Registry of Enteric Pathogens. Among patients 1,026 (2.10%) deaths were registered up to one year after infection. 3,353 (0.69%) deaths were identified among 487,150 people in the reference group. Patients infected with one of the four enteric pathogenic species had a 3.2 times higher mortality than referents (95 % confidence interval (CI) 3.0-3.5). After adjusting for co-morbidity this was reduced to 2.3 (95 % CI 2.2-2.5). The relative mortality within the first 30 days of infection (acute mortality) was high in all four bac-

terial groups (*Salmonella*: RR 11.8, *Campylobacter*: RR 5.0, Shigella: RR 31.8 and Yersinia: RR 4.7), compared with the reference group. Furthermore we found an excess long-term mortality up to six month after infection with a *Campylobacter* (RR 1.6) or Yersinia (RR 2.1) species, and up to 1 year in *Salmonella* species (RR 1.3). In the group of patients without known pre-existing illness, we found an excess mortality among *Salmonella* (RR 2.4) and Yersinia (RR 2.8) infected patients up to one year after infection compared to the reference group. **Conclusion:** The four food borne bacterial species were all associated with a significant acute mortality, even when pre-existing conditions were taken into account. As a new finding, *Salmonella*, *Campylobacter* and Yersinia were associated with a significant long-term excess mortality. Only a part of this excess mortality could be explained by co-morbidity, in particular HIV-infection, metastatic cancer and leukemia. Our data suggest that current estimates of the burden of foodborne diseases underestimate the number of deaths from bacterial gastrointestinal infections.

Board 79. Meningococcemia-Liked Syndrome (*Streptococcus suis* type 2) is New Emerging Zoonotic Disease in Thailand, 1999 - 2000

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Background: On August 27, 2000, local epidemiologist in Lumpun Provincial Health Office (PHO) was notified from community hospital in Lumpun province where is in the northern part of Thailand that there was two suspected meningococcal meningitis cases. Then the rapid response team investigated this event during August 27 - September 30, 2000. **Objectives:** To verify diagnosis and the outbreak, to describe the outbreak, to determine mode of transmission and risk behaviors, to recommend prevention, control and further surveillance. **Methodology:** Reviewed medical record of both cases. Active cases finding by interview physicians, review medical records in previous year and search for contact case in community. The definition of the case was high grade of fever, severe myalgia and petichiae/echymosis with *S. viridans* or *S. suis* finding from blood or CSF or urine culture. And environmental survey was conducted within that village. **Results:** Two cases were male, 44 and 40 years old. Dates of onset were August 21, 2000 and August 25, 2000. The places at illness were different subdistrict but in the same district. Both of them died from sepsis and shock on August 26, 2000 and August 27, 2000, respectively. Clinical signs and symptoms were fever, severe myalgia and echymosis at face and trunk. The laboratory finding from hemo-culture of both cases were *Streptococcus suis* type 2. Medical record reviewing during Jan 1999 - July 2000, eight cases that met case definition were found. All of them were male, 44 years old mean of age (40 - 50 years old), all died. Date of onset of first case was 26 March, 1999. From epidemic curve, it showed 3 times of outbreak and the last time showed common source outbreak. 7/10 cases had history of few days taking raw pork or raw pork's blood before ill and had history of heavy alcoholic consumption more than 10 years. All of them had no history of feeding or contact with lived or dead pigs for 30 days before ill. **Discussion:** Previously in Thailand, there had no document of severe S. suis type 2 infection. From these outbreaks, we suspected meningococcemia and we could verify diagnosis and outbreak that caused from *S. viridans* or *S. suis*. The mode of transmission was taking raw pork or raw pork's blood and the risk was heavy alcoholic consumption. **Action Taken:** Health education was done in communities. In Lumpun province, the new surveillance for seeking meningococcemia-like syndrome from *S. viridans* or *S. suis* has been conducted the whole province and expand to adjacent provinces. Then we can find this syndrome in another two provinces.

Board 80. Investigation of an *Escherichia coli* O111:NM Outbreak in a Daycare in South Dakota

C. D. Carlson

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Background: *Escherichia coli* O111:NM is one of many non-O157 shiga toxin producing *E. coli* (STEC) known to cause diarrheal illness in humans. Very few outbreaks of non-O157 STEC have been reported in this country. Surveillance conducted by the State Public Health Laboratory (SPHL) the past two years has shown that this is one of the more common non-O157 serotypes isolated in SD. The SD Department of Health initiated the investigation after receiving a report of a shiga toxin positive, stool specimen. **Methods:** The index case was detected through the state's passive surveillance system on September 28, 2001. The initial investigation revealed that the patient attended a home daycare. Further investigation identified two additional symptomatic children from the same daycare. Stool samples tested at the SPHL were positive for shiga toxin by EIA on both additional symptomatic children. Stool samples were plated using standard culture methods. Individual colonies were tested for shiga toxin production by EIA. Toxin positive isolates were typed by pulsed-field gel electrophoresis (PFGE) using the standard PulseNet protocol for *E. coli* and sent to the Centers for Disease Control and Prevention (CDC) for serotyping. **Results:** The onset date of the initial case was Sept. 20, 2001. Possible sources of exposure identified included pet rabbits and the father's occupation at a feed mill. Little information was obtained from the food history. No other family members were ill. The second case had an onset of Sept. 25, 2001 with this child's brother becoming ill on Oct. 3, 2001. The only risk factor observed for these cases was contact with the index case at the daycare. The shiga toxin positive isolates on all three cases were identified by the SPHL as *Escherichia coli* and all had indistinguishable pulsed-field gel electrophoresis patterns. Laboratory results from CDC indicated all were serotype O111:NM. They were also positive for several virulence factors by PCR including shiga toxin 1 and 2, enterohemolysin and the attaching and effacing gene. All cases had positive stool samples for at least 3 weeks after onset of illness. **Conclusions:** This is the first identified outbreak of the O111:NM serotype in South Dakota. The source of this outbreak has not been clearly identified. The length of time from the onset of illness to diagnosis (8 days) resulted in a poor food history. The length of time between onset dates and the typical incubation period of STEC would suggest person to person transmission resulted in the 2 additional cases. Efforts need to be made to increase awareness of this type of organism and decrease the time between onset and reporting.

Board 81. Stool Specimen Practices in Clinical Laboratories, FoodNet Sites, 1995-2000

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Background: Clinical laboratory practice influences pathogen isolation rates and may affect the interpretation of laboratory-based surveillance data trends. To determine laboratory practice in the Centers for Disease Control and Prevention's Foodborne Diseases Active Surveillance Network (FoodNet) sites,

microbiologists at clinical laboratories which process stool specimens from FoodNet residents were surveyed in 2000 and results were compared to previous surveys conducted in 1995 and 1997. In 2000, FoodNet sites included Connecticut, Georgia, Minnesota, and Oregon and select counties in California, Colorado, Maryland, New York, and Tennessee. **Methods:** We ascertained laboratory methods for routine testing of stool specimens for *Salmonella*, *Shigella*, *Campylobacter*, *Escherichia coli* O157:H7, *Yersinia*, and *Vibrio* species, and estimated the number of stool specimens processed per year by clinical laboratories. FoodNet conducted active surveillance in those laboratories for all culture-confirmed cases of those pathogens. **Results:** Four hundred fifty-six laboratories processed stool specimens from FoodNet residents; the laboratories processed an estimated 440,000 stool specimens per year. The number of stools processed per 100,000 persons in all sites was 1504(range, per site, 823 to 2675 per 100,000 persons.) These laboratories reported routinely testing for *Salmonella*, *Shigella*, and *Campylobacter*; only 63% of laboratories routinely tested for *E. coli* O157:H7, 50% for *Vibrio*, and 49% for *Yersinia*. Among all stools submitted, the mean isolation rate for *Campylobacter* was 1.2% (range: 0.8% to 1.7%), 0.9% for *Salmonella*, (range: 0.5% to 1.1%), 0.4% for *Shigella* (range: 0.2% to 0.5%), and 0.2% for *E. coli* O157:H7 (range: 0.1% to 0.4%). Among the 160 laboratories surveyed in all three years, the proportion that reported routinely testing for *E. coli* O157:H7 increased from 59% in 1995 to 68% in 2000. Discussion: Variation in the identified rate of culture-confirmed illness caused by these pathogens may be explained, in part, by variation in laboratory practice; other potential factors include variation in physician practice and rates of illness in the population. Adherence to recently published IDSA/CDC guidelines for diagnosis and management of diarrheal diseases may help to balance concerns for patient management and public health surveillance in the era of managed health care.

Board 82. Surveillance for Guillain-Barré Syndrome in Oregon

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Background: Guillain-Barré syndrome (GBS) is an acute demyelinating condition that may complicate *Campylobacter* or upper respiratory infections. GBS is not reportable in Oregon, and its incidence is not known in that state. We sought to determine the burden and the proportion of GBS cases attributable to *Campylobacter* infection in Oregon. **Methods:** *Campylobacter* infections reported in Oregon during 1997 were reviewed. Oregon 1997 hospital discharge data (HDD) were queried for ICD-9 code 357.0. Hospitals with cases so identified were asked to review their own records for additional cases. Duplicates due to repeat admissions were removed. Data were abstracted from discharge summaries and laboratory records. Cases were classified as definite, probable, possible or non-cases according to published criteria. **Results:** Eighty-two cases of GBS were identified through the initial HDD query, including 24 cases identified by hospitals. Four medical charts were unobtainable. Twenty-two (28%) of the remaining 78 were classified as definite cases, 12 (15%) were probable cases, 10 (13%) were possible cases, and 34 (44%) were non-cases. Treatment modalities included plasmapheresis (32%), and IVIG (54%). The majority of the patients were discharged home (64%), 32% were discharged to extended-care facilities, and one person died. The mean number of days in the intensive care unit was 13 days. The statewide incidence of definite, probable, and possible cases was 1.4/100,000. Persons ≥ 65 years of age older had a higher incidence than younger persons (2.1 vs 1.3/100,000). Men had higher rates than women (1.6 vs 1.2). Of the 44 definite, probable or possible cases, 8 (18%) reported preceding gastrointestinal illness; 3 (7%) had confirmed *Campylobacter* infection. Seven-hundred thirty-seven cases of laboratory-confirmed *campylobacteriosis* were reported in Oregon during 1997. **Conclusion:** GBS caused 1 death and substantial morbidity in Oregon in 1997. Diagnosed *Campylobacter* infection was associated with at least 7% of GBS. About 0.4% of laboratory-confirmed *Campylobacter* infections were complicated by GBS. Efforts to prevent *campylobacteriosis* are likely to result in a decreased incidence of this serious complication.

Board 83. Trends in Indigenous Foodborne Disease (IFD) and Deaths, England and Wales - 1992 to 2000

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Background: Commitment to food safety is evidenced by high profile governmental initiatives around the globe. To measure progress towards targets policy makers need to know the baseline from which they started. **Aim:** To describe the burden (mortality, morbidity, new presentations to general practice, hospital admissions and hospital occupancy) and trends of indigenous foodborne disease (IFD) in England and Wales between 1992 and 2000. **Methods:** Routinely available surveillance data, special survey data, hospital episode statistics (HES) and National Statistics mortality data were collated and arithmetic employed to estimate the burden and trends of IFD in England and Wales. Adjustments were made for underascertainment of disease through national surveillance and for foreign travel. The final estimates were compared with those from the United States of America. **Results:** In 1995 there were an estimated 2,365,909 cases, 21,138 hospital admissions and 717 deaths in England and Wales due to IFD. By 2000 this had fallen to 1,338,772 cases, 20,759 hospital admissions and 481 deaths. In terms of disease burden the most important pathogens were *campylobacters*, *salmonellas*, Clostridium perfringens, Verocytotoxin-producing Escherichia coli (VTEC) O157 and *Listeria monocytogenes*. The ratio of food-related illness in the USA to IFD in England and Wales in 2000 was 57:1. Taking into account population rates this ratio fell to 11:1 and converged when aetiology and disease severity were considered. **Conclusion:** Reducing IFD in England and Wales means tackling *campylobacter*. Lowering mortality rates, however, also requires better control and prevention of *salmonellas*, Cl. perfringens, *L. monocytogenes* and VTEC O157.

Board 84. Outbreak of Multidrug-resistant *Salmonella* Newport Associated with Consumption of Italian-style Soft Cheese, Connecticut

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Background: In the previous few years, multidrug-resistant *Salmonella* Newport (MDR-SN) has emerged in multiple states as an important cause of human illness. In Massachusetts where a sustained increase has been seen, infection with MDR-SN was associated with exposure to dairy farms. In April 2001, the Connecticut (CT) Department of Public Health (DPH) Epidemiology Program noticed through routine surveillance an increase in reports of S. Newport isolates and began an investigation. Initial typing by pulsed-field gel electrophoresis (PFGE) suggested that the increase was caused by a single MDR strain, indistinguishable from the Massachusetts strain. **Methods:** To determine the magnitude and source of the outbreak, we reviewed previous surveillance data and conducted a case-control study and an environmental investigation. A case-patient was defined as a person reported to the DPH with illness onset April 1-25 and an isolate of the same PFGE type as the initial cases. Two or more controls for each case-patient were obtained

through progressive digit-dialing matching on local prefix and age group. Environmental investigation included collecting raw milk and cheese samples from the subsequently implicated cheese manufacturer and leftover cheese from ill cheese consumers. Samples were cultured for *S.* Newport and assayed for alkaline phosphatase. **Results:** Before April, only sporadic cases of *S.* Newport with a matching PFGE pattern were reported, averaging one every 2-3 months since January 2000. From April 1 through May 31, 26 MDR-SN isolates were reported. Case-patients lived in five CT counties; median age was 56 years (range: 15-88); 20 (77%) were female. Twenty-three case-patients received antibiotics for their illness. Eight cases were hospitalized, none died. The 15 case-patients included in the case-control study were more likely than their 40 controls to have consumed any of three fresh soft Italian style cheeses (100% versus 38%, $p<0.0005$). Results from consumption of basket cheese revealed the strongest association (73% versus 0%, $p<0.00001$). The implicated cheese maker obtained raw milk from a large multistate consortium. The cheese making process involved a heating step but not a formal pasteurization step. The outbreak strain was isolated from a sample of raw milk, but not cheese. Alkaline phosphatase was detected in four of eight cheese samples obtained from ill persons during the outbreak period. **Conclusions:** This outbreak was most likely caused by periodic inadequate heat treatment of contaminated raw milk used to make soft cheese. Beginning the on-site cheese making process with raw milk might add an unnecessary element of risk to cheese making, particularly for fresh soft cheese. The emergence of an MDR strain of *S.* Newport as a cause of human illness associated with dairy farm contact and/or consumption of dairy products appears to be a growing problem in the U.S.

Board 85. An Outbreak Of Typhoid Fever In Florida Associated With An Imported Frozen Fruit

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An outbreak of typhoid fever involving at least 16 persons in Florida during the winter of 1998-99 was investigated using case control, environmental and laboratory methods. The genomic profiles of the 15 confirmed cases were identical. Consumption of fruit shakes made with frozen mamey, a tropical fruit, was significantly associated with illness (matched odds ratio=7.6, 95% confidence interval, 1.4 to 81.3). Laboratory testing showed the fruit was heavily contaminated with fecal coliforms; no *Salmonella* enterica serovar Typhi (S. Typhi)was isolated. The frozen mamey was prepared in plants in Guatemala and Honduras. No further cases occurred after the frozen product was recalled. As our nation's food sources become increasingly globalized, outbreaks of exotic diseases linked to contaminated imported food will become increasingly common. This outbreak highlights the need for new approaches to ensuring the safety of our food supply.

Board 86. Higher Incidence of *Listeria* Infections among Hispanics: FoodNet, 1996-2000

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Background: Listeriosis, a disease caused by infection with *Listeria monocytogenes*, carries high morbidity and mortality. Infection with *L. monocytogenes* has been most commonly associated with the consumption of unpasteurized milk, soft cheeses, hot dogs, and deli meats. Prominent outbreaks among Hispanic communities in Los Angeles and North Carolina have been associated with the consumption of Mexican-style soft cheese made with unpasteurized milk. We sought to determine if people of Hispanic ethnicity have an increased rate of listeriosis in general. **Methods:** Active surveillance for listeriosis has been conducted in FoodNet sites since 1996. In 2000, listeriosis surveillance was conducted in eight FoodNet sites (California, Connecticut, Georgia, Maryland, Minnesota, New York, Oregon, Tennessee) encompassing approximately 29.5 million persons, or 11% of the US population. We analyzed demographic data on all cases of culture-confirmed listeriosis identified by FoodNet from 1996 to 2000. **Results:** From 1996 to 2000, a total of 474 culture-confirmed cases of listeriosis were reported in FoodNet sites. The five year average incidence for all sites was 0.4 per 100,000 population, ranging from 0.3 in MN to 0.7 in CT. The average incidence was 0.2 per 100,000 among non-Hispanics and 0.7 among Hispanics during the study period. Among non-Hispanics, the incidence was 0.2 in Native Americans, 0.2 in blacks, 0.2 in whites, and 0.4 in Asians. Although the incidence remained higher in Hispanics across almost all age groups, the disparity between Hispanics and non-Hispanics was greatest among infants < 1 year of age (11.9 per 100,000 vs. 1.0 per 100,000 respectively) and among Hispanic women of childbearing age (15-39 years, 1.1 per 100,000 vs. 0.1 per 100,000 respectively). The highest incidence of illness among Hispanic women of childbearing age was observed in the 30-34 age group (2.7 per 100,000). When comparing incidence by gender, Hispanic females (0.9 per 100,000) had a notably higher incidence than Hispanic males (0.5 per 100,000); incidence was similar by gender for non-Hispanics. **Conclusion:** In FoodNet sites from 1996 to 2000, there was a higher incidence of listeriosis among Hispanics compared with non-Hispanics, particularly in infants and women of childbearing age. Hispanic infants had a 12-fold greater incidence of listeriosis than their non-Hispanic counterparts; for Hispanic women 30-34 years of age, the incidence was 13-fold greater than for non-Hispanic women in the same age group. Additional studies of listeriosis focusing on these groups are needed to determine specific risk factors for infection. To reduce the burden of listeriosis, prevention strategies and educational campaigns that focus on protecting infants and women of childbearing age should be targeted towards the Hispanic community.

Board 87. Comparability of FoodNet and United States Populations

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Background: A key objective of the Centers for Disease Control and Prevention's Foodborne Disease Active Surveillance Network (FoodNet) is to estimate the burden of foodborne illness in the United States. FoodNet activities, however, are conducted within selected state health departments. The selection of these sites was not chosen to be representative of the U.S. population. We therefore evaluated the comparability of the FoodNet population to the U.S. population on the basis of several demographic characteristics and health indicators. **Methods:** Using 1996 U.S. Census data, we performed a demographic comparison of the original FoodNet population (Minnesota, Oregon and selected counties in California, Connecticut and Georgia) and U.S. population on the basis of age, gender, race and urban residence (metropolitan statistical area (MSA) distribution). Using Community Health Status Indicator (CHSI) Project data, we also compared the two populations on the basis of population density (persons per square mile) and percent at or below poverty. For the purpose of this investigation, poverty is defined as having a household income less than the poverty thresholds established by the U.S. Census Bureau. These thresholds vary by family size and composition.

Results: The original FoodNet (count: 14,281,096) and U.S. (count: 265,189,794) populations had similar age and gender distributions, but differed slightly with regard to race. The Asian population was overrepresented (FoodNet: 6%, U.S.: 4%). The Black and Hispanic populations were underrepresented (FoodNet: 11% and 6%, U.S.: 13% and 12%, respectively). The populations also differed in their proportion of urban residents (FoodNet: 99%, U.S.: 80%). County-level comparison indicated a lower population density among the 135 FoodNet counties (FoodNet: median= 31 persons per square mile; U.S.: median= 41 persons per square mile). The FoodNet population also had a smaller percentage of persons living at or below poverty (FoodNet: 11%; U.S.: 15%). **Conclusions:** The generalizability of FoodNet studies is somewhat limited due to slight demographic differences (e.g., Hispanic and Asian populations). Despite these differences, however, the distribution of the FoodNet population across several other demographic factors and health indicators is similar to that of the U.S. population. These data support the generalizability of FoodNet data to the U.S. population for the purpose of understanding the epidemiology of foodborne illness. Every year since its inception, the FoodNet catchment area has increased from approximately 14 million in 1996 to 34 million in 2001. Further analysis is being conducted to compare the expanding FoodNet population with the U.S. population.

Board 88. Age, Ethnic and Racial Disparity in *Salmonella* sertotype Enteritidis (SE): FoodNet, 1998-2000

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Background: *Salmonella* serotype Enteritidis (SE) emerged as the most common *Salmonella* serotype in the United States in the mid-1990s, reaching a peak in 1995. SE infections are most often associated with consumption of raw or undercooked shell eggs. The objective of this analysis is to describe the variation in SE incidence rates among the CDC's Foodborne Disease Active Surveillance Network (FoodNet) sites by state, age group, race, and ethnicity to determine where prevention efforts might be targeted. **Methods:** Since 1996, FoodNet sites have been conducting active laboratory-based surveillance at clinical laboratories for selected foodborne pathogens including *Salmonella*. Clinical laboratories forward *Salmonella* isolates to public health laboratories for serotyping. In 2000, FoodNet sites included Connecticut, Georgia, Minnesota, and Oregon, and selected counties in California, Tennessee, Maryland, and New York (29.5 million); 11% of the U.S. population. **Results:** In 1998-2000, 11,657 *Salmonella* cases were ascertained, of which 12% (1425) were SE. Enteriditis was the 2nd most common serotype. SE incidence rates were 1.9 per 100,000 in 1998, 1.7 in 1999 and 2.0 in 2000. Average annual incidence was highest in Maryland (4.8/100,000), followed by Connecticut (3.7) and was lowest in Georgia (0.9). The average annual age-specific incidence of SE was highest among children <5 years of age (4.2/100,000) and 5-9 years of age (2.1/100,000). There was no difference in age-specific incidence rates by gender. Of the 939 (66%) SE cases over 3 years of age whose race/ethnicity was known, average annual incidence was highest among Blacks (2.0/100,000) followed by Hispanics (1.2), and Whites (1.1). Incidence among Blacks was highest in Maryland (3-year average 7.4/100,000). **Conclusions:** Incidence of SE varied by site with the highest incidence in Maryland and Connecticut. Children under 5 years of age had an incidence of SE twice as high as other age groups. The incidence of SE in Blacks was higher than in other racial or ethnic groups. These differences in SE incidence warrant further study to identify risk factors for infection that may explain these variations. Surveillance data are useful for identification of groups for targeted educational programs to reduce the incidence of SE infection.

Board 89. A Pilot Study in FoodNet of the Use of Stool Collection Kits Delivered to the Home to Improve Confirmation of Etiology in Gastroenteritis Outbreak Investigations

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Background: In 68% of foodborne disease outbreaks reported to the Centers for Disease Control and Prevention (CDC), no etiologic pathogen is identified. In two-thirds of outbreaks of unconfirmed etiology, no stool specimens are submitted for laboratory testing. We studied the utility of using stool collection kits delivered to the homes of patients to improve rates of specimen submission and identification of an etiology in foodborne disease outbreaks. **Methods:** CDC and Foodborne Diseases Active Surveillance Network (FoodNet) sites in California, Maryland, and Tennessee initiated a prospective pilot project to collect stool specimens using kits during gastroenteritis outbreaks. Each site designed, implemented, and evaluated easy-to-use kits specific to the needs of their populations and health department laboratories. All kits included instructions, shipping labels, transport and packaging material, and a stool collection "hat" for the toilet. Two sites used a single specimen collection container, and one site used separate bacterial and viral collection containers with different media. The sites employed commercial and health department couriers and U.S. mail to deliver and retrieve the kits. **Results:** From April 1 to October 31, 2001, stool collection kits were deployed in 12 outbreaks (7 in Tennessee, 4 in Maryland and 1 in California), involving 248 ill persons. Kits were distributed to 59 ill persons, and 42 (71%), which included > 1 specimen from 11 of the 12 outbreaks were returned to state laboratories. Of these, 28 were returned via courier and 14 by U.S. mail. "Inability to produce a specimen" after receiving the kit from the health department was the most common reason for non-submission. The mean time from start of the outbreak investigation to receipt of specimens at the laboratory was 4.9 days. Of the 11 outbreaks for which kits were returned, an etiologic organism was confirmed in eight (72.7%); 6 Norwalk-like virus, 1 *Staphylococcus aureus*, and 1 *Salmonella* serotype Enteritidis. **Conclusion:** In over two-thirds of gastroenteritis outbreaks in which these stool collection kits were successfully deployed, an etiologic organism was identified. Delivery of kits to patients homes to improve rates of stool collection in outbreaks in which specimens might otherwise not be submitted could substantially reduce the number of outbreaks with an unknown etiology. However, these preliminary findings are based on a small number of outbreak investigations. The cost-effectiveness and feasibility of routine use of these kits requires further evaluation.

Board 90. Eating in Restaurants: A Risk Factor for Foodborne Illness? Findings from FoodNet to Be Explored by EHS-Net

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Background: Over 80% of Americans eat out at least once per week, and 46% of the U.S. food dollar is spent on food away from home. The Centers for Diseases Control and Prevention's Foodborne Disease Active Surveillance Network (FoodNet) provides a unique opportunity to investigate the potential relationship between foodborne illness and consumption of food outside the home. **Methods:** We compiled results of a random digit dialing telephone survey and several multi-state case-control studies, pertaining to consumption of food outside the home as a risk factor for foodborne illnesses. **Results:** Among 12,755 respondents to the 1998-1999 population survey, 83% said that they eat out at least once per week, and 16% ate out an average of 5 or more times per week. In a case-control study of *Salmonella* serotype Enteriditis with 182 cases enrolled, among persons with no recent international travel, consumption of chicken outside the home was associated with a matched odds ratio (mOR) of 2.1 (95% CI 1.2-3.4) and a population attributable risk of 25%. In a case-control study of E. coli O157:H7 with 200 cases enrolled, among persons consuming ground beef, eating a hamburger at a restaurant that was not part of a major fast-food chain was associated with a mOR of 10 (CI 1.3-82). In a case-control study of *Salmonella* serotype Heidelberg with 44 patients enrolled, illness was associated with eating eggs prepared outside the home (mOR=6.2, CI 1.2-31.7), particularly runny eggs (mOR=11.1, CI 1.22-63.1), with population attributable risks of 33% and 56%, respectively. In a case-control study of 64 persons with fluoroquinolone-resistant *Campylobacter*, among persons without recent international travel, illness was associated with eating chicken or turkey at a commercial establishment (mOR 4.3, CI 1.2-15). **Conclusions:** Findings from a number of FoodNet case-control studies suggest that consumption of food outside the home is associated with increased risk of specific foodborne illnesses. Refining data on the period of exposure for common risk factors will be important in better understanding this issue. The CDC's Environmental Health Specialist Network (EHS-Net) is a new program developed to improve our understanding of environmental causes of illness. Its initial focus will be evaluating risk factors associated with eating outside the home. Given the numbers of persons eating in restaurants regularly, further study is warranted to better understand the nature of those risks.

Board 91. Drinking Water Exposures and Perceptions among 1998-1999 FoodNet Survey Respondents

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Background: In 1996, Congress mandated that EPA and CDC produce a report to define a national estimate of waterborne illness attributable to municipal drinking water. As part of the report process, it was determined that there was a need to better characterize the drinking water consumption, behaviors, and exposure outcomes of the U.S. population. **Methods:** The Emerging Infections Program's Foodborne Diseases Active Surveillance Network (FoodNet) conducts population surveys that collect demographic, medical and food consumption information. EPA and CDC integrated water consumption and exposure questions into FoodNet surveys administered via random digit dialing to households within 7 FoodNet sites from February 1998 through February 1999. **Results:** Among 12,755 respondents, 63.8% identified municipal water, 17.8% bottled water, and 15.0% private well water as their primary source of drinking water. Residents of rural or farm areas were more likely to drink private well water than municipal or bottled water (p=0.001). Reasons for drinking bottled water included improved taste or odor (49.1%), avoiding chemicals (28.0%), and avoiding germs (16.5%). Bottled-water drinkers with children were more likely to express concern about germs in water (p=0.02). Thirty percent of tap water drinkers treated their water. The most cited treatment method, filtration (76.0%), was associated with higher income and higher education (p<0.001). Those with annual incomes less than $15,000 who treated their water favored pitcher filters or boiling their water. The reasons for choosing to treat water did not vary by income or education. Respondents (65.0%) did not know if their filter removed *Cryptosporidium*. Respondents did not consistently use the primary source of drinking water to prepare beverages. One-third of those who drank bottled or treated tap water reported using untreated tap water to prepare cold beverages. Diarrheal episodes (3 or more stools lasting 1 day or more or impairing daily activity, except episodes linked with chronic illness) did not show any significant associations with water exposures by univariate analysis. **Conclusion:** The results from the 1998-1999 population survey indicate socioeconomic factors and geographic location may influence the type of drinking water source and selection of treatment. Responses generally indicate that the public chooses water treatment for palatability, rather than to prevent harm from possible chemical or microbial contaminants. Continued data collection will indicate whether these patterns and beliefs remain temporally and geographically consistent as more FoodNet sites are included and will assist in the development of a national estimate of waterborne illness.

Board 92. Population-based Incidence of Infection with Selected Enteric Bacterial Pathogens for Children under 5 Years of Age, FoodNet, 1996-1998

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Background: Previous studies have shown that the disease burden of bacterial enteric infections falls disproportionately on children under 5 years old. This study describes population-based incidence rates of laboratory-confirmed infections with *Campylobacter*, *E. coli* O157, *Listeria*, *Salmonella*, *Shigella*, and *Yersinia* in children < 5 years of age in the CDC's Foodborne Diseases Active Surveillance Network (FoodNet), 1996-1998. **Methods:** Culture-confirmed cases of infection with these 6 pathogens were ascertained through active laboratory surveillance. The FoodNet catchment area included Minnesota, Oregon, and selected counties in California, Connecticut, Georgia, Maryland and New York. Incidence rates for each pathogen per person-year of observation (py) were calculated by year, site, season, sex, and age. Age-specific postcensus estimates for the 3-year period were used to calculate the FoodNet population. Incidence rate ratios and 95% confidence intervals (CIs) were used to estimate relative risk (RR) in those < 5 years. **Results:** There were 3,488,746 py for children < 5 years and 51,115,328 total py for all ages; children <5 accounted for 7% of total py. For children < 5 years, there were 5,210 cases of infection with any of the 6 pathogens, accounting for 21% of cases for all ages. By pathogen, the number of cases and percent of cases for < 5 years out of all reported FoodNet cases

was: *Campylobacter* 1505 (13%); *E. coli* O157 359 (29%); *Listeria* 25 (10%); *Salmonella* 1941 (27%); *Shigella* 1133 (28%); *Yersinia* 247 (53%). Culture-confirmed cases per 100,000 py for those < 5 were 43.1 for *Campylobacter*, 10.3 for *E.coli* O157, 0.7 for *Listeria*, 55.6 for *Salmonella*, 32.5 for *Shigella*, and 7.1 for *Yersinia*. For age < 5, RRs compared with age 5 and older for the respective pathogens were 2.1 for *Campylobacter*, 5.7 for *E. coli* O157, 1.4 for *Listeria*, 5.1 for *Salmonella*, 5.4 for *Shigella*, and 15.3 for *Yersinia*. Incidence rates varied widely across the 7 FoodNet sites. In general, for the 5 pathogens other than *Listeria*, sites with higher incidence rates for age < 5 also had high rates for age 5 and older, compared with other sites. However, for *Campylobacter*, *E. coli* O157 and *Shigella*, sites with higher rates for age < 5 also had a greater contrast between age < 5 and age 5 and over than did other sites. **Conclusion:** This population-based study confirmed a disproportionate disease burden for these enteric bacterial infections in children < 5 as both percent of cases and per 100,000 py. The absolute and relative disease burden for age < 5 years differed by pathogen and by FoodNet site. This disease burden suggests that investigation of risk factors specific to this age group and a review of current prevention and control strategies and their enhancement specifically for young children might lead to appreciable reductions in illness.

Board 93. Changing Epidemiological Patterns of *Salmonella* serotype Enteritidis in Barbados: Implications for Tourism and Trade

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Objective: To determine the etiology, sources and risk factors for *Salmonella* Enteritidis (SE) infections in Barbados, to compare its epidemiology with that of SE infections in Trinidad and to develop preventive measures. **Methods:** Retrospective (1996-1998) and prospective (August 1998-November 2000) descriptive epidemiological studies were conducted to determine the occurrence, distribution and potential risk factors for SE infections in Barbados. To determine the etiology for SE infections, a matched case control study of 30 cases and 60 age- and neighborhood-matched controls was conducted between February 1999 to November 2000. Standard written questionnaires were used for the prospective and case control studies, administered through face to face interviews. SE outbreaks were also investigated. *Salmonella* isolates were serotyped and phagetyped using standard methods. Data was analyzed in Epi Info version 6.04c software. **Findings:** The isolation rate per 100,000 population of SE increased from 1.1 in 1990 to 10.0 in 1999. Children < 10 years were most susceptible to SE infections (44 % cases, 39 infections per 100,0000). No distinct seasonal pattern was observed in the occurrence of SE cases. SE infection was found to be associated with the consumption of undercooked eggs (matched odds ratio [mOR]=43.5, 95% confidence interval [CI]=6.79-1737,p<0.00001) and undercooked chickens (mOR 8.23, 95%CI =1.57-73.6, p<0.01). In particular soft boiled eggs (mOR = 29.0, p<0.0001), scrambled eggs with soft yolks (mOR=8.39, p<0.001) and caesar salad (mOR =10, p<0.001) were the main implicated undercooked egg-containing foods. Three hotel SE outbreaks, involving visitors and 6 family outbreaks were investigated. Caesar salad, soft boiled and scrambled eggs, and undercooked chickens were implicated. Of the 60 isolates phagetyped, PT8 was most prevalent (33 cases, 55%), followed by PT4 (19 cases, 32%), PT2 (6 cases, 10%), PT24a (1 case) and PT11 (1 case) Ten cases (17%) were hospitalized , and 2 died (case fatality rate 6.7%). **Conclusion:**. This is the first reported analytical study of SE infections in Barbados. It highlights that in Barbados, the consumption of undercooked eggs and undercooked chickens are the major vehicles for SE infections, unlike our previous findings in Trinidad. SE PT8 and PT4 predominate. This is the first time that undercooked chicken has been associated with SE infection in the Caribbean, and it is also the first time that PT2 has been identified in the Caribbean. The findings of this study have important implications for public health, food safety, trade and tourism in Barbados. It has demonstrated the increasing impact of SE infection in local and visitor population which requires a "Farm to Table" for effective prevention and control.

Board 94. Hospitalizations Among Cases with the Most Common Serotypes of *Salmonella*: FoodNet, 1996-2000

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Background: *Salmonella* is a leading cause of gastrointestinal illness in the United States. Although there are over 2000 known serotypes of *Salmonella*, four serotypes account for the majority of reported infections. This analysis assessed severity of illness among the major serotypes of *Salmonella* cases reported to the Centers for Disease Control and Prevention's Foodborne Disease Active Surveillance Network (FoodNet), as measured by hospitalization rates and duration. **Methods:** A case of salmonellosis was defined as the isolation of a *Salmonella* species from any clinical source in a resident of the FoodNet catchment area during the years 1996-2000. In 1996, the catchment area included Minnesota, Oregon, and selected counties in California, Connecticut, and Georgia; subsequently, selected counties in New York, Maryland (1998) and Tennessee (1999) were added. The top four reported *Salmonella* serotypes were abstracted from the data set and analyzed for hospitalization and length of hospital stay. The median duration of hospitalization was calculated for each serotype and the proportion of hospitalized cases was compared, by serotype, using the chi-square test. **Results:** Between 1996 and 2000, 15,931 cases of *Salmonella* infection were reported to FoodNet. One hundred ninety-two cases with incomplete hospitalization data were excluded from this analysis. Of the 15,739 remaining, 2671 (17%) were hospitalized. Four *Salmonella* serotypes (*S.* Typhimurium, *S.* Enteriditis, *S.* Heidelberg, and *S.* Newport) comprised 53% of the hospitalized cases. Hospitalized patients with one of these serotypes had a median hospital stay of 3 days (range 1-157). *S.* Typhimurium accounted for 4015 (26%) cases; 778 (19%) were hospitalized and had a median hospital stay of 3 days. There were 2144 (14%) cases of *S.* Enteriditis; of which 322 (15%) were hospitalized with a median hospital stay of 4 days. *S.* Heidelberg represents 961 (6%) cases; 207 (22%) were hospitalized and had a median hospital stay of 4 days. There were 1045 (7%) cases of *S.* Newport, of which 102 (10%) were hospitalized with a median hospital stay of 3 days. **Conclusion:** The propensity of individual *Salmonella* serotypes to cause hospitalization among residents of FoodNet sites varies, ranging from 10% (*S.* Newport) to 22% (*S.* Heidelberg). However, the median duration of hospitalization among cases infected with the most frequent serotypes of *Salmonella* is similar, suggesting similar recovery rates independent of the serotype causing infection. Further studies are needed to determine reasons for the elevated hospitalization rates between *S.* Heidelberg and *S.* Typhimurium.

Board 95. Restaurant-Associated Behavior from the FoodNet Population Survey, 1998-99

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Background: A large proportion of foodborne outbreaks reported in the United States are associated with restaurants, but little is known about risk factors for sporadic acute gastrointestinal illness associated with restaurants. It is estimated that 46% of the average U.S. household's food-dollar is spent in restaurants. **Methods:** From March 1998 through February 1999, the Centers for Disease Control and Prevention's Foodborne Diseases Active Surveillance Network (FoodNet) conducted a random-digit dialing telephone survey to better understand factors potentially associated with acute diarrheal illness. The survey was performed in Connecticut, Minnesota, and Oregon and selected counties within California, Georgia, Maryland, and New York (population 21 million persons). We attempted to interview 150 persons each month in each state. Persons of all ages were eligible. Respondents were asked about restaurant patronage in the past 7 days and food preferences. **Results:** The questionnaire was administered to 12,755 persons. Of these, 463 (4%) reported eating at a fast food or sit-down restaurant frequently (≥7 times in the past 7 days). Among males, 7% ate out frequently as compared to 3% of females ($p<0.001$). Over 10% of persons between the ages of 16 and 25 years of age and 6% of young adults (26-45 year-olds) ate out frequently. Blacks (7%) were more likely to eat out ≥7 times in the previous week than whites (4%, $p<0.001$). Of all respondents, 10% ordered their restaurant hamburgers cooked rare or medium-rare. Of these, 87% considered a hamburger having pink on the inside to be cooked, compared to 20% of those who ordered medium, medium-well, or well-done restaurant hamburgers ($p<0.001$). One third (33%) of rare or medium-rare hamburger eaters cut their hamburgers to check how they were cooked as compared with two-thirds (66%) of non-rare hamburger customers ($p<0.001$). **Conclusions:** A large proportion of this survey's respondents ate ≥7 meals per week at fast food and sit-down restaurants. A substantial number of respondents admit to preferring established higher-risk foods, such as undercooked hamburgers, when they eat out. Further studies are necessary to explore the association between frequent restaurant patronage and acute diarrheal illness.

Board 96. Marked Regional Variation in the Incidence of Laboratory-Confirmed Bacterial Foodborne Illness: FoodNet, 2000

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Background: Each year in the United States, an estimated 5 million persons contract bacterial foodborne illnesses. The Foodborne Diseases Active Surveillance Network (FoodNet) is the principal foodborne disease component of the CDC's Emerging Infections Program. FoodNet strives to monitor the burden of foodborne illnesses and interventions designed to reduce them. **Methods:** In 2000, FoodNet conducted population-based active surveillance for laboratory confirmed cases of *Campylobacter*, *E. coli* O157, *Listeria*, *Salmonella*, *Shigella*, *Vibrio*, and *Yersinia* infections in Connecticut, Georgia, Minnesota, and Oregon, and selected counties in California, Maryland, New York, and Tennessee (total population 29.5 million). FoodNet contacts approximately 450 clinical laboratories at least monthly to ascertain cases. **Results:** 12,125 cases were identified; 4640 *Campylobacter*, 4237 *Salmonella*, 2324 *Shigella*, 631 *E. coli* O157, 131 *Yersinia*, 101 *Listeria*, and 61 *Vibrio*. The incidence per 100,000 population was highest for *Campylobacter* (15.7), followed by *Salmonella* (14.4), and *Shigella* (7.9). Lower incidences were reported for *E. coli* O157 (2.1), *Yersinia* (0.4), *Listeria* (0.3) and *Vibrio* (0.2). Substantial variation in incidence was reported among sites. The incidence of *Campylobacter* infections ranged from 6.6 per 100,000 in TN to 38.2 in CA. The incidence of *Salmonella* infections was less variable ranging from 8.9 in OR to 18.0 in GA. Rates for infections with specific *Salmonella* serotypes also varied; infections with *S.* Typhimurium ranged from 1.9 in CA to 3.7 in TN, *S.* Enteritidis from 1.0 in NY and TN to 5.1 in MD, and *S.* Newport from 0.3 in OR to 3.5 in TN. *Shigella* infections ranged from 1.1 in NY to 18.8 in MN. *E. coli* O157 infections ranged from 0.5 in MD to 4.6 in MN. Incidence also varied by age, especially for *Campylobacter* and *Salmonella* infections; for children <1 year of age, the incidence was 88.4 and 33.6, respectively, substantially higher than for other age groups. **Conclusion:** *Campylobacter* was the most frequently diagnosed pathogen; however, substantial regional variation occurred. The incidence of *Campylobacter* and *Salmonella* among infants is particularly high. Focused research into the reasons for these local differences may provide information about prevention that is of general use. Further prevention efforts are needed to meet the Healthy People 2010 objectives for *Campylobacter* (12.3/100,000 population), *Salmonella* (6.8/100,000 population), and *E. coli* O157 (1.0/100,000).

Board 97. The Burden of Diarrheal Illness in FoodNet, 2000-2001

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Background: An estimated 76 million food-related illnesses occur annually in the United States. Since 1996, the Centers for Disease Control and Prevention's Foodborne Disease Active Surveillance Network (FoodNet) has conducted periodic surveys of the population to determine the prevalence of diarrheal illness, and frequency at which persons with diarrhea seek medical care and submit stool specimens. These data are useful in determining the burden of foodborne diseases. **Methods:** The FoodNet population survey was designed to ascertain demographic, health, and food preference information among residents of Connecticut, Georgia, Minnesota, Oregon, and select counties in California, New York, Maryland, and Tennessee (population 29.5 million). The 131-item questionnaire was administered by telephone using standard Behavioral Risk Factor Surveillance System methodology. One member of each household contacted was randomly selected to complete the interview. Participants were asked about activities in the month prior to interview. We attempted to interview 150 persons per month in each of the FoodNet sites between March

2000 and February 2001. We defined acute diarrheal illness as ≥ 3 loose stools in 24 hours with impairment of daily activities or duration of diarrhea >1 day. **Results:** Of the 14,647 persons interviewed, 5761 (39%) were male; the median age was 41 years. Of the 14,046 respondents who denied a chronic gastrointestinal disease, 659 (5%) reported an acute diarrheal illness during the month prior to the interview. The prevalence of illness was highest among children less than 5 years (9%) and lowest among those over 65 years (2%). Rates of illness were similar among education, income, gender, and residence groups but ranged from 2% in Asian/Pacific Islanders to 10% in those of mixed race. Of those with an acute diarrheal illness, 18 (3%) reported blood in their stool, 152 (23%) sought medical care; of those seeking medical care 26 (17%) were asked to submit a stool specimen, and 73 (48%) were prescribed antibiotics for their illness. Only 7 (27%) of the 26 who submitted stool samples were prescribed antibiotics. Discussion: Diarrheal illness continues to impose a large burden of disease with a marked prevalence and high proportion of ill persons seeking medical care. However, few persons seeking medical care submitted a stool specimen, illustrating that there are many more ill persons for each laboratory-confirmed infection. Including a factor of 0.7 to account for test sensitivity, these data indicate there are roughly 36.5 cases of diarrheal illness for each diagnosed infection. This is similar to multipliers used to develop recent estimates, and suggests that changes in reported incidence may reflect changes in illness rates rather than changes in health seeking behavior.

Board 98. Isolation and Characterization of *Campylobacter jejuni* Isolates Obtained from Asymptomatic Human Volunteers

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Background: *Campylobacter jejuni* is the foremost cause of bacterial gastroenteritis in the United States. It is also demonstrating increased resistance to antibiotics, especially the fluoroquinolones. In Maryland, the incidence of gastrointestinal disease due to *C. jejuni* (6.8 cases/100,000 population) is significantly less than that caused by *Salmonella* (17.7 cases/100,000 population). In order to ascertain if there is an asymptomatic state for *Campylobacter* that might contribute to the decreased incidence of symptomatic disease, the Centers for Disease Control and Prevention's Foodborne Diseases Active Surveillance Network's (FoodNet) University of Maryland site analyzed fecal specimens from healthy human volunteers. **Methods:** Stool specimens were collected from Maryland residents who had not experienced a significant episode of diarrhea nor had taken antibiotics in the six months prior to specimen donation. Specimens were processed by adding an aliquot of stool into 5 ml of *Campylobacter* enrichment broth. Following a 48 hr incubation at 42^0C, an aliquot of the enrichment culture was transferred to a *Campylobacter* blood agar plate and incubated an additional 48 hr at 42^0C in a microaerophilic environment. Colonies were identified as *C. jejuni* if they were Gram negative rods, grew at 42^0C on the selective media, were both oxidase and catalase positive, and hydrolyzed both hippurate and indoxyl acetate. **Results:** Stools from 27 of the 222 asymptomatic volunteers (12.2%) yielded colonies that were identified as *C. jejuni*. Six of these asymptomatic isolates, along with 12 clinical isolates obtained from hospitalized patients, were analyzed for the presence of two putative virulence genes using the polymerase chain reaction. None of the asymptomatic isolates were positive for the presence of cytolethal distending toxin (CDT) genes, while 8/12 clinical isolates contained CDT genes. In vitro, CDT induces cell cycle arrest at the G_2 phase and ultimately cell death. In addition, the CiaB gene (associated with secretion of bacterial virulence factors) was not amplified in any of the asymptomatic isolates but was amplified in 11/12 clinical isolates. **Conclusion:** *C. jejuni* may be found in the gastrointestinal tract of individuals who do not have overt signs of disease nor a recent history of significant diarrheal illness. Currently the remaining asymptomatic isolates are undergoing analysis for the presence of CDT, CiaB and other putative virulence genes. Functional cell invasion assays and antibiotic susceptibility tests are also being performed to better characterize the differences between isolates that cause clinical disease and those that do not.

Board 99. Comparison of Disease Severity Between Outbreaks of Known and Unknown Etiology with ≥ 10 Ill Persons, FoodNet Sites, 1999-2000

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Background: Approximately 550 foodborne disease outbreaks are reported to CDC annually and two-thirds of these have an unknown etiology. Several factors, including disease severity and specimen collection and testing, are thought to contribute to a successful investigation. **Methods:** To compare disease severity between outbreaks of known and unknown etiology with ≥10 ill persons, we reviewed outbreak data collected in FoodNet sites in 1999 and 2000. FoodNet, the CDC's Foodborne Diseases Active Surveillance Network, includes Connecticut, Georgia, Minnesota, and Oregon and portions of California, Maryland, New York, and Tennessee, representing approximately 29 million persons (11 % of the United States population). A foodborne outbreak is defined as two or more cases of a similar illness resulting from ingestion of a common food. Etiology was determined using the guidelines for confirming a foodborne disease outbreak [MMWR 2000; 49(No. SS-1):54-61]. **Results:** From 1999 to 2000, 185 foodborne disease outbreaks with ≥10 ill were reported from FoodNet sites. Six outbreaks of ≥10 ill persons per million population were reported in FoodNet (range 2 per million persons in TN to 11 per million persons in MN.) Of these, 96 (52%) were outbreaks with a known etiology. Among these, 57 (59%) were due to Norwalk-like virus, 17 (18%) to *Salmonella* spp., 6 (6%) to *Escherichia coli* O157, and 16 (17 %) to other etiologies. Among the 96 outbreaks of known etiology, the median number of persons with vomiting was 12 (range 0 to 186), with diarrhea was 18 (range 0 to 243), and with fever was 9 (range 0 to 148). Among the 89 outbreaks of unknown etiology, the median number of persons with vomiting was 11 (range 0 to 72), with diarrhea was 14 (range 1 to 72), and with fever was 5 (range 0 to 30). In 18 (19%) outbreaks of known etiology, 50% or more of those ill sought health care; this compares to 2 (2%) outbreaks of unknown etiology. Outbreaks with a known etiology were also more likely to be outbreaks where ≥50% of those ill were hospitalized [4 (4%) outbreaks vs. 0 (0%) outbreaks] and where≥ 25% of those ill had bloody diarrhea [14 (15%) vs. 1 (1%)]. **Conclusions:** A little more than half of the foodborne disease outbreaks with ≥10 ill persons reported to FoodNet from 1999 to 2000 had a known etiology. Outbreaks of known etiology were more likely to result in health care visits, hospitalizations, and bloody diarrhea, possibly prompting a more aggressive investigation including microbial testing. Additional efforts are needed to determine the etiology of outbreaks with less severe symptoms. The use of courier services and mail-in kits to increase the number of clinical specimens submitted for etiologic testing during outbreaks may increase pathogen yield in outbreaks where patients are less likely to seek medical care.

Board 100. Outbreak of *Salmonella* Enteritidis Among Scandinavian Tourists Returning from Greece: The Need for Communication in the Detection of Outbreaks in Tourist Destinations

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Background: Greece is a popular holiday resort for Scandinavians. By July 2001, the Norwegian Institute of Public Health (NIPH) had received notifications of an unusually high number of cases with *Salmonella* Enteritidis among tourists returning from Greece. The National Reference Laboratory for Enteropathogens at NIPH noticed a cluster of cases with uncommon *Salmonella* Enteritidis (S.E.) of phage type 14b. An increase in the same phage type was also registered at the Swedish Institute for Infectious Disease Control (SMI) and the Finnish National Public Health Institute (KTL). In previous years, only sporadic cases infected by S.E. phage type 14b have been reported to Scandinavian surveillance systems. **Methods:** For the descriptive study, a case was defined as a person living in Norway, Sweden or Finland with a positive finding of S.E. phage type 14b after travelling to Greece within the incubation period for *Salmonella* Enteritidis. In addition, in order to identify possible source(s) of infection, case-control studies were conducted in Norway and Sweden. The Norwegian case control study was restricted to tourists who had been in the same area of western Crete between 30 July and 2 September. Twenty-five cases were matched with 45 controls by time of travel and tour operator. Isolates from patients were characterised by standard biochemical assays and phage typing methods at the reference laboratory. **Results:** The first case was reported in Norway on 28 May 2001. The first peak of cases was observed in mid-August, corresponding to the summer holidays in Scandinavia, and a second peak in mid-October corresponding to the autumn holiday. By 1 December, 301 cases had been reported in Scandinavia, 89 in Norway, 149 in Sweden and 63 in Finland. Fifty-one percent of the cases had been infected in Crete. The median age was 35 years and the sex ratio (M/F) was 0.9. In the Norwegian case control study, consumption of chicken was associated with illness (OR = 3.3, 95% CI: 1.0 - 11.3). Results from the Swedish study and the environmental investigation in Greece are not yet available. **Discussion:** Because the place of infection is not included in most *salmonella* notification systems, it is likely that the S.E. phage type 14b outbreak reported in Scandinavia represents only "the ears of the hippopotamus" of a larger outbreak in Europe. Poultry was the probable vehicle of infection. Collaboration among national institutes of public health can be an important tool in the detection and alert of outbreaks that occur in tourist destinations. Infections are often reported only in the tourists' home country, because they often prefer to seek medical care after returning. Therefore public health authorities in the tourist destinations may not be aware of the problem.

Board 101. Foreign-Travel-Associated Salmonellosis and Shigellosis: Oregon 2000-2001

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Introduction: Salmonellosis and shigellosis are important enteric diseases, and both are reportable in Oregon; during 2000 the incidences were 8.4 confirmed cases/100,000 population and 2.4 per 100,000 (excluding outbreak cases), respectively. Efforts to reduce their incidence by making food safer are under way. However, the extent to which salmonellosis and shigellosis in Oregon are attributable to foreign travel (FT) is unknown. **Methods:** Oregon's FoodBorne Diseases Active Surveillance Network (FoodNet) program has conducted active, laboratory-based surveillance for *Salmonella* and *Shigella* since 1996. Clinical laboratories report *Salmonella* and *Shigella* cases to local public health officials and submit all isolates to the Oregon State Public Health Laboratory for subtyping. Local health department case investigations are submitted to the Oregon Department of Human Services Office of Disease Prevention and Epidemiology for analysis. The case-investigation forms solicit information on FT during the five days before illness onset for non-typhoidal salmonellosis, three days for shigellosis, and 21 days for typhoid fever. We evaluated case travel histories by pathogen for the years 2000-2001 and compared them to travel histories reported during the same years in a FoodNet telephone survey of a stratified random sample of Oregonians. **Results:** Excluding outbreak cases, from January 2000 through October 2001, 518 salmonellosis and 168 shigellosis cases were reported from Oregon residents, for a total of 686 sporadic cases. Case-investigation forms were submitted for 665 (97%) of these. 59 (11%) of the salmonellosis cases and 46 (27%) of the shigellosis cases were associated with FT. FT was associated with 9 (82%) of 11 cases with *Salmonella* Typhi and 21 (32%) of 65 with *Salmonella* Enteritidis, but only 4 (3%) of 144 with *Salmonella* Typhimurium. 22 (31%) of 72 of *Shigella sonnei* cases and 16 (19%) of 86 *Shigella flexneri* cases were associated with foreign travel. Of the 105 FT-associated cases, 55 (52%) had traveled to Mexico; 24 (23%) to Asia; 9 (9%) to Africa; 8 (8%) to other Latin American countries; 5 (5%) to Europe; and 4 (4%) to other areas. In the 2000-2001 FoodNet population survey of 1,600 Oregon residents, only 1% reported FT in the seven days before the interview. **Conclusions:** 15% of sporadic salmonellosis and shigellosis reported in Oregon are associated with FT. Some of this may reflect a bias as to who is cultured; nevertheless, the striking differences in reported FT by *Salmonella* serotype suggest that much of the observed association is real. Studies are needed to identify the sources of these infections abroad.

Board 102. Restaurant-Associated Foodborne Outbreaks in Oregon, 1996-2001

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Background: Food preparation errors in restaurant kitchens expose the general population to viruses, bacteria and parasites. Much is known about the food preparation errors in restaurant (and other) kitchens that produce foodborne illness. Less is known about the proportion of restaurant-associated foodborne outbreaks attributable to these errors. **Methods:** We reviewed in detail summaries of foodborne outbreaks investigated by Oregon state and local health department epidemiologists from 1996 through 2001. We defined an outbreak as two or more non-householders who develop similar gastrointestinal illness at about the same time and are epidemiologically linked to a common source. Foodborne outbreaks were grouped by where the food was prepared (restaurants, private kitchens, institutions, or other settings). We then idenified restaurant-associated outbreaks that could have been prevented in the restaurant's kitchen. **Results:** From 1996-2001, Oregon epidemiologists investigated a total of 135 foodborne outbreaks. Of these, 64 (47%) occurred among restaurant patrons, 29 (22%) among persons who ate food prepared in institutions, 20 (15%) among persons who ate food prepared in private kitchens, and 22 (16%) among persons who ate food prepared in other settings. Of the 64 restaurant-associated foodborne outbreaks, causative agents were confirmed by laboratory testing in 19 (30%) and a food was convincingly implicated in 19 (30%). Four outbreaks were the result of eating products contaminated before they reached the restaurant; in 26 outbreaks food preparation errors

were not documented on the investigation summaries. Thirty-two outbreaks (50%) could have been prevented in the restaurant kitchen. These outbreaks were attributed to food handlers with Norwalk virus preparing food eaten raw (n=22); food not appropriately "hot-held" or thoroughly cooked (n=9); and cross-contamination of an uncooked food with a raw ingredient of animal origin (n=1). **Conclusions:** Restaurant-associated foodborne outbreaks account for nearly half of all outbreaks investigated. This may reflect the fact that such outbreaks are more likely to be reported than outbreaks originating in other settings. The most common cause of preventable outbreaks in restaurants was Norwalk virus, which has a human reservoir and which spreads as a result of poor food handler hygiene. Prevention research should focus on within-restaurant changes that make it difficult for food handlers not to wash their hands after using the toilet.

Board 103. Clinical and Molecular Investigation of a *Salmonella* Typhimurium DT104 Outbreak Due to Consumption of Raw Beef

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Background: *Salmonella enterica* serotype Typhimurium, definite phage type (DT)104 is a zoonotic pathogen. Since 1990 it has become an increasingly common cause of human gastroenteritis worldwide. In Israel the first human cases were reported in 1994. This strain is frequently associated with multidrug resistance to antimicrobial agents. The common R-type in Israel is ACST (A. ampicillin; C. chloramphenicol; S. streptomycin; T. Tetracycline). **Objectives:** To determine the epidemiological, clinical and molecular characteristics of an outbreak of severe gastroenteritis in a close community of East Asian workers. **Materials And Methods:** A comprehensive epidemiological investigation was carried out by the Ashkelon District Health Office employing interviews and survey of medical records. *Salmonella spp*. isolated from clinical sources and from suspected beef and cow blood samples were identified and tested by classical laboratory methods (serotyping, phagetyping and antibiotic resistance typing). The epidemiological and serological data were complemented by molecular investigation, using pulse field gel electrophoresis (PFGE). **Results:** In July 2001, fifty nine individuals of an East Asian group of workers developed severe diarrhea. Twenty five were hospitalized. Two patients developed secondary bacteremia. *Salmonella* typhimurium DT104 was isolated from the stool of all the 25 patients and the two blood samples. The epidemiological investigation revealed a suspected common source: Raw beef eaten by all on the day before onset of symptoms. The estimated attack rate in the exposed population was 100%. The median incubation time was 18h. The same *S*. typhimurium DT104 was isolated from samples of the suspected beef and cow blood. Application of PFGE with the restriction enzymes *Xba*I and *Avr*II to all isolates revealed the same PFGE pattern for all human and food isolates. The clonality was confirmed by a common drug resistance pattern (ACSTN; N. nalidixic acid). **Conclusions:** The main characteristic of the reported outbreak is its definite focal pattern. We assume that this food borne outbreak is correlated with the specific food handling practice. Similar events have been reported worldwide, emphasizing the global importance of *Salmonella* typhimurium DT104.

Board 104. Salmonella Newport in Georgia, 1998-2000

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Background: The rate of reported serotyped *Salmonella* infection in GA between 1998 and 2000 was 16.4 *10-5 person/years (p/y), which is one of the highest rates in the United States. S. Typhimurium is the most common serotype in GA and in the country, but S. Newport, the second most common serotype in GA, is 16% of *Salmonella* isolates in GA compared to only 8% in the United States. Understanding the descriptive epidemiology of S. Newport in GA will guide development of targeted environmental studies and hypothesis-testing epidemiologic studies.

Methods: S. Newport data were collected through GA Emerging Infections Program's (EIP) active surveillance system and through passive reporting to the Georgia Division of Public Health (GDPH). Only reports that included Health District (HD), age and *Salmonella* serotype were used in the analysis. A three-year average rate for each of the nineteen Health Districts (HDs) was calculated. Analysis was done with EpiInfo 6 and Excel.

Results: The three-year overall rate of S. Newport in GA was 2.66*10-5 p/y. Most HDs have a rate less than 4.5*10-5 p/y except for two adjoining south-central GA HDs where the rates were 16.23*10-5 and 13.66*10-5 p/y. More than 50% of GA S. Newport cases were children <5 years old. The three-year average rate of S. Newport in children <5 years old was 19.40*10-5 p/y compared to a rate for those 5 years old and older of 1.33*10-5 p/y. These data have encouraged focus on the south-central GA HDs and on those <5 years old. The rate of S. Newport in these south-central districts in children 5 years old and older is 6.3*10-5 p/y which is still high for the state but low compared to the rate in children <5 years old of 123.45*10-5p/y. Although cases of S. Newport occur throughout the year, an increase is seen in July with a peak in September or October. This increase is also marked in the two south-central GA HDs with high rates of S. Newport infection.

Conclusion: The high rate of reported S. Newport in two south-central GA HDs suggests that studies in these areas focusing on activities, habits and food consumption of children less than 5 years old will be most useful. Environmental studies should also be considered in this geographic region of the state during late summer and early fall. Targeted environmental and epidemiologic studies may identify the route of transmission of S. Newport to young children in south GA and result in effective prevention programs.

29 Malaria

Monday, March 25, 10:00 a.m.
Grand Hall East

Board 105. The Thrombospondin Related Autonomous Protein (TRAP) from *P. falciparum* Interacts with the Liver D-glucuronyl C5-epimerase in Humans

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Malaria remains one of the major infectious diseases of the world, affecting the health of hundreds of millions of people. A series of molecular and cellular interactions occur during passage of the parasite through human blood and liver cells. The sporozoite binds to specific receptors on liver cells that include glycoaminoglycan chains of heparin sulfate proteoglycans. The co-receptor on sporozoites involves, in part, the thrombospondin domains on the circumsporozoite protein and on TRAP (thrombospondin related

autonomous protein). Using Plasmodium falciparum pfTRAP as "bait" in the yeast two-hybrid system, we have screened a human liver cDNA library for interacting proteins. We have found that D-glucuronyl C5-epimerase (gC5E) interacts with pfTRAP. A molecular dissection of this interaction shows that a 79 amino acid region of pfTRAP, containing the unique RGD region interacts with gC5E. We have tested this interaction using the full-length cloned gC5E using various in-vivo and in-vitro methods. Finally, we have shown that the pfTRAP-gC5E interaction is unique to pfTRAP and not to another closely related protein Plasmodium cynomolgi TRAP, in which the RGD region is absent. The uniqueness of this interaction and its implications in parasite invasion are discussed.

Board 106. Reemergence of Malaria Related to Climatic Factors in U.S. Forces and Republic of Korea Soldiers and Civilians 1993-2000

B. J. Killenbeck[1], J. Gaydos[2], J. Pavlin[3], A. Anyamba[4], T. Klein[5], H. C. Lee[5]

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In 1948, the World Health Organization (WHO) estimated the prevalence of Malaria at about 300 million people infected, possibly causing 3 million deaths per year. The Republic of Korea (ROK) enjoyed several Malaria-free decades and the WHO declared the ROK malaria free in 1979. But, in 1993 *P. vivax* reemerged near the western edge of the Demilitarized Zone (DMZ) and cases tripled in 1995 and quadrupled in 1997. The cause of this reemergence is unknown. Many studies have used single or multiple remote sensing techniques to derive models to evaluate climatic variables that directly/indirectly influence environmental factors that may independently or collectively influence the transmission of vector-borne diseases. Factors like vegetation cover, landscape structures, and water bodies that may be potential breeding sites can be measured to see if these variables are associated with the rate of human cases. Instruments used for these studies have been Landsat's Multispectral Scanner and Thematic Mapper, the National Oceanic and Atmospheric Administration's Advanced Very High Resolution Radiometer, and France's Systeme Pour l'Observation de la Terre. Validating such studies present many confounding variables that have to be controlled or explained, for example, the interaction of socio-economic changes and mobility of populations are difficult to quantify. Additionally, documenting changes in public health practices and systematic data collection are very challenging obstacles. **Methods:** We analyzed metrological data for Korea provided by the Global Historical Climatology Network and the National Climatic Data Center along with Outgoing Longwave Radiation (OLR) anomaly time series 1981 to 2000. Results. **Results:** from this analysis indicate several observable shifts over time of increasing surface temperature coupled with a series of corresponding increased positive OLR anomalies, which imply decreased cloud coverage indicating decreased precipitation. **Conclusion:** We conclude that the observed trends, particularly increasing temperature may have enhanced the parasite development inside of mosquitoes, therefore changing the feeding frequency and allowing the vector to transmit the disease earlier and longer in its life cycle. This may help to explain the increase in malaria cases along the DMZ in the ROK.

Board 107. Non Pharmacological Methods to Prevent Malaria in an Urban Community in India : Is It Working ?

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Background: Chennai city in accounts for over 70% of the urban malaria in this southern state of India. This is inspite of wide spread use of anti-mosquito like personal protection measures. The question arises whether these are really effective.

Objective: To measure the protection from malaria of the personal protection measures used against mosquito bites

Design: Case-Control Study Setting: The corporation health clinics, which serve as primary level malaria clinics for Chennai.

Participants: New febrile patients with blood smear positive or negative for malarial parasites were grouped as cases and controls respectively. 84 cases and 87 controls were studied.

Main Outcome Measure(s): Proportion exposed to protective measures in cases and controls.

Results: OR of 0.97(0.53,1.78)(p=0.940) was detected, for the use of self-protective measures against malaria. The usage of coil showed 7% protection (0.41,2.09) (p=0.849). Logistic regression analysis showed 19% (0.40,1.65) (p=0.572) protection on the use of netted windows in houses. The power of the study was 63%.

Conclusions: The protective measures used by the population do not appear to offer any protection against malaria. The reasons for the lack of protection need to be studied further with regard to the quality and duration of action of the repellants, the nocturnal biting habits of mosquitos.

Board 109. Target Based In vitro Assays for New Antimalarial Drug Development

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Malaria remains a major global health problem with over 40 % world's population at the risk of the disease. The problem has been further aggravated due to spread of the drug resistance. Identification of novel lead molecules, which are active against the resistant strains of the parasite, is highly necessary for new antimalarial drug development. Current approaches of combinatorial chemistry generate large number of novel chemical entities. Improved technologies for isolation and identification of novel compounds from natural resources has provided promising new molecules. Target based in vitro assays may expedite the process of new lead identification and optimization. We have developed and standardized some in vitro assays which are based on some vital molecular functions of malaria parasite.The target functions show significant selectivity for the malaria parasite.

During intraerythrocytic proliferation large amount of hemoglobin is degraded by malaria parasite. This process generates toxic free heme. Malaria parasite is equipped with distinct metabolic process for detoxification of heme through its conversion to a crystalline black brown pigment commonly known as hemozoin. Biosynthesis of hemozoin (b-hematin) is a target for action of several blood schizontocidal antimalarials. We have developed a filtration based micro plate assay for in vitro b-hematin formation. The assay is highly robust and cost-effective. Sensitivity of this assay is almost similar to the tedious and expensive radiometric assay. The assay has been validated with several standard antimalarials.

The erythrocytes infected with malaria parasites are continuously exposed to oxidative stress. Reduced glutathione is a major antioxidant which plays essential role in defense of malaria parasite to the oxidative stress. This is kept in the functional state by a FAD containing enzyme, glutathione reductase (GR). The enzyme from Plasmodium falciparum shows distinct differences over the mam-

malian counterparts. The selective inhibitors of GR may be the promising antimalarials. Recombinant P. falciparum as well human glutathione reductases have been prepared from the E. coli cultures. The enzymes have been purified by affinity chromatography. A spectrophotometric microplate assay for GR has been standardized. The assay has been validated with some standard GR inhibitors. The purified malarial and human GR proteins may be used for high throughput screening and identification of selective enzyme inhibitors. Recently we also identified a putative gene for glutathione s-transferase (GST) from the P. falciparum genome data-base. The gene has been cloned by PCR and over expressed in E. coli cultures. GST may have important role in drug resistance in malaria parasite. Assays for several other target functions are being developed. Availability of these tools may expedite new drug development

30 Molecular Epidemiology I

Monday, March 25, 10:00 a.m. Grand Hall East

Board 108. Echovirus Type 13 Associated Outbreak of Viral Meningitis in Israel, 2000

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In the summer and fall of 2000 an outbreak of viral meningitis due to Echovirus type 13 (Echo13) occurred in the central, most populated region of Israel. Similar outbreaks due to Echo 13 where reported at the same time in Germany, England and Wales[1,2] and a year later in the USA[3]. Echo 13 did not cause outbreaks in these countries previously, and had been isolated very rarely. We report here the history of Echo 13 activity in Israel for the last 20 years and describe characteristics of the cases diagnosed by the Central Virology Laboratory (CVL). Between 1980 and 1999 Echo 13 was isolated only twice: from a healthy contact of an AFP case in 1998 (a 5 years old), and from an AFP case in 1999 (an 11 years old). Between July and October, 2000 the laboratory isolated Echo 13 from 91 patients with aseptic meningitis hospitalized in 6 medical centers in the central region of Israel, from Hadera in the North to Rehovot in the South. The Monthly distribution of the laboratory confirmed enteroviral infections during the outbreak period are summarized in the table below.

Month	CSF				Stool			
	No. samples	No. Echo 13 (%)	No. other entero viruses	Total No. of isolates (%)	No. samples	No. Echo 13 (%)	No. other entero viruses	Total No. of isolates (%)
July	113	33(29)	3	36(32)	25	4(16)	4	8(32)
Aug	160	28(17.5)	2	30(18.7)	40	6(15)	3	9(22.5)
Sept	92	11(12)	1	12(13)	26	1(3.8)	0	1(3.8)
Oct	55	7(12.7)	1	8(14.5)	30	1(3.3)	0	1(3.3)
Total	420	79(18.8)	7	86(20.5)	121	12(9.9)	7	19(15.7)

The age distribution of 72 patients was 40 (55%), 28 (38.9%), 2 (2.8%) and 2 (2.8%) in age groups 0-4y, 5-14y, 15-19y and 20-41y, respectively. Females were 44% and males were 56%. The age distribution was similar to those reported in Germany and the US (app 95% of the cases were below 15y) but different from the outbreak reported in England and Wales where 68% of the cases were in patents over age 15y[1, 2,3]. A preliminary sequence analysis of the 5'UTR of the Israeli 1998 and 1999 isolates and 12 isolates from July 2000 revealed a 97.4% homology between the 1998 and 1999 isolates, and 98.7% homology between the 2000 isolates (which were all nearly identical) and each of the 1998 and 1999 isolates. Comparatively, the 5'UTR homology between the Echo 13 isolates and an Echo 7 isolate from 2000 was in the range of 91.5 and 94 %. A more detailed molecular and antigenic analysis of Echo 13 isolates worldwide may lead to the understanding of the emergence of this virus as the causative agent of viral meningitis outbreaks. 1. Eurosurveillance Weekly 2000;4 at <http:www.eurosurv.org/> 2. Comm. Dis. Rep CDR Wkly 2000:10277, 280.MMWR 14, 2001 50:36, 777-780.

Board 110. Molecular Detection of Human Calicivirus in Young Children with Acute Gastroenteritis in Spain, During 1997

N. Negredo[1], E. Roman[2], R. M. Dalton[1], I. Wilhelmi[3], **A. Sánchez Fauquier**[1]

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Human Calicivirus are increasingly being recognized as one of the viral aetiological agents that cause acute gastroenteritis. However, to date routinely detection has not been possible. HuCV can be categorized into two genera named Norwalk-like virus (NLV) and Sapporo like viruses (SLV). NLV is the major cause of outbreak and sporadic gastroenteritis in adults. SLV has been associated mainly to gastroenteritis in non-hospitalisated children. To establish the importance of HuCV among Spanish children a large prospective study has been carried out in children attended in a hospital's pediatric emergency room. A total of 822 stool specimens were collected from children under 4 years during the period of a year. Samples in which no enteric pathogen was detected (neither bacterial nor viral) by routine diagnosis test were analysed by NLV specific RT-PCR. This infectious agent was detected in 54 (27%) of 201 samples tested by RT-PCR. A selection of this samples are being analysed by sequence analysis of a fragment POL coding region for their phylogenetic grouping (genotype). From this study, we could estimate the annual incidence rate of sporadic acute gastroenteritis due to HuCV. This rate was calculated in 4,23 annual cases/1000 children under 4 years. In addition, hospitalisation incidence rate of HuCVs infected children was 0,52 annual cases/1000children under 4 years. In this study the annual incidence rate of sporadic acute gastroenteritis closed to HuCVs was 4,23 annual cases/1000 children under the age of 4 years. In addition, hospitalisation incidence rate of HuCVs infection was 0,52 annual cases/1000children under the age of 4 years.

Board 111. Seroprevalence of SEN Virus Among Individuals at High or Low Risk for Infection with Blood–Borne Pathogens in Manitoba

M. R. Dawood[1], G. Smart[2], L. A. Forrester[3], A. Giulivi[3], K. D. Kaita[4]

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Objectives: 1- To determine the seroprevalence of SEN-V among individuals at high or low risk for infection with blood-borne pathogens (BBP). 2- To compare the nucleotide sequences of different SEN-V isolates in Manitoba. **Methods:** Twenty patients with no known risk factors for infection with BBP, 10 from a hepatology clinic and 50 patients from HIV clinics were included

in the study. Participants were assigned study codes and were asked to complete a questionnaire regarding their history of liver related diseases, injection drug use (IDU), blood transfusion (BT) and hospitalization. DNA was extracted from serum samples using Qiagen DNA Mini kit followed by PCR amplification. The oligonucleotide primers were able to amplify a 348 bp segment from the different SEN-V genotypes and other related viruses. Amplicons were analyzed on 2% agarose gel electrophoresis. The 348 bp segments from positive cases were subject to nucleotide sequence analyses using ABI Prism 310 genetic analyzer and nucleotide sequences were compared to sequences in the gene bank database. **Results:** SEN-V was detected in forty cases. The positivity rates among individuals from 2 clinics with no known risk factors are 10% and 60%. The positive patients from these 2 clinics have only history of hospitalization. The SEN-V prevalence rates among individuals seen in the hepatology or the HIV clinics are 60% and 54% respectively. Nucleotide sequence analyses was performed on all the positive specimens. The sequence analyses of the amplicons indicated close relation to SEN-V but not to TTV, YONBAN or SANBAN viruses. Isolates from individuals at low risk of SEN-V infection indicated that one patient has mixed genotype infection and six of genotypes B (1), C (1), D (1), F (1) and H (2). The nucleotide sequence analyses of the 33 specimens from high risk individuals indicated that 22 patients are infected with more than one genotype. The other 11 individuals were infected with genotypes A (2), B (1), F (1), H (4) and 3 do not match the sequences of the published SEN-V genotypes. **Conclusion:** The high prevalence of SEN-V among individuals with low risk for blood-borne pathogen infection may indicate that the virus can be transmitted by other means other than IDU or BT. The nucleotide sequences demonstrate that 86% and 33% of patients with low and high risk respectively are infected with single genotype. The infection with more than one genotype may indicate that infection with one genotype may not protect against infection with other genotypes.

Board 112. The Characteristic of the *Francisella tularensis* Mediaasiatica

A. M. Aikimbayev, T. N. Kunitsa, G. A. Temiraliyeva, B. A. Atshabar, L. Y. Lukhnova

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There are 4 types of tularemia natural foci in Kazakhstan: foothills-stream, flood-lands-marsh, steppe, tugai. Into the first three foci *F.tularensis* holarctica circulate. Masgut Aikimbayev [1966, 1967] in 1965 studying the fermentative activity of 56 tularemia microbe strains, isolated in the natural tugai foci of Kazakhstan, found out that some of these strains reiterate only a number of features of two subspecies of tularemia microbe (holarctica, nearctica). Possessing ferment -citrulline ureidase and making acid from glycerol, its can't make acid from glucose and maltose, are little pathogenic for the laboratory rabbits. The author proposed to isolate the given variety as subspecies *F.tularensis* mediaasiatica. Besides these signs it has been determinated, that strains *F.tularensis* mediaasiatica in comparison with *F.tularensis* holarctica are susceptible to erythromycin and macrolides. All the strains of tularemia microbe of the *F.tularensis* mediaasiatica subspecies are agglutinated by the licensed tularemia serum, received from immunisated by *F.tularensis* holarctica animals. The microbe is well coloured with tularemia luminescent serum both in smears out of the bacterial culture and in smears from the animals' organs. The circulation of the given tularemia microbe subspecies in general takes place among Meriones tamariscinus and Lepus tolai Pall.; the epizootic process often involves Ondatra zibethica, small mice-like rodents and Rhombomis opimus. The main carriers are ticks — D.dagestanicus, Rhipicephalus pumilio. *F.tularensis* mediaasiatica does not posses oxidase activity, and are catalase positive (oxidase-, catalase +). The majority of strains of tularemia microbe of the *F.tularensis* mediaasiatica subspecies produce tularecins and at the same time are sensible both to their own tularecins and to tularecins produced by other subspecies of tularemia microbe. The literature cites data concerning the use of olegonucleotide hybridization analysis under the study of tularemia microbe of the *F.tularensis* mediaasiatica. On the basis of an oligonucleotide hybridization analysis that detects a single base substitution in 16S rRNA, Sandstrom et al.[1972] have determined that *F.tularensis* mediaasiatica generally share significant identity to *F.tularensis* tularensis. For identification of tularemia microbe subspecies at the taxonomic level the multilocus VNTR- analysis is especially important.

Board 113. Molecular Epidemiology of an Outbreak Caused by *Salmonella enterica* Serovar Newport in Argentina

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Between July 28 and August 25 2001, a total of 70 cases of gastroenteritis were reported at the "Juan Pablo II" Pediatric Hospital, in the Province of Corrientes, Argentina. Among these cases, *Salmonella spp*. was isolated as the only pathogen from the stools of 52 infants under 8 years old. All these isolates were susceptible to 12 antimicrobial agents assayed. The strains were submitted to the National Reference Laboratory, where the biochemical and serological tests were performed and the isolates were identified as *Salmonella enterica* serovar Newport. In our country, *S.* Newport is not frequently isolated, being Enteritidis and Typhimurium the most prevalent serovars up to now. In order to establish the genetic relationship among the *S.* Newport isolates, a total of 25 isolates were analyzed by pulsed field gel electrophoresis (PFGE) using the restriction enzyme *Xba*I. For comparison purposes, 16 strains of *S.* Newport isolated from sporadic cases in different time periods and from distinct regions of the country were included in the study. The genotypic analysis revealed that all the isolates from the children in the Province of Corrientes showed an identical PFGE profile, confirming that the outbreak was caused by a single strain. In contrast, the isolates from sporadic infections exhibited different DNA band patterns, that shared between 7.4% and 80.4% of the bands with the outbreak profile.

Board 114. Isolation and Molecular Subtyping of *Listeria monocytogenes* from Pristine, Urban, and Agricultural Sources

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Although previous reports describe the ecology and transmission of *Listeria monocytogenes* (Lm) in and among food processing environments, there are few reports describing the occurrence of Lm among environments outside those used for food production. These few reports suggest that Lm is distributed ubiquitously and transmission dynamics may be difficult to assess. To assess the occurrence and molecular diversity of Lm in different environments in New York State (NYS), we cultured pristine, urban, and agricultural environments for Lm. Lm subtypes were compared with all reported Lm from animal and human listeriosis in the prior five years. Samples were obtained from soil, plant materials, and water from all environments. In addition contact and floor sponges were taken from urban areas and stool specimens were obtained from all farms. Four separate sites each were chosen for urban and pristine environments. Agricultural sites were sampled when bovine or goat cases were reported to the Cornell University Veterinary Diagnostic Laboratory. One control farm (without reported listeriosis) was chosen for each case farm. Samples were enriched in *Listeria* Enrichment Broth for 24 and 48 hours at 30 ºC and then streaked for isolation on Oxford medium.

Typical colonies were confirmed as Lm biochemically and by polymerase chain reaction detection of the *hly* gene. All Lm isolates were genetically characterized by automated ribotyping (Qualicon™). There were 7/176 (4%) Lm positive urban specimens, 2/163 (1%) Lm positive pristine specimens, and 45/238 (19%) Lm positive farm specimens. Urban isolates were represented by five different ribotypes. DUP-1038B accounted for 13% of the human and 2% of the animal listeriosis in NYS in the 5 years prior. DUP-1045B accounted for 3% of the human cases and <1% of the animals cases. DUP-1039 was found only in <1% of animal listeriosis cases. Both 116-702-S-3 and 116-704-S-5 were unique ribotypes that were not previously described. Among pristine isolates, there were 2 ribotypes. DUP-1045A represented <1% of all human and no animal cases. DUP-1053C was not found in any clinical cases. From 31 farm isolates, there were 12 ribotypes. Five of the 12 were found previously among both human and animal cases, 4 were found only among human cases, 2 were found only among animal cases, and 1 was never found among either animal or human cases. While this study was aimed at determining the genetic diversity of Lm among different environmental sources outside the normal conceptualized foodborne transmission route, we found that a much higher proportion of Lm was readily cultured from farm and urban environments than from pristine environments. Our results show that a considerable diversity of Lm genotypes exists in non-food related environments and that high density animal populations (such as farms) may provide a favorable environment for the survival and transmission of Lm.

Board 115. UPGMA: Are We Correctly Describing the Relationships Between Bacterial Isolates?

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Introduction: Genetic relatedness clustering techniques for bacterial isolates, such as the unweighted pair group method using arithmetic averages (UPGMA), are used for the study of phylogenetic trees. Even though UPGMA is used to describe the relationships among the isolates and yield an unequivocal dendrogram, distortions of the original data can occur and more than one dendrogram can be obtained form the same dataset — tie dendrograms. In this study, we present a procedure to address these issues. **Methods:** Three articles with published distance matrices for cluster analysis with bacteria were selected from the literature to serve as an example for the techniques described. For each distance matrix, the order of the isolates was shuffled 1,000 times and all possible dendrograms were constructed. In the case of more than one dendrogram, the ones that presented the least distortion in the original distance structure, measured by the cophenetic coefficient (CC) were chosen. If more than one tie dendrogram had the smallest CC, an isolate-wise analysis was performed to compare the specific differences between them. The distortion in the original distance in each dendrogram was compared using two parameters to check if: 1) the original distance between an isolate in one cluster and all isolates not in that cluster is smaller than the cluster height and 2) the original distance between the isolates within a cluster is bigger than the height of the next cluster. **Results:** All three datasets yielded more than one dendrogram — 2, 3 and 8 respectively. In the first, the CC was around 0.97, and the published dendrogram was retrieved in 50% of the replications. In the second, the CC was around 0.70, and the published dendrogram could not be reproduced. In the last one, the CC was around 0.91 and the published dendrogram appeared in 10.3% of the replications. The isolate-wise distortion was much greater for the example with the smallest CC, and so were the differences between specific isolates in the tie dendrograms. **Discussion:** Multiple dendrograms can be obtained for the same dataset, depending on the presence of tied distances. The great majority of statistical packages yield only one dendrogram, which is arbitrarily chosen depending on the order of the data. Although it is believed that a CC greater than 0.70 is sufficient to guarantee a low rate of distortion, we show that even values as high as 0.90 can present significant isolate-wise distortions. The examples presented illustrate the necessity of a closer analysis of results drawn from dendrograms constructed with UPGMA, to check for severe distortions, and to check for tie dendrograms. We suggest that whenever UPGMA is employed, the analysis should include all possible dendrograms obtained from the data, along with their CC, and a refined isolate-wise analysis of the dendrograms with the highest CC should be performed.

Board 116. Development of a Multilocus Sequence Typing (MLST) Scheme for *Listeria monocytogenes*

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The foodborne pathogen, *Listeria monocytogenes*, is responsible for a number of outbreaks of listeriosis worldwide. The high fatality rate associated with this foodborne pathogen combined with its ability to grow at refrigerated temperatures have prompted the FDA and FSIS (USDA) to establish a zero tolerance for ready-to-eat foods. These periodic outbreaks result in costly outbreak investigations and large food recalls. To investigate the population biology of this organism and to aid in the development of a molecular typing tool based on nucleic acid sequence, multilocus sequence typing (MLST) was set up by choosing eight different metabolic genes of which 450-550 bp of sequence were obtained. A diverse set of 140 isolates were chosen from a large collection of clinical, environmental, and food isolates representing sporatic episodes and food outbreaks from 1971-2000. This diverse set of isolates represents serotypes (1,1a, 1b, 1c, 1/2a, 1/2b, 1/2c, 3b, 4, 4b, 4d, 4e, 6b, and 7) and, for comparison, these isolates were all characterized by pulsed-field electrophoresis using Asc I and, if necessary, Apa I. Geographically, the isolates were obtained from North America, South America, and Europe. This typing method will provide a ongoing view into the population structure of this species as well as a better understanding of its global epidemiology.

Board 117. PFGE Diversity Among Salmonella Heidelberg in the United States

F. W. Virgin, Jr., K. A. Kubota, E. M. Ribot, S. B. Hunter

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PulseNet is the national network of public health laboratories that perform molecular subtyping using pulsed-field gel electrophoresis (PFGE) on foodborne bacterial pathogens. PFGE patterns are shared and compared for the purpose of cluster identification through a national database located at the at the Centers for Disease Control and Prevention (CDC). PFGE patterns are submitted by U.S. Public Health Labs, food regulatory agencies, as well as Canadian public health laboratories through PulseNet North. The PulseNet national database for *Salmonella* serotype Heidelberg was established in 1998. In addition to the S. Heidelberg isolates submitted by PulseNet laboratories, the national database also includes PFGE patterns from retrospective isolates from 1985, 1990, and 1995 that were sent to CDC. All isolates were PFGE typed using PulseNet standardized protocol for *Salmonella*. XbaI is used as the primary restriction endonuclease to digest total DNA. The endonuclease BlnI was also used for some of the isolates. Gel images were analyzed using Molecular Analyst v 1.5 (Bio-Rad, Hercules, CA) and dendrograms were calculated using the Dice coefficient and UPGMA. Within the S. Heidelberg database there were 85 unique XbaI PFGE patterns. Five hundred twenty-eight isolates in the database which were restricted with XbaI have been assigned pattern numbers. Two hundred ninety-

five (56%) of those isolates were designated pattern JF6X01.0022. Of the 295 isolates, 104 were digested with BlnI. Out of the 104 isolates, 82% were indistinguishable and were assigned the pattern number JF6A26.0001. The remaining 19 isolates were assigned 10 different pattern numbers represented by 1 to 5 isolates. Isolates with patterns JF6X01.0022 and JF6A26.0001 were seen in 1985, 1990, and 1995. Although there appears to be PFGE pattern diversity within S. Heidelberg, a predominant clone has emerged circulating among strains in the U.S. This data supports a previous study showing the continual presence of this clonal strain since 1985. It appears that PFGE is useful in two ways. Since there are over 80 unique patterns within the Heidelberg database, PFGE can be used to distinguish among isolates that are not patterns JF6X01.0022 and JF6A26.0001. Finally, it can also be useful in identifying the predominance of the clonal strain.

Board 119. Correlation of Epidemiologic Trends in Meningococcal Infection with the Strains of Neisseria Meningitidis Causing Invasive Disease

M. McEllistrem[1], P. Pass[2], J. A. Kolano[1], L. H. Harrison[1,2]

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Background: The incidence of meningococcal disease in persons 15-24 years of age increased from 1990-97, before declining in 1998-99. An increase in this age group is characteristic of a clonal outbreak of meningococcal disease. From 1990-99, the incidence of meningococcal disease steadily increased among persons at least 25 years old. **Methods:** Pulsed-field gel electrophoresis (PFGE) was performed on N. meningitides isolates obtained from active, laboratory based surveillance from Maryland during 1992-99. PFGE-based clonal groups were defined as strains at least 80% genetically related by dendrogram. The degree of genetic relatedness between strains was calculated using the mean of the Dice coefficients. **Results:** Among the 84% (246/293)of the cases with known serogroups, 46% (29/62) of persons 15-24 years old were infected with a serogroup C strain compared to 21.5% (20/93) of adults at least 25 years old ($p < 0.01$). Likewise, 32% (19/62) of persons 15-24 years old were infected with a serogroup Y strain compared to 44% (41/93) of adults at least 25 years old ($p = 0.09$). From 1992-97, the mean of the Dice coefficients was 83.7 for persons 15-24 years old versus 67.1 for children < 15 ($p < 0.01$) and 66.8 for persons at least 25 years old ($p < 0.01$). During 1999, 88% (7/8) of the serogroup C infections in persons 15-24 years old were due to an unique PFGE pattern which was not present in previous years. Seventy-six (58/76) percent of the serogroup Y strains could be classified into 2 clonal groups (1 and 2). The proportion of clonal group 2 strains increased from 11% (1/9) in 1992 to 57% (12/21) in 1999 ($p = 0.01$, Chi square for trend); this trend was seen among adults atleast 25 years old, but not in the < 15 and 15-24 year age groups. **Conclusion:** During the rise in meningococcal incidence in persons 15-24 years old, serogroup C strains were more genetically related in this age group than in the other two age groups. Interestingly, during the decline of meningococcal disease, a serogroup C clone emerged in persons 15-24 years of age. Among adults at least 25 years old, the increase in meningococcal disease was partially due to an increase in one serogroup Y clonal group.

31 New or Rapid Diagnostics I

Monday, March 25, 10:00 a.m.
Grand Hall East

Board 120. A Rapid Modified Antibody-Capture Enzyme-Linked Immunosorbent Assay (ELISA) for Detection HSV-1 Primary Infection in Human

M. Ravanshad[1], M. Roostaee[1], A. Mostafaee[2], F. Sabahi[1]

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Objective: Development and application of an enzyme-linked immunosorbent assay (ELISA) for detection and measurement of IgM antibody to herpes simplex virus type 1 (HSV-1) in human sera. **Methods:** An antibody-capture ELISA based on the reaction between anti-human IgM, prepared in rabbits, and IgM of serum samples and HSV-1 conjugated with horesradish peroxidase was developed and applied. Five hundred sera from healthy persons and 26 sera from persons with primary HSV-1 infection were tested for the presence of IgM antibody against HSV-1. The specificity and sensitivity of the test were compared with a commercial test kit, and was acceptable. **Results:** Based on the results obtained from this method, it was shown that this method is suitable to detect IgM to HSV-1. Seven point three percent of healthy sera were positive for IgM. The sensitivity and specificity of the test was measured and were 94.4% and 93.91% respectively. **Conclusion:** Detection of HSV-1 IgM provides a sensitive, rapid and economic method for the diagnosis of HSV-1 primary infection. The ELISA test developed in this study had acceptable sensitivity and is a suitable method for the detection of HSV-1 primary infection.

Board 121. Evaluation of Eight Rapid Screening Tests for Acute Leptospirosis in Hawaii

P. V. Effler[1], A. K. Bogard[1], H. Y. Domen[1], A. R. Katz[2], H. Y. Higa[1], D. M. Sasaki[1]

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Leptospirosis is a major public health problem throughout the world. Clinical recognition of leptospirosis is challenging and the definitive serologic diagnostic assay, the microscopic agglutination test (MAT), is time-consuming and difficult to conduct. Various serologic screening tests have been developed but their performance among ill persons in the US has not been established. Eight screening tests were compared on 379 sera obtained from a series of 236 patients (33 with confirmed infection) collected in 1998 and 1999. The median number of days between illness onset and specimen collection was nine. The overall sensitivity, by specimen, for each test was as follows: IHA (MRL Diagnostics-Cypress, Calif.): 29%; INDX Leptospira Dip-S-Tick™ (PanBio InDx, Inc., Baltimore, MD): 52%; Biognost™ IgM IFA test (Bios GmbH Labordiagnostik, Gräfelfing, Germany): 40%; Biolisa™ IgM ELISA (Bios GmbH, Labordiagnostik, Gräfelfing, Germany): 48%; Leptospira IgM ELISA™ (Pan Bio Pty Ltd., Brisbane, Australia): 36%; SERION ELISA classic Leptospira™ (Institut VirionoSerion GmbH, Würsburg, Germany): 48%; LEPTO Dipstick™(Organon-Teknika, Ltd, Amsterdam, The Netherlands): 34%; Biosave™ latex agglutination test (LATEX) (Bios GmbH Labordiagnostik, Gräfelfing, Germany): 86%. Test specificity ranged from 85% to 100% among all tests except LATEX which was significantly lower, at 10%. Test sensitivity was particularly low (<25%) for all tests (except LATEX) on specimens collected during the first week of illness. This is the most comprehensive field trial

of leptospirosis screening tests reported to date. The data indicate that IgM detection tests have limited utility for diagnosing leptospirosis during the initial evaluation of patients seen in Hawaii, a time when important therapeutic decisions are made. Improved leptospirosis screening tests are needed.

Board 122. Enhancing Surveillance for Influenza Virus by Incorporating Newly Available Rapid Diagnostic Tests

P. Effler, M. Ieong, M. Nakata, T. Tom

State of Hawaii Department of Health, Honolulu, HI

Objectives: To determine the effect of incorporating influenza rapid testing into public health virologic influenza surveillance activities.

Methods: Beginning with the 1999-2000 influenza season, physicians throughout Hawaii ordering a viral culture for patients with suspected influenza were also offered influenza rapid testing. We compared the number and results of viral respiratory cultures sent to the Hawaii Department of Health (HDOH) and the number of providers who participated in influenza surveillance over consecutive influenza seasons. Data from 37 virology laboratories elsewhere in the United States were reviewed for comparison.

Results: HDOH received 306, 396, 1112, and 2169 specimens for influenza culture during the 1997-1998, 1998-1999, 1999-2000 and 2000-2001 influenza seasons, respectively, and the number of influenza isolates recovered was 73, 64, 137, and 491 respectively. The number of Hawaii providers submitting one or more influenza cultures rose from 34 to 196 between the 1998-1999 and 1999-2000 seasons; the number of cultures submitted at comparison laboratories rose just 5% during this same period.

Conclusions: In our setting, incorporating rapid tests into public health surveillance greatly increased the number of specimens submitted for viral culture and the number of influenza isolates recovered. Coupling rapid tests with cultures appears to be an effective incentive for physicians to participate in virologic surveillance.

Board 123. New Express Method of Virus-Cell Interaction Dynamic Monitoring and Diagnostics.

A. S. Fedchuk[1], O. P. Fedchuk[2], A. O. Fedchuk[2], P. O. Fedchuk[3]

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We propose new original and objective express-method for virus-cell interaction dynamic monitoring. Fractal approach was chosen because it is stated experimentally that main systems and organs of human organism beginning from cellular level have fractal structure. Samples of Hep-2 cells cultivated for 24 and 48 hours were used as the substrate for further infection with Herpes simplex virus of US-1 strain. The substrates were pretreated with E-aminocaproic acid (EACA) and tested 8, 16, 24 and 48 hours after infection. The non-pretreated cell culture samples were tested as well. Thickness and homogeneity of samples were checked using interferometric techniques. Diffraction patterns (DP) of the specimens containing system of virus-cell interacting particles were generated due to the specific changes of their optical density and afterwards registered by VZM 1000 Color LabVideo system. Thus obtained DP were transmitted to Intel Pentium III 600 MHz PC and processed using original image processing software elaborated in our group. As a result of few minutes long PC work, one could obtain an objective parameter — fractal dimension D, which is much more sensitive than those obtained using regular techniques such as direct counting of pre-colored infected cells in optical microscope. All types of specimens under consideration in present work were tested as well through traditional techniques and the results were compared with one another. Sufficient differences in D values were registered even at early stages (8 hours and even less) of viral infection. We could state that proposed method will be of exceptional need in drug design research and clinical practice because of its sensitivity and express nature.

Board 124. New NAT Assays for Quantitative Detection of Non-Enveloped Model Virus, PPV, in Blood Product Safety Studies

G. G. Prikhod'ko, H. Reyes, I. Vasilyeva, H. Xue, J. He, A. Ralston, T. F. Busby

American Red Cross Holland Laboratory, Rockville, MD

Improvement in donor selection and plasma screening has resulted in a tremendous reduction of risk in transfusion- and plasma product-transmitted infections over the past two decades. In 1999, European Union regulators began to require that all plasma be tested by nucleic acid amplification technology (NAT) assays for HCV if derivatives made from such plasma were to be sold in Europe. This announcement provoked and accelerated the development and implementation of NAT assays for blood and plasma screening in the United States and other developed countries. Virtually all whole blood and plasma donations collected in the United States are been screened for both HCV and HIV-1 by NAT assays. Moreover, recently evaluated NAT assays for detection of HBV and B19 in plasma pools are expected to reduce the risk of viral transmission via transfusion and plasma products. Still the blood supply remains vulnerable to new and reemerging infections, since several hepatitis and other viruses have been discovered. For this reason, current US and European guidelines and regulations recommend using at least 2 viral clearance techniques to create plasma products that more closely approach zero risk for pathogen transmission. Porcine parvovirus (PPV) has been recognized as a model virus for non-enveloped human viruses like parvovirus B19 and HAV in viral inactivation/removal studies. The standard, cell-based PPV-specific ($TCID_{50}$) assay provides a quantitative analysis of PPV-containing samples within 6 to 7 days with a sensitivity of approximately 2 $\log_{10}$ $TCID_{50}$. However, neither a referenced method for the quantitative PPV NAT assay nor a kit for quantification of PPV has been published or become available on the market. We developed two PPV NAT assays (a PPV-specific nested-Q-PCR assay and a PPV-specific LightCycler nested-PCR assay) that are designed to be used with widely distributed PCR systems from companies such as Perkin Elmer, MJ Research and Roche Molecular Biochemicals. Both assays are simple and reproducible, and provide an accurate quantification of PPV (single copy of PPV per PCR run) within several hours. The assays contain a PPV DNA standard, against which all PPV controls can be calibrated, and the proof test of the PPV-specificity of amplified products. PPV NAT assays were evaluated in PPV inactivation studies, quantification of PPV in human plasma and in nanofiltration of α 1-proteinase inhibitor (API) spiked PPV samples.

32 Environmental Changes

Monday, March 25, 10:00 a.m.
Grand Hall East

Board 125. Behavioral Environmental Influence on Pathology and Outcome of Chronic Viral Hepatitis

Y. Shcherba

St.Petersburg State Medical University, Scientific Research Institute of Influenza of the RAMS, Saint Petersburg, RUSSIAN FEDERATION

Background/Objectives: Nowadays it is well known that behavioral environmental epidemiology can predict acute and chronic communicable diseases of public health importance,

including the newly emerging or re-emerging infections. In this investigation we have undertaken to assess the influence of underlying or superimposed drug abuse on the pathomorphogenesis of chronic viral hepatitis and evaluate its possible prognostic significance. **Methods:** Prospective and retrospective epidemiological, clinical and histoenzymological investigation of liver tissue obtained with the help of liver biopsy in 400 patients with chronic hepatitis B, C or B and C with and without intravenous opiate and ephedrine addiction. **Results:** In chronic viral hepatitis patients without drug abuse an increase in the number of capillarized sinusoids, marked by enzymes alkaline phosphatase and 5-nucleotidase, and decrease in the activity of the second link tissue oxidation enzyme NAD-diaphorase were determined in the blood-hepatocytic barrier. The changes were much greater in the group of associate B and C etiology. In chronic viral hepatitis patients with drug abuse the number of capillarized sinusoids was very large and the enzyme activity was persistently very low, regardless of the particular etiology — B, C or B and C respectively. **Discussion/ Conclusions:** The data obtained are in accordance with the fact of severe deleterious drug interference with the oxidation-reduction process in living tissues and intensive capillarization of the liver sinusoids, being especially expressed in opiates. Simultaneous B and C viral infection of the liver in association with drug abuse, both being the very consequences of the behavioral environmental influences, can cause greater alteration and subsequent structural damage to the blood-hepatocytic barrier. The study demonstrated that the quantitative data obtained correlated sufficiently well with the severity and outcome of chronic hepatitis B, C or B and C (the extent of inflammation, fibrosis and cirrhotic transformation).

Board 126. Bioecological Assessment and Environmental Control by Women's Reproductive Function Indices

E. Ailamazyan[1], **T. Belyaeva**[2]

[1]St.Petersburg Institute of Obstetrics and Gynecology, Saint Petersburg, RUSSIAN FEDERATION, [2]St.Petersburg State Medical University, St.Petersburg Institute of Obstetrics and Gynecology, Saint Petersburg, RUSSIAN FEDERATION

Objectives: To sustantiate a new method of bioecological assessment and environmental control by women's reproductive function indices. **Methods:** More than 250000 women with and without pregnancy and 50000 newborn infants have been examined prospectively and retrospectively. The women's clinical, biochemical, hormonal, immunologic, instrumental data testifying to their reproductive function in the areas with and without various unfavourable ecological influences (industrial, agricultural and sanitary) have been compared. **Results:** The most informative women's reproductive function criteria for the assessment of and monitoring the ecological situation in the region in this respect were selected. They included: the rates of the hazard of interrupted pregnancy (incompetent pregnancy), gestosis, premature delivery, labor activity anomalies, hypogalactia, fetal hypotrophy, chronic intrauterine hypoxia, in-delivery fetal hypoxia and asphyxia, perinatal mortality, newborn morbidity, ovarian hormonal insufficiency, menopausal age, osteopenia degree in early postmenopause, and climacteric syndrome degree. The quantitative values of the criteria selected can be used for the assessment of the ecological situation of the region in this respect as being favourable/unfavourable. **Conclusions:** Making use of the suggested criteria and corresponding indices gives the possibility to ensure and carry out ecological regional cartography and individual prophylaxis of ecologically dependent obstetric, gynecologic, perinatal and neonatal pathological conditions.

33 Foodborne Illness and Antibiotic Resistance

Monday, March 25, 10:30 a.m.
Centennial Ballroom I

Campylobacter coli – What's the Big Deal?

S. J. O'Brien, G. K. Adak, S. M. Long, I. A. Gillespie, J. A. Frost

Public Health Laboratory Service, London, UNITED KINGDOM

Background: In the 1980s *campylobacter*s emerged as the most common bacterial cause of acute gastroenteritis in North America and Western Europe. Routine surveillance and special studies have consistently shown that, within the genus, *Campylobacter coli* lies second to *C. jejuni* as a cause of human illness. Data on the impact of *C. coli* infection were scarce because strains were infrequently speciated and incidence studies were lacking. However following the completion of the Study of Infectious Intestinal Diseases in England and the Sensor Study in the Netherlands, incidence data are now available for two industrialized countries. The development of a method for estimating the impact of food-related illness by the United States Centers for Disease Control and Prevention (CDC) has made it possible to explore the impact of *C. coli* infection within the context of all food-related disease. **Methods:** We refined the CDC method for quantifying the impact of food-related disease to correct for imported infection. We estimated the number of illnesses, presentations to primary care physicians (presentations), hospitalizations, days of care in hospital (days) and deaths due to indigenous foodborne *C. coli* in England and Wales in 2000 and compared these data with those for other pathogens. **Results:** Indigenous foodborne *C. coli* infection resulted in 24560 illnesses, 11695 presentations, 990 hospitalizations (for 5500 days) and 6 deaths. *C. coli* infection led to more hospitalizations than all foodborne pathogens other than *C. jejuni* and *Salmonella enterica* serotype Enteritidis and more illness and presentations than Shiga-toxin producing *Escherichia coli*, *Salmonella enterica* serotype *Typhimurium* or *Listeria monocytogenes*. **Conclusion:** The importance of *C. coli* as a foodborne pathogen has been underestimated, possibly because it lies in the shadow of *C. jejuni*. This is the first time that the impact of illness due to this pathogen has been considered against the background of all other causes of food-related infectious intestinal disease on a national scale. Our analyses show that *C. coli* is an important pathogen in its own right and that control of this pathogen is a necessary part of any strategy that is developed to reduce the burden of food-related illness. However in order to control *C. coli* we must learn more about its epidemiology and microbiology.

Is Drinking Water a Risk Factor for Endemic Cryptosporidiosis in the Immunocompetent General Population of the San Francisco Bay Area?

A. Khalakdina[1,2,3], D. J. Vugia[2,4], J. Nadle[2], J. M. Colford, Jr.[1,2]

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Background: Cryptosporidiosis is a protozoan enteric illness that has received much attention in immunocompromised persons and in outbreak settings (frequently waterborne). There are, however, no population-based studies on the risk factors for

community-acquired cryptosporidiosis in the immunocompetent general US population. **Methods:** We undertook a case-control study in 8 counties in the San Francisco Bay Area as part of a national study to ascertain the major routes of transmission for endemic cryptosporidiosis in this population. Our specific goal was to evaluate any risk associated with drinking water. Cases were recruited from among those identified by a population-based, active surveillance system that is in place in the region. At least two age-matched controls per case were recruited using random-digit dialing schemes for three possible types: household, neighborhood and different water district. Cases (n=26) and controls (n=62) were interviewed by telephone using a standardized questionnaire that included extensive questions about the following exposures in the 2-week period prior to the onset of illness in the index case: drinking water, recreational water, food items, travel, animal contact, and person-to-person fecal contact. For adults, additional questions were asked about sexual practices. **Results:** In multivariate conditional logistic regression analyses the major risk factor for cryptosporidiosis was travel to another country (matched OR=24.12; 95% CI: 2.64-220.62) (Table). **Conclusions:** Our study found a high association between foreign travel and cryptosporidiosis. No significant association with drinking water was detected. These findings can be used both to design larger studies of endemic cryptosporidiosis and to guide the analyses of national data that have already been collected.

Cryptosporidiosis among the immunocompetent, San Francisco Bay Area: Multivariate OR (95% CI)

Exposure	All Controls(n=62)	Neighborhood Controls(n=45)
Drink boiled water	1.00 (reference)	1.00 (reference)
Drink filtered or bottled water	2.29 (0.11–46.52)	2.11 (0.08–54.71)
Drink tap water	3.56 (0.11–46.52)	2.91 (0.15–54.91)
Travel to another country	34.66 (3.58–27.96)	24.12 (2.64–20.62)

Washington Clinical Laboratory Initiative – Assessment of Laboratory Practice

J. M. Counts

University of Washington, Seattle, WA

The University of Washington Clinical Laboratory Initiative is a demonstration project, that is part of the National Laboratory System (NLS), funded by CDC. The goal of the NLS is to strengthen critical laboratory testing for public health surveillance and investigations through systematic assessments of laboratory practice, focused training, improvement of diagnostic testing through the promotion of consensus testing standards and responsive laboratory delivery systems that provide diagnostic testing for the diagnosis, treatment and surveillance of infectious diseases. The Initiative is conducted in collaboration with the CDC, Foundation of Health Care Quality and numerous other stakeholders in the state of Washington as a quality improvement initiative. The current focus of the Initiative is the assessment of laboratory practice that addresses antimicrobial susceptibility testing in public health, hospital, commercial, and physician office laboratories. National studies have indicated that antimicrobial susceptibility testing (AST) may not be of the quality necessary to ensure appropriate patient care and effective surveillance. Data will be presented from studies, conducted by the Clinical Laboratory Initiative, which identified serious deficiencies in laboratory practice such as utilization of outdated NCCLS tables, failure to respond appropriately to case studies, which address contemporary AST issues, and failure to utilize appropriate number and type of antimicrobials in AST which may contribute to erroneous results leading to treatment failures and false assumptions about antimicrobial resistance.

Real-Time International Surveillance of Antimicrobial Resistance by the Enter-net Surveillance Network

I. S. Fisher[1], N. Gill[1], B. Reilly[2], H. Smith[3], J. Threlfall[3], on behalf of the Enter-net participants[4]

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Background: Many fora and reports have highlighted the importance of surveillance of antimicrobial resistance across a range of organisms over the last few years. Illness from enteric pathogens often presents with self-limiting symptoms, but this is not always the case, particularly for the immunocompromised or those with severe infection. With no new antimicrobials on the immediate horizon it is vital to monitor the efficacy of current treatments and identify the emergence of resistance to those currently in use. However international surveillance of resistance has always been dogged by the question of comparability of results. In 1998 Enter-net — the international surveillance network for the enteric pathogens *salmonella* and shiga-toxin producing *E.coli* — undertook an international study to compare the qualitative (resistant, intermediate resistance or sensitivity) results of antimicrobial susceptibility testing to ascertain whether international surveillance could successfully be achieved. Forty-eight strains were sent to each of the 18 National Reference Laboratories in the network to be tested using their own methods against the panel of 11 antimicrobials recommended by Enter-net so that the results could be analysed and the degree of concordance (or non-concordance) between them could be determined. Over 8,500 tests for antimicrobial susceptibility were undertaken and, with the exception of low-level resistance to ciprofloxacin, it was clear that there was a great deal of concordance between the results, over 99% of the tests for resistance yielded the same results. Therefore data on antimicrobial resistance were incorporated into the specification for the international databases created by Enter-net. Results Provisional data for 2000 (the last full year for which data are available) show that in the *salmonella* database antimicrobial susceptibility testing results are available for almost 18,000 strains. Of these 6,098 (47.1%) were fully sensitive, 5,343 (41.2%) showed resistance to between one and four antimicrobials, and 1,513 (11.7%) strains were resistant to five or more antimicrobials. **Conclusion:** International surveillance of antimicrobial susceptibility results has been achieved. Comparable data on these results are being collated in the international Enter-net databases. Although the inclusion of data on testing results has begun relatively recently, its true value will be seen in the course of the next few years as the data become more complete and significant, and trends and the emergence of newly resistant strains are identified. In addition the exchange of antimicrobial resistance data has proved invaluable in confirming outbreak strains of *salmonella* infections on an international basis.

34 Vectorborne Diseases I

Monday, March 25, 10:30 a.m.
Regency Ballroom V

The Emergence of Rift Valley Fever in the Arabian Peninsula, 2000

H. El Sakka[1], R. Graham[1], E. Mohareb[1], D. Salma[1], S. Lewis[1], A. El Kholy[2], M. Ibrahim[2], F. Mahoney[1,3]

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Background: On September 17 2000, the Yemen Ministry of Agriculture and Irrigation (MoAI) and Ministry of Health (MOH) received reports about the occurrence of disease compatible with Rift Valley Fever (RVF) in the Tihama region of Yemen. Under terms of a cooperative agreement to rapidly respond to outbreaks, a WHO mission was quickly organized to provide assistance in the outbreak investigation. The Saudi Arabian Ministry of Health has described a simultaneous outbreak of RVF in the Jizan region of KSA.

Methods: Using standardized case investigation forms and mobile surveillance teams, a computerized database was established to monitor the outbreak. Laboratory capacity was developed to perform serologic assays for IgM-class antibody to Rift Valley Fever virus. A cross-sectional survey was conducted to evaluate attack rates and risk factors for disease.

Results: Case finding - Between August 7 to December 31, 2000, 1358 suspect case-patients were identified including 147 (11%) persons who died. The mean age of suspect case-patients was 31.4 years (range 1 month- 95 years). Among 555 case-patients with serological testing, 142 (26%) had IgM class antibody to RVF virus, 20 (4%) were weakly reactive. The clinical spectrum of disease was typical of RVF and included patients with benign and complicated disease (eg hemorrhagic disease, hepatitis, retinitis, and encephalitis). Overall, laboratory confirmed disease occurred in 14 districts in 5 different governorates. The majority of case-patients (>75%) reported exposure to sick animals, handling an abortus or slaughtering of animals in the week prior to illness. Among the 721 persons tested in the cross-sectional survey, 151 (21%) had serologic evidence of past or recent infection with RVF virus. Risk factors for disease included exposure to animal abortus (OR 3.3; $P < 0.05$), animal contact, (OR 3.1; $P < 0.05$) and contact with sick family members (OR 2.2; $P < 0.05$). Thirty six percent of participating households reported a similar outbreak in 1998 with waves of abortions and sudden death in the farm animals.

Conclusions: The outbreak response was highly effective in mobilizing resources in a rapid manner. Surveillance efforts documented widespread disease among humans and animals throughout the northern Tihama. Enhanced surveillance efforts are ongoing to monitor the potential for RVF virus to become endemic in the region.

Microheterogenicity of the Volgograd Clone of West Nile Virus

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In August and September 1999, an outbreak of West Nile (WN) encephalitis/fever occurred in the Volgograd region of South Russia (> 600 human clinical cases). WN clinical cases were diagnosed in Volgograd region in 2000 and 2001 also (31 and 15 patients). Brain specimens from non-survivors were positive in specific RT-PCR assays confirming the presence of WN virus. We have sequenced the fragment of WN viral envelope (E) gene obtained from the brain tissue samples of 16 Volgograd patients with clinical and pathomorphological signs of aseptic meningoencephalitis. Fourteen patients died from September 3 to September 7, 1999. Nucleotide substitutions occurred at 5 of the 512 positions of the E gene fragment of 14 isolates. So 5 genovariants (VLG-1, AF412270; VLG-2, AF412271; VLG-3, AF412272; VLG-6, AF412273; VLG-11, AF412274) were presented. Variant VLG-1, found in 9 isolates, prevailed significantly ($p = 0004$, chi-square test). Within group mean p-distance was equal 0.0019 ± 0.0009 (pairwise p-distance ranged from 0 to 0.0059). All substitutions were in third codon, only one of them lead to amino acid change (Met-Ile in VLG-3). As far as all patients contracted the disease at the same time and at the same place, these isolates appeared belonging to the same clone. Minor differences might arise as a result of "genetic noise" or adaptation to host or vector. After additional analysis of GenBank WN sequences submitted from the USA 1999-2000 and Israel 1999-2000, we suggested to define conventionally the WN clone as the group of strains having within group mean p-distance less than 0.005 and the maximal pairwise p-distance less than 0.015 for nucleotide sequence. The E gene fragment of two WN isolates from Volgograd 2000 were identical to VLG-1 genovariant, that argued for the endemicity of this clone for the region. The nearest relatives of the Volgograd WN clone are the mosquito isolates from Romania-1996 [AF260969] and Kenya-1998. Their mean p-distances from the Volgograd clone were equal 0.006 ± 0.003, pairwise distance ranges from 0.0020 (one substitution without amino acid change in VLG-3 isolates in comparison to Romania-1996M isolate) to 0.0078 (four substitutions). According to our definition, Volgograd, Romanian and Kenyan strains belong to the same clone. The comparison of the complete genome of one Volgograd isolate [AF317203] and Romania-1996M isolate confirmed this hypothesis. The strains differed from each other in 46 nucleotide positions, 43 of them were located in coding region. 35 mutations were silent so the strains differed in 8 amino acid only. So the homology of WN-Volgograd-4 and WN-Romania-1996M strains was 99.77% for aa sequence and 99.58% for nt sequence. Although Volgograd-1999/2000, Romania-1996M, and Kenya-1998-mosquito isolates demonstrate an unusual degree of similarity, the exact mode of the clone introduction into Russia remains unclear.

Rapid Screening and Identification of West Nile Virus in Captive and Wild Birds Using Non-Invasive Environmental Samples and a Portable TaqMan RT-PCR

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Zoo animal populations in large cities could serve as excellent sentinels for the epidemiological surveillance of West Nile (WN) virus or other diseases if sample collection and screening for pathogens could be made easier and faster. Current rapid testing methods for WN include RT-PCR amplification of viral RNA from tissues, which is useful only if infected animals die. We describe the development of a Taqman RT-PCR assay for the specific real-time detection of WN and Kunjin (KUN) viruses suitable for environmental samples that can be performed in less than two hours on a portable instrument. A set of oligonucleotide primers and a single fluorogenic probe were designed to target a conserved area within of the 3'noncoding region common to all known sequences of WN

and KUN. Preliminary evaluation and optimization of the assay were performed on cell culture derived stock viruses representing WN, KUN and multiple flaviviral near neighbors. The assay successfully detected all WN and KUN strains tested but did not amplify closely related flaviviruses. Archived RNA samples from tissues, blood, cloacal and orpharyngeal swabs, and guano representing zoo and wild birds populations as well as serially collected serum and guano from birds experimentally infected with WN were obtained for evaluation of the assay. RNA was extracted from the later sample set using the Qiagen, QIAamp viral RNA mini kit. Testing of archived RNA samples from captive and wild animal populations previously identified as infected with WN and control animals indicated that the Taqman assay had 100% correlation with viral isolation and gel based RT-PCR results for all sample types and species tested. Testing of serum and guano samples from experimentally infected crows revealed a 100% correlation between Taqman and viral isolation and plaque assay results for serum and guano for all samples with viral titers of at least 10e+3.0 PFU/ml. These results indicate that the assay may be suitable for testing for WN in guano samples from live birds. Preliminary results appear promising and highlight the potential use of this assay for screening for WN or KUN. The ability to test multiple sample types including non-invasive guano samples from live birds facilitate the potential use of the assay as a rapid tool for the epidemiological surveillance and diagnostic investigation of West Nile and Kunjin viruses.

West Nile Virus First Transmission Season in Florida, 2001 – More than 400 Horse Cases and 170 Chicken Seroconversions but Only Sporadic Human Disease

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With endemic St. Louis Encephalitis virus and Eastern Encephalomyelitis virus transmission in Florida, the state has a well established arbovirus surveillance program mainly by using sentinel chicken flocks, monitoring equine arboviruses and by enhanced passive human encephalitis case investigation. In anticipation of the arrival of West Nile (WN) virus in the state, an interagency task force was formed and, based on the experience from states in the North East, protocols for additional surveillance using dead bird reporting, dead bird testing and horse testing were established.

After the virus was first detected in Florida in early July 2001, intensive surveillance efforts over the following 4 months uncovered evidence of WN virus infections in 763 wild birds, 404 horses, 175 sentinel chickens and 11 people. West Nile virus infected wild birds were found in 65 of the 67 Florida counties. However, unlike the predominantly urban 1999 and 2000 epizootics in New York and other northeastern states, the epicenter of the Florida epizootic was in the mostly rural north and north central Florida. Only 7% of WN virus positive dead birds, 4% of WN virus positive horses and 17% of WN virus positive chicken found statewide, were from counties in the central and southern parts of the state, the focus of SLE virus transmission in Florida.

Eight human cases were diagnosed from 7 north and north central Florida counties. Three additional cases were diagnosed in Monroe County (the Florida Keys). Seven case-patients were males, median age was 50 years and onset dates ranged from July 13 to October 28, 2001. Seven were hospitalized with no fatalities. All human cases were preceded by detections of virus infections in animals in the state. However, only seven of the eleven cases were preceded by reports of WN virus detection in birds or horses in the local county.

The reasons for the limited number of human WN virus cases are unclear.

Surveillance data and disease prevention messages were publicized on the web, in news letters and in regular state and local press releases, measures that have been shown to increase the public awareness of the need to protect themselves against mosquito bites in previous outbreaks. In addition, extensive mosquito control efforts were undertaken in counties with mammalian virus transmission. Ecological and behavioral characteristics of the local mosquito vector(s) may also be of importance. Mosquito collection data suggest the human disease vectors may be one or several local species in the Culex family. Virus isolations have also been made from *Anopheles atropos, Culiseta melanura, Ochlerotatus atlanticus* and *Oc. taeniorhynchus*.

35 Molecular Diagnostics and Epidemiology I

Monday, March 25, 10:30 a.m.
Centennial Ballroom III

A Molecular Approach to the Epidemiology of *Giardia guodenalis* in a Peruvian Shantytown

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Giardia duodenalis is a protozoan parasite that causes severe diarrhea, abdominal pain and rapid weight loss. As the most common intestinal parasite of humans in developed countries, *G. duodenalis* has been named in several U.S. outbreaks occurring in daycare centers and small communities. The situation, however, is far worse in developing countries where living conditions are often crowded and sanitation is poor. In fact, these conditions create an environment where people are continually exposed to infection. This setting has proven especially devastating for children, whose immune systems are not developed enough to fight off repeated *G. duodenalis* infections. Children with multiple infections early in life do not develop equally with their age-matched counterparts. While infectious from person to person, controversy remains as to whether or not the organism is transmissible from animals to humans. Furthermore, transmission patterns within an endemic community are poorly understood. This study attempts to provide insight into these issues by examining an endemic locality in Peru. Because the organism is passed in the feces, stool samples were collected from 12 households and their dogs living in a shantytown outside of Lima, Peru from May 20 to July 31, 2001. Households consisted of five to nine members, and their ages ranged from 0 to 58 years. Fecal samples were collected weekly from 81 humans and 4 dogs. Samples were microscopically screened for *G. duodenalis*, and positive fecal samples were purified using differential centrifugation techniques. *G. duodenalis* DNA was extracted from purified samples using a QIAamp DNA Stool Mini Kit. To identify different strains of *G. duodenalis* affecting the shantytown, a genomic region variable among *G. duodenalis* strains was analyzed. The small subunit ribosomal (SSU) RNA gene was targeted utilizing the polymerase chain reaction and primers RH4 and RH11. A 292-bp product was produced from positive samples and sequenced to compare strains. Infections were tracked graphically taking into consideration each participant's age, infection duration, and the infecting *G. duodenalis* strain. During the study, 37 of 81 human participants microscopically screened positive for *G. duodenalis*, while one of four dogs screened positive. Comparison of the SSU-RNA sequences from human isolates reveals the predominance of two distinct genotypes within the endemic locality (the dog isolate could not be sequenced). However, only a single *G. duodenalis* genotype was found among infected members from the

same household during the study. These results suggest that infection may occur from a single source, and that transmission is likely to occur among household members.

Increasing Detection of Malaria in U.S. Hospitals Using the OptiMAL Rapid Diagnostic Test

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There are greater than 1,000 cases of malaria diagnosed each year in the United States. While most cases are imported, U.S. malaria cases have also been attributed to blood transfusion or local mosquito transmission. Reported numbers, however, may be artificially low because most U.S. hospital laboratory technologists have limited experience in identifying malaria parasites and are only infrequently requested to screen for this disease. In this study, a rapid malaria diagnostic test, the OptiMAL (Flow Inc., Portland, OR) was introduced to selected U.S. hospitals in an effort to assist and increase the identification of malaria cases. The OptiMAL test is an immunochromatographic test that both identifies and speciates malaria parasites based on detection of parasite lactate dehydrogenase (pLDH) from a drop of patient blood. Results are visually read as colored bands on a nitrocellulose strip. In this study, a total of 83 patients with suspect malaria were tested by both microscopy and OptiMAL. Patients reporting to these hospitals had recently traveled from Nigeria, Kenya, Uganda, Senegal, Gambia, Ghana, Sudan, Iraq, India, Ecuador, Indonesia, or Bangladesh. Results indicated that 19 were positive for malaria by bloodfilm (13 falciparum, 6 vivax) while 18 were positive by OptiMAL (13 falciparum, 5 vivax). Initially, there was one discrepant sample wherein the bloodfilm was positive and the OptiMAL was negative. However, further evaluation of the patient blood sample by that state's Dept. of Health revealed that the patient was infected with Babesia spp. and not malaria. Thus the OptiMAL was correct and the initial blood film reading was incorrect. To date, we report 100% sensitivity and 100% specificity in the U.S. hospital study using the OptiMAL with eight additional months left in the study. Participating hospitals have reported that the OptiMAL rapid malaria test was well accepted and enthusiastically welcomed by those working in their diagnostic laboratories. Integration of the OptiMAL rapid malaria diagnostic test into the U.S. healthcare infrastructure can provide an important and easy to use diagnostic tool for the detection of malaria.

Incidence and Type Distribution of Astrovirus Among Spanish Children

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Our understanding of the epidemiology of astrovirus-associated acute gastroenteritis is changing markedly with each improvement in detection methods. The incidence of astrovirus infection in children less than 4 years of age diagnosed with acute gastroenteritis in a hospital of Madrid during one year was determined by the combination of two methods (EIA and RT-PCR). In this study, faeces from 822 children diagnosed in a Hospital's paediatric emergency room were analysed. In every sample, the presence of astrovirus was analysed by EIA (IDEIA, DAKO). Besides, samples in which no enteric pathogen was detected (neither bacterial nor viral) were analysed by astrovirus specific RT-PCR. Astrovirus was detected in 36 (4.38%) of 822 specimens tested by EIA (IDEIA, Dako) and in 50 more specimens (6.08%) by RT-PCR. This represents 10.5% (86) of all children tested for enteric pathogens, including viral and bacterial, over the survey period. Using RT-PCR as a method of detection of astrovirus this viral agent can be considered as the second cause of acute gastroenteritis of viral origin. A selection of the 86 astrovirus positive samples of this study are being analysed by RT-PCR and nucleotide sequencing of 348pb within the capsid protein precursor region of the genome for their phylogenetic grouping (genotype). Preliminary results point out that HAst-1 could be the predominating genotype in this study.

Detection and Typing of Enterovirus in Cerebrospinal Fluid

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Enteroviruses are the most common cause of acute aseptic meningitis and meningoencephalitis. Reverse transcription-polymerase chain reaction (RT-PCR) assays have recently been developed for the detection of enterovirus RNA directly from clinical samples. The primers used in most of these assays are targeted to conserved sequences within the 5' noncoding region (5' NCR) of the enterovirus genome. Primers targeted to the VP1 sequence of enteroviruses have facilitated the molecular typing of enteroviruses. We have assessed RT-PCR assays with primers targeted to two genomic regions (5' NCR and VP1). Cerebrospinal fluid (n =1545) received at our encephalitis PCR laboratory since July 1997 were examined. Each clinical sample was assayed for the presence of 11 different viruses, including enterovirus. Primers targeted to the conserved 5' NCR of the enterovirus genome were used routinely for diagnostic detection. PCR products were visualized on agarose gels stained with ethidium bromide. Amplicons of the expected size were recovered and sequenced to confirm the identity of the viruses. A total of 207 cases of enterovirus infections were identified. Seventy percent of all cases occurred during the months of August, September, and October. Molecular typing of enterovirus was performed with degenerate primers targeted to the VP1 region. The sequences of the amplicons were compared with a database containing the sequences of all 66 human enterovirus serotypes. Of 83 cases examined for the presence of VP1 sequences, 49 (59.1%) were echovirus 18, 23 (27.7%) were echovirus 13, 8 (9.6%) were echovirus 30, 2 (2.4%) were echovirus 6, and 1 (1.2%) was coxsackie A9. Our data suggests that (1) RT-PCR with primers targeted to the enterovirus 5' NCR region provides a rapid and sensitive procedure for routine laboratory diagnosis of enterovirus infections, and (2) RT-PCR with primers targeted to VP1 provides a useful tool for the identification of enterovirus. The typing of enteroviruses is important for epidemiologic studies of enterovirus disease outbreaks.

36 Late Breakers I

Monday, March 25, 10:30 a.m.
Centennial Ballroom IV

37 Smallpox Response

Monday, March 25, 10:30 a.m.
Centennial Ballroom II

38 First Encounters with New Diseases: The Clinician's Perspective

Monday, March 25, 11:30 a.m.
Regency Ballroom VI/VII

39 Zoonotic Diseases

Monday, March 25, 1:00 p.m.
Centennial Ballroom I

Shared Animal and Human Influenza Viruses: A Role in the Next Pandemic?

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The H5N1 virus that infected chicken and humans in Hong Kong in 1997 had poor human-to-human transmissibility. Would it have given rise to a full-blooded rather than an incipient pandemic if had it undergone prior reassortment with a prevailing human influenza virus in a pig to acquire the gene(s) that facilitate this? Does the H5N1 virus still pose a pandemic threat given the isolation of different genotypes from fatal infections of chicken in Hong Kong in 2001? Does the H9N2 virus pose a greater pandemic threat than H5N1 given the isolation in Hong Kong recently of one lineage from children with influenza-like illness and another from pigs? The recent isolation of H4N6 virus from pigs with pneumonia in Canada extends the range of known avian H subtypes isolated from naturally infected pigs. Could the pig play a consolidating role in a chain of events as a mixing vessel for the reassortment of avian and human influenza viruses in the genesis of the next pandemic virus?

The Emergence of Infectious Diseases Among Wildlife and the Origin of Human Zoonoses

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Using the criteria that define emerging infectious diseases (EIDs) of humans, we can identify a significant group of EIDs affecting wildlife, many that have caused mass mortality events and population declines. A key example is chytridiomycosis, a recently discovered fungal disease of amphibians implicated in global population declines and species extinctions. Our research strongly suggests that the causative agent has been disseminated internationally via globalized trade in amphibians. House finch mycoplasmal conjunctivitis; canine distemper in lions, African wild dogs and marine mammals, infectious salmon anemia and the majority of wildlife EIDs have been driven by anthropogenic introduction of hosts and/or pathogens to new geographic regions ("pathogen pollution"). What can these phenomena teach us about disease emergence in human populations? The majority of human EIDs are zoonotic, either classically or in the broadest sense due to recent pathogen evolution following a host jump. The complex multi-host life cycles of some pathogens and abundance of unknown pathogens with zoonotic potential presents a serious challenge to surveillance and prediction of emergence. This requires analysis of the factors that alter contact and transmission rates between populations. Our analysis shows that for wildlife EIDs these factors are almost entirely anthropogenic environmental changes. They include close parallels of commonly cited drivers of human EIDs and reflect a historically unprecedented level of interaction between humans, domestic animals and wildlife. Many are poorly understood, but clearly have the potential to alter transmission and contact rates and promote zoonotic emergence. These include habitat fragmentation, urban sprawl, blocking of wildlife migration routes, deforestation, encroachment, overfishing and others. Ecologists and conservation biologists have developed a wealth of knowledge on the direct impacts of these changes on wildlife populations, but have largely ignored their impact on pathogen transmission. We propose that predicting zoonotic emergence will be possible for some pathogens, but only by a fusion of these approaches and closer collaboration between disciplines. This integration requires us to step outside the security of our narrow fields and tackle complex issues in related disciplines. For medics and public health researchers, this means understanding ecosystem processes, conservation biology and wildlife population biology.

40 Innovative Surveillance Systems

Monday, March 25, 1:00 p.m.
Centennial Ballroom II

41 Foodborne/ Waterborne Disease

Monday, March 25, 1:00 p.m.
Centennial Ballroom III

42 Public Health Policy/Law

Monday, March 25, 1:00 p.m.
Centennial Ballroom IV

Legal and Policy Issues To Consider Before a Bioterrorist Attack

R. E. Hoffman

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A bioterrorism attack has the potential to overwhelm public health agencies, hospitals, and health care providers, especially if the bioterrorist agent may be transmitted from person to person. The response will require coordination among these groups as well as local, state, and federal political leaders, public information specialists, emergency managers, public safety workers, law enforcement officials, and mental health workers. The key to an effective response is assuring that all possible workers and support staff are given adequate personal protective equipment and organized into teams of sufficient numbers with efficient communications. To this end, it is recommended that existing legal authority be reviewed and revised or drafted as necessary. Consideration should be given to assessment of emergency public health powers as well as reduction or elimination of legal obstacles that prevent private entities and public agencies from working together in a public health crisis for the welfare of the community. Laws, regulations, executive orders, and emergency plans should be flexible and not unduly restrictive or burdensome so that those leading the response can

use the best laboratory methods, forensic science, and epidemiology to adapt rapidly to highly unusual circumstances facing the community and nation. The response to an attack can be optimized through detailed planning and training. Issues surrounding the use of restrictive measures, such as isolation and quarantine, for large numbers of persons will be discussed. Examples of Colorado bioterrorism response laws, regulations, and draft executive orders will be presented.

West Nile Virus in New York City

W. Lopez

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In late August of 1999 a cluster of encephalitis cases was detected in Queens County, New York City, through the fortuitous combination of early notification to the City Health Department by a treating physician and amazing detective work on the part of city epidemiologists. Quick consultations ensued between the city Department of Health (CDOH), the state Department of Health (SDOH) and the federal Centers for Disease Control and Prevention (CDC), and human specimens were submitted to them for laboratory analysis. In the days that followed those discussions were expanded to include the Mayor's Office of Emergency Management (OEM), the state Department of Environmental Conservation (DEC), and the federal Environmental Protection Agency (EPA). The city responded immediately by applying larvicide to standing bodies of water and by spraying the pesticide Malathion in northern Queens by helicopter to control adult mosquitoes. A few weeks later the causative agent was determined to be West Nile virus (WNV), a type of encephalitis that had never before been transmitted in the western hemisphere.

New York City's experience as the epicenter of WNV offers many lessons for the practitioners of public health and of public health law. WNV reminds us all of the need to maintain a public health infrastructure that does not lose sight of the old threats, and of how they were brought under control, even in the face of new emerging threats such as bio-terrorism. Nuisance control and abatement is one of the oldest public health mandates, and one of the most traditional uses of the police power to protect the public from the neglect and/or abuse of the individual. WNV requires the re-engineering, re-invigoration, and also the re-learning, of nuisance control practice and of its underlying laws, all in an age of needed environmental conservation. Indeed, WNV has forced the public health and environmental governmental establishments to work together in ways that have sensitized both to the importance of the other's role. In the end, the mission of both, as with all of government, is similar and complimentary; i.e., to provide for the health, safety and welfare of the public.

Perhaps the most fundamental lesson of the WNV experience is the reaffirmation of the fact that the public health practitioner, today, cannot implement public health policy and interventions without sound legal advice that is cognizant of not only the nuances of traditional public health law, but also of the law that governs kindred agencies. In effect, public health law is broader and more complicated than in the past. The WNV experience in New York City shows how closely law intertwines with policy and programmatic initiatives. Hopefully, it also shows how law, instead of being an obstacle to sound policy, can be a vehicle that facilitates a better public health outcome.

43 Disease Eradication

Monday, March 25, 1:00 p.m.
Regency Ballroom V

44 Emerging Zoonoses I

Monday, March 25, 3:00 p.m.
Regency Ballroom V

Emergence of Canine Visceral Leishmaniasis in Dogs in North America

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Beginning in the late summer of 1999, foxhounds at a hunt club in Dutchess Co., NY, developed illness with manifestations that included bleeding, wasting, seizures, hair loss, skin lesions, kidney failure, and swollen limbs and joints; several dogs died. *Leishmania* spp. was isolated from lymph nodes and other tissues of 15 seropositive dogs. investigation was expanded and screening of foxhounds in other states has revealed evidence of widespread infection. Through April, 2001, sera from more than 10,000 foxhounds and other hunting dogs throughout North America have been tested and positive titers were detected in 1.8%. At least one seropositive dog was detected in 60 different kennels of foxhounds in 21 U.S. states and 2 Canadian provinces. The organisms isolated from 40 hounds in multiple states and provinces were typed at the Institute of Public Health (Rome) and determined to be *L. infantum* MON1. The routes of transmission in these dogs remain unclear. Phlebotomine species exist in most of these areas, however, vector transmission has not been demonstrated and epidemiologic characteristics of the infection do not support vector transmission. Serotesting of pet dogs (n~600) and wild canids (n=300), many of them from geographic localities close to infected foxhounds, have not revealed evidence of infection. Foxhounds commonly live in close contact with each other and mixing of dogs from hunt clubs in different states is common; therefore, direct dog-to-dog transmission may occur. To date there have been no cases of autochthonous human visceral leishmaniasis reported in the United States. Investigations are continuing to identify infections in dogs and other potential hosts, to determine how the infection is being transmitted, and to determine the potential public health significance.

Detection and Genetic Analysis of Swine Hepatitis E Virus in Farm Waste

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Hepatitis E virus (HEV), an unclassified calici-like virus, was first detected in hepatitis outbreaks caused by gross fecal contamination of water supplies in endemic countries. Increasing evidence suggests that HEV may be a zoonotic agent whose full range of natural hosts has yet to be defined. Serologic evidence indicates that antibodies to HEV are present in swine from Australia, Canada, China, Germany, Korea, Nepal, New Zealand, Taiwan, Thailand, the United States (US) and Vietnam. Evidence of HEV-related antibodies have also been reported in rats, rhesus monkeys, chickens, dogs, sheep, goats, and cattle. The sequences of HEV-like viruses from swine and chickens have recently been published; swine virus is closely related to human isolates of HEV, while the chicken related HEV is genetically different. Swine HEV has pre-

viously been detected in individual or pooled fecal samples by RT-PCR. Barn waste that is composed of fecal matter, urine and other substances and is commonly stored in pits or lagoons, also may contain HEV shed from animals, but sHEV detection in such material has not been reported. HEV presence in such waste would have implications for swine waste management systems. We processed 5 liters of liquid barn waste (lagoon-type) collected in the fall of 2000 (2 liters) and in the spring of 2001 (3 liters) from a midwestern facility in the US for the detection of sHEV. Each one-liter sample was separated into solid and liquids by a low speed centrifugation. The liquid fraction was concentrated, extracted, and reconcentrated to produce ~ 10 ml samples. The solids were re-extracted to produce two fractions: liquid and solid. Each of these fractions was processed separately to produce 2 more 10 ml samples, for a total of three ~10 ml concentrates from each liter of liquid manure. RNA extracts of the concentrates were analyzed by RT-PCR for sHEV with primers specific for sHEV from the ORF-2 region of the genome. All fifteen samples were RT-PCR positive and serial 10-fold dilutions revealed that concentrates averaged ~10 5 per ml. Sequencing of amplified DNA yielded two different sequences corresponding to the fall and spring collection times, respectively. Comparison with available sequences in this HEV ORF 2 region revealed that these sequences were genotype III. This genotype contains the previously published swine HEV sequence (US- Sw1, also from the Midwestern US) and two sequences from sporadic human cases recently identified in the US. In summary, we have isolated from liquid swine manure waste two different sequences of sHEV that are distinct from the other published midwestern sHEV. The concentration method used will be useful for detection of sHEV in mixed waste from different barns, farms, or herds.

Enhanced Laboratory-based Surveillance of Shiga Toxin-producing Escherichia coli O157, the Netherlands

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In January 1999 an enhanced surveillance of Shiga toxin-producing Escherichia coli (STEC) O157 was implemented in the Netherlands. All laboratories report positive cases to the public health services and submit isolates for typing to the reference laboratory. Public health services collect clinical and risk factor information of patients. In February 2000, a questionnaire was sent to all laboratories to assess the criteria for testing, diagnostic tools used, and participation in the surveillance. Between January 1999 and June 2001, 93 symptomatic cases were reported, 25% aged 0-4 years. Based on O-, H- and stx-typing, two types dominated: O157:H7, stx2 (47%) and O157:H-, stx1, stx2 (24%). Distributions of types were similar for HUS and non-HUS patients. However, less stx1-positive strains (mainly also stx2-positive) were isolated from hospitalised cases (30% vs 41% for non-hospitalised cases, not significant) and urination problems were less often reported by patients with stx1-positive strains (20% vs 49%, Chi2=4.5, p=0.03). Pulsed-field gel electrophoresis, using Xba I, showed 17 clusters of isolates with at least 95% fragments in common. Although several had a known relationship (mainly household), 13 clusters (also) included isolates with an unknown epidemiological link. Within 6 clusters, based on the interval between dates of onset of illness, a common source for the infections was imaginable. Of all patients, 52% reported a known risk factor, such as contact with farm animals or manure, consumption of raw or undercooked beef, raw milk, raw-milk cheese or contact with a symptomatic individual. Compared to data from control persons from a general practice-based study on gastroenteritis, especially contact with farm animals (manure) was reported clearly more often by STEC patients (21% vs 7%), suggesting that this might be an important risk factor for STEC O157 in our country. For a 1-year old boy, this could be confirmed: indistinguishable PFGE patterns were obtained for isolates from the boy and goats at the petting zoo that he visited. Response to the laboratory survey was high (97%). Ninety-five percent of laboratories tested for STEC O157. The majority (88%) used culture on (CT-)SMAC as detection method. Confirmation was primarily performed with commercially available latex agglutination assays (95% of laboratories) and biochemical characterisation with the API 20E test (42%). Most laboratories (92%) used selection criteria for testing: bloody diarrhoea and other clinical information were reported by 81% of laboratories and young age by 10%. It is concluded that STEC O157 seems a limited public health problem in the Netherlands. However, testing is mainly performed selectively using clinical and age criteria. PFGE results suggest that small clusters regularly occur, but often go unnoticed. Molecular typing is a useful tool for cluster identification in routine surveillance.

Outbreaks of Multidrug-Resistant *Salmonella* Serotype Typhimurium Infections Associated with Small Animal Veterinary Facilities in Idaho, Minnesota and Washington, 1999

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Background: An estimated 1.4 million persons are infected with *Salmonella* annually in the United States. While the majority of these infections are acquired from eating contaminated foods, *Salmonella* also is transmitted through contaminated water and contact with reptiles, farm animals, and pets. Outbreaks of human *Salmonella* infections associated with veterinary facilities have been infrequently reported and most such outbreaks occurred in large animal (e.g., cattle, horses) facilities. Outbreaks associated with small animal (e.g., dog, cat) facilities are rare. **Methods:** Routine laboratory-based *Salmonella* surveillance was conducted in Idaho, Minnesota, and Washington; clinical laboratories forwarded *Salmonella* isolates to the state public health laboratories for serotyping. Field investigations were conducted by the state health departments. Selected *Salmonella* isolates were forwarded to CDC for phage typing and antimicrobial susceptibility to 17 antimicrobial agents using broth microdilution (Sensititre®). Selected *Salmonella* isolates from the state veterinary diagnostic laboratory in Minnesota also were forwarded to the state public health laboratory for pulsed-field gel electrophoresis (PFGE). **Results:** In 1999, outbreaks of *Salmonella* serotype Typhimurium associated with small animal veterinary facilities were reported in Idaho, Minnesota, and Washington. In Idaho, 10 of 20 employees of a veterinary clinic became ill after employees cared for kittens ill with diarrhea; ill employees reported no other common exposures. Specimens were not collected from the kittens, but stool specimens from five ill persons yielded *S.* Typhimurium resistant to ampicillin, chloramphenicol, sulfonamides, streptomycin and tetracycline (R-type ACSSuT). In Minnesota, *S.* Typhimurium DT104 R-type ACSSuT was isolated from 9 cats at an animal shelter that died from enteritis. These isolates were indistinguishable by PFGE from isolates from 7 ill persons, 6 of whom reported a connection with the animal shelter. In Washington, *S.* Typhimurium DT104 R-type ACSSuT was isolated from three ill employees or clients of a veterinary facility. Specimens from 14 cats associated with the facility also yielded *S.* Typhimurium DT104 R-type ACSSuT. **Conclusion:** Three states reported outbreaks of multidrug-resistant *S.* Typhimurium infections among employees or clients of small animal facilities. In each facility, employee or client illness followed illness in animals. These outbreaks demonstrate the need for increased hygiene within small animal facilities and at home, especially after handling of animal feces.

An Outbreak of *Salmonella* Javiana Associated with Amphibian Contact – Mississippi, 2001

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Background: Although *Salmonella* Javiana is the fifth most commonly isolated *Salmonella* serotype among humans in the United States, the risk factors and sources for infection are largely unknown. Infection with *S.* Javiana occurs primarily in infants and young children and appears to be restricted to specific geographic regions of the country. During the summer of 2001, an outbreak of *S.* Javiana infections occurred among young children in greater Jackson, Mississippi, providing an opportunity to examine risk factors for infection. **Methods:** We conducted a case-control study to identify risk factors for infection. We defined a case as infection with *S.* Javiana between August and September 2001 in a Mississippi resident. Two age-and county- matched controls per case were randomly selected from the Mississippi state birth registry and through sequential digit dialing. Pulsed-field gel electrophoresis (PFGE) was performed on all *S.* Javiana isolates from stool cultures. **Results:** We enrolled 55 case patients and 109 controls. Among patients, thirty-three (58%) were female and the median age was 24 months (range 3 months to 70 years). Symptoms included fever (85.5%), abdominal pain (82.6%), and bloody diarrhea (44%). The median duration of illness was 7 days. Nine (16.4%) patients were hospitalized; none died. Molecular subtyping of 51 isolates yielded 18 distinct PFGE patterns, suggesting multiple sources of infection. The most common pattern was found in 20 (39%) isolates. Thirty-two (58%) case-patients reported exposure to amphibians (frogs, toads and turtles), defined as owning an amphibian, touching an amphibian, or seeing an amphibian on one's property, compared with 32 (31%) controls (matched odds ratio 3.3, p=0.003). In addition, consumption of watermelon was associated with *S.* Javiana infection, but the frequency of this exposure was low and could only account for six (12%) infections. **Conclusions:** Amphibians may be a reservoir for S. Javiana. In our study, contact with amphibians and and their environments was a risk factor for infection. Such exposures may be more common among toddlers, who are likely to have increased hand to floor contact, potentially explaining why *S.* Javiana disproportionately affects young children. Interestingly, the geographic distribution of certain amphibian species mimics that of *S.* Javiana infection; both cluster in the Southeastern United States. Public health officials should promote proper hand washing after contact with amphibians to decrease the risk of infection with *S.* Javiana.

Outbreaks of Salmonellosis at Elementary Schools Associated with Dissection of Owl Pellets

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Background: On May 22, 2001 the Washington County Department of Public Health and Environment (WCDPHE) received reports from two physicians of children from the same elementary school with acute febrile gastroenteritis. Symptoms included high fevers and bloody stools, and *Salmonella* had reportedly been cultured from the stool of one child. The school nurse reported high absenteeism rates during the same week. **Methods:** Staff from the WCDPHE and Minnesota Department of Health interviewed students from the elementary school about illness history, meals at school, and school-related activities. Food service at the school was evaluated. A case was defined as a school attendee who developed diarrhea (≥3 stools in a 24-hour period) and fever on or after May 14. Animals and animal materials used in school activities were cultured. *Salmonella* isolates were subtyped by pulsed-field gel electrophoresis (PFGE). **Results:** Of 352 students, 205 (58%) were interviewed. Of students interviewed, 39 (19%) met the case definition. *Salmonella* Typhimurium was cultured from the stool of 27 cases; all but one isolate had an indistinguishable PFGE pattern (designated TM353). Dates of illness onset ranged from May 17 to May 25. Illness was associated with being a member of the science club (odds ratio [OR], 38.0; 95% confidence interval [CI], 5.0-308; p<0.001) and being a member of the after-school latchkey program (OR, 7.0; 95% CI, 3.0-17.0; p<0.001). On May 16, science club members dissected owl pellets (i.e., regurgitated indigestible fur, bones, from a recent meal) on a table in the school's cafeteria. Concurrently, the latchkey program was being held in the cafeteria. The same table was used for snacks for the latchkey children following science club and for lunch the next day before it was sanitized. Subsequent to this outbreak, an outbreak was identified among science club members at a second elementary school. In this outbreak, seven of nine students became ill after dissecting owl pellets on May 24; *S.* Typhimurium TM353 was recovered from six of these students. The pellets in both outbreaks originated from a single barred owl that was housed at a local nature center. Cultures of left over pellets and fresh feces from the owl yielded *S.* Typhimurium TM353. The owl shed *S.* Typhimurium in its feces for at least 4 months (when culturing was discontinued). Prior to the outbreaks, the owl's diet consisted of mice and chicks from commercial sources; TM353 was recovered from all four chicks left over from the shipment used to feed the owl prior to and during the outbreaks. **Conclusions:** These are the first reported outbreaks of salmonellosis due to contact with owl pellets. As with all animal-derived materials, handling of owl pellets should be followed by sanitation of contact surfaces and thorough hand washing. Sterilized owl pellets for use in educational activities can be obtained from commercial sources.

45 Bioterrorism

Monday, March 25, 3:00 p.m.
Centennial Ballroom II

Public Health Laboratory Response to an Anthrax Incident in Connecticut

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In mid-November of 2001, a case of anthrax was confirmed in a 94-year-old woman in Connecticut. The Connecticut Department of Public Health (DPH) laboratory had been processing various kinds of specimens up to that point but the number of specimens processed, the urgency to produce results and the demand for data increased dramatically after the incident. The Bio-Response Action Team (BRATs, a volunteer group of microbiologists) was fully activated along with considerable administrative support. We will present our practical experience as well as data on the numbers, variety and temporal distribution of the greater than 2100 specimens we have processed to date as well as descriptive information on the technical changes that were made in the laboratory to accommodate the changing demands. We hope that this information will help other state health laboratories to better prepare for a similar incident

Rapid Molecular Identification of *B. anthracis* in New York State in Response to Recent Bioterrorism Incidents

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In the three years prior to September 11th, 2001, the NYSDOH received and tested an average of six suspect bioterrorism specimens a year for *Bacillus anthracis*. From September 11th until December 14th, 850 specimens were received for *Bacillus anthracis* testing. Our response plan to this crisis included modifications to our existing protocols as well as the decision to use germination followed by the polymerase chain reaction (PCR) as the primary method for detection of *B. anthracis* and culture as a confirmatory method. Three separate PCR assays were developed which required prior assessment of sensitivity, specificity, as well as overcoming potential PCR inhibitors often found in environmental samples. We found that our PCR assays can detect <25 bacteria and have 100% specificity when tested against *Bacillus* spp., and other non-*Bacillus* bacteria. Analysis of past bioterrorism specimens revealed that a significant number of samples contained inhibitors to PCR which necessitated methods to inactivate inhibitors in environmental specimens. A total of 26 substances were analyzed for PCR inhibition including common household powders, laboratory agents, soil, blood samples, several envelope types, photographs, and past bioterrorism samples. The majority of PCR inhibitors were removed by a DNA extraction together with a modification of the components of the PCR reaction mix. When tested on biothreat samples, only 30 of the 838 specimens containing PCR inhibitors that were not removed. The samples that demonstrated persistent inhibition in PCR assays as well as PCR-positive samples were cultured. An integral part of our identification/confirmation scheme for *B. anthracis* includes phage sensitivity and direct fluorescent antibody of both the cell wall and capsule. Of the 850 specimens received, 838 were processed; 778 were negative by PCR and 47 were negative by culture for *B. anthracis*. Additionally, 11 samples were positive by both PCR and culture, one sample was positive by PCR but negative by culture, and one sample was negative by PCR and positive by culture, with only one colony of *B. anthracis* isolated. The new streamlined protocol has improved our turn-around time for ruling out *B. anthracis* from two to five days before this crisis to our current 7-18 hours. The current protocol also can now accommodate close to 200 specimens per day if necessary whereas previous methodology limited our laboratory capacity to testing 5 specimens per day. We are also working on incorporating new CDC-developed ABI Prism 7700 and Smart Cycler assays that should further increase capacity and/or decrease turn-around time. This experience demonstrates the need to build a strong public health infrastructure in order to increase laboratory surge capacity as well as advanced training to deal with the increasing threat of bioterrorism events.

Laboratory Response in the Commonwealth of Virginia to the Intentional Release of *Bacillus anthracis*

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The intentional release of *Bacillus anthracis* in the United States has resulted in increased laboratory testing to identify and confirm the presence or absence of *B. anthracis* in clinical specimens and environmental samples. To address an unprecedented demand to process, test and store a large number of potentially infectious legal samples, the Division of Consolidated Laboratory Services (DCLS) in the Commonwealth of Virginia, rapidly reviewed and revised protocols for sample collection, transport, submission, chain-of-custody, triage, and evidence storage and retrieval. Pathways to establish communication of test results to law enforcement and local public health departments were redefined. The Laboratory Response Network (LRN) protocols, reagents, and control organisms, were used to process over 800 samples consisting of 127 clinical samples, 614 suspicious mail items and/or powders, and 84 other environmental samples. Three of 47 clinical isolates submitted for confirmation were positive for *B. anthracis*, as determined by gamma phage lysis, M'Fadyean staining, and direct fluorescent antibody tests for *B. anthracis* cell wall-associated polysaccharide and capsule. In addition, *B. anthracis* specific DNA was amplified from these isolates using three independent real time polymerase chain reactions. No *B. anthracis* colonies were obtained from environmental samples submitted for testing. However, 101 isolates containing gram positive rods with characteristics that were morphologically indistinguishable from *B. anthracis* on sheep blood agar plates were detected. All of these isolates were non-hemolytic and 78% were non-motile. None of the 101 isolates exhibited gamma phage lysis and all isolates requiring further characterization were negative by direct fluorescent antibody tests for *B. anthracis* cell wall-associated polysaccharide and/or capsule and real time PCR for *B. anthracis*. Further characterization of *B. anthracis*-like colonies is on going. Spores were detected by malachite green staining in six letters that contained a visible powder. Cultures of the powder yielded beta-hemolytic, motile, gram positive rods that were further characterized as being in the *B. cereus* group. These activities allowed DCLS to process high volumes of samples in an accurate and timely manner.

Monitoring of Human Exposure to *Bacillus thuringiensis* after Aerial Applications for Insect Control

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Aerial applications of Foray 48B, which contains Bacillus thuringiensis (Bt) strain HD1 (Btk HD1), were carried out on May 09-10, May 19-21, and June 08-09, 1999 to control European gypsy moth, Lymantria dispar, populations in Victoria, British Columbia, Canada. An assessment of the health impact of Btk was conducted by the Office of the Medical Health Officer of the Capital Health Region, during this period. Environmental (air and water) and human (nasal swab) samples, collected before and after aerial applications of Foray 48B, both in the spray zone and outside of the spray zone, were analyzed for the presence of Btk HD1-like bacteria. Random Amplified Polymorphic DNA (RAPD) analysis, cry gene specific polymerase chain reaction (PCR), and Dot-blot DNA hybridization techniques were used to screen over 11,000 isolates of bacteria. We identified bacteria with genetic patterns consistent with those of Btk HD1 in 9,102 of 10,659 (85.4%) isolates obtained from the air samples, 13 of 440 (2.9%) isolates obtained from the water samples, and 131 of 171 (76.6%) isolates from the nasal swab samples. These analyses suggest that bacteria applied from airplanes over urban areas result in both extensive environmental contamination and human exposure, even if individuals are in doors at the time of the application.

Threat Letter Menace: The Fiji Experience

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Objective: To process and identify the suspected material sent in threat letters to embassies and other local offices.

Methods: Pathology laboratories at the CWM hospital serves as the referral laboratory for the country. Microbiology lab processes the routine diagnostic specimens it receives from the hospital. It also provides its services to the police for its forensic investigations. Threat letters were sent to embassies, government offices, and offices of the prominent citizens. They were reported to police, who cordoned off the premises, obtained the specimens of suspected materials from those threat letters and sent to micro-

biology lab for identification, and sealed the office where these letters were opened. Microbiology lab processed these specimens, identified them with available lab resources, and advised the police accordingly. Offices where these letters were opened remained sealed during this period.

Results: A total of 11 specimens were sent to lab for processing. First of these was sent to an embassy, and the letter originated from overseas. Rests all sent to local offices and persons and were sent locally. All of these contained white powder, which immediately drew the suspicion of possible anthrax spores. They were processed as per CDC guidelines, and other reference textbooks. Microbact TM, API 20 E TM and API 50 CH TM were used for confirmation for their identity. None of them were found to be containing spores of *B. anthracis*.

Conclusions: Following the events of September 11 in USA and subsequent anthrax scare, similar tactics was used for creating panic and confusion among the people. Although possibly of anthrax spores sent to any one remained a remote possibility, is succeeded in creating a sense of apprehension, scare, and heightened state of alert. It also resulted in enormous waste in terms of work hours for the offices where these were sent, and extra burden in lab processing, resulting in resource drains on facility of limited resources.

Enhanced Emergency Department Surveillance System Following the World Trade Disaster – New York City, September 14 to October 10, 2001

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Background: After the events of September 11, 2001, the NYCDOH was under a heightened alert status for bioterrorist attacks in the city. As a result, an Emergency Department (ED) syndromic surveillance system was implemented with the assistance of CDC to monitor for an increase in disease syndromes that might represent a bioterrorist event. The system included the largest deployment of Epidemic Intelligence Service Officers in CDC history. **Methods:** From September 13th - 29th, CDC staff were stationed at 15 sentinel EDs on a 24-hour basis ("full staffing") and between September 30th and October 10th stationed at 12 EDs on an 18-hour basis due to resource limitations ("part staffing"). A standardized form was used to classify each visit into one of 12 distinct syndrome categories and to obtain demographics. Six of these syndrome categories represented prodromal manifestations of illness that may be caused by bioterrorist agents. Visits were classified by the ED physician, nurse, or EIS officers and based on discharge diagnosis and data was entered on-site. Data and ED census numbers were transferred to the NYCDOH every 24 hours. Data was analyzed daily for individual hospital and geographically-based statistical increases ("alarms") by syndrome. Retrospective analysis of the data was completed using SAS 8.0 to detect trends of syndromes and differences in reporting between coverage hours. **Results:** The NYCDOH received daily reports from 12 EDs during the entire surveillance period. Comparison of total visits recorded with ED census data indicated 85% of visits were recorded during "full staffing" while 75% of visits were recorded during "part staffing" ($\mu 2=997$, $p<0.0001$). Statistical "alarms" occurred 16 times with an "alarm" size of 2 to 105 visits. Each "alarm" was investigated by chart review through on-site CDC staff and no infectious disease outbreaks were detected. Of the total visits classified, 12.8% of visits were trauma related, 5.5% were related to exacerbation of an underlying respiratory condition, and 1.5% were associated with an unexplained death with history of fever. All other syndromes accounted for less than 1% of all ED visits. **Conclusions:** Daily analysis of the ED visits provided the opportunity for timely detection of increases in clinical syndromes citywide. On-site CDC staff promptly investigated statistical "alarms". The system was sensitive, detecting small increases in syndromes, but required 53 to 83 full-time staff to function optimally. The usefulness of implementing this type of surveillance in response to a high profile event should be further evaluated to assess the validity of syndromic coding and the timeliness of "alarm" investigations.

46 Chronic Diseases

Monday, March 25, 3:00 p.m.
Centennial Ballroom III

Failure to Detect *C. pneumoniae* in Atherosclerotic Specimens from Major Arteries of 93 Patients

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Background: Seroepidemiological studies have indicated a possible association between chronic *Chlamydia pneumoniae* (Cp) infection and atherosclerosis. Several studies, using different diagnostic methods have demonstrated Cp or its components in atherosclerotic lesions. Interestingly, these findings have not been confirmed by all researchers. **Methods and Results:** Punch specimens of the aortic wall of 61 patients undergoing coronary-aortic bypass graft, and carotid atheromas of 32 patients undergoing carotid endarterectomy, were examined for Cp by cell culture (HEp-2 cells), and two PCR assays in two different laboratories. Anti Cp IgG antibodies were found by MIF and ELISA in 67.5% and 55.4% of patients' serum specimens; IgA in 22.7%, and 35% respectively. Anti Cp IgM was found in one patient only. All cultures and PCR tests for Cp were negative. **Conclusions:** In our study population, we found no evidence that Cp exists within atheromatous arteries. The speculated association between Cp infection and atherosclerosis remains controversial and warrants further investigation

Prevalence of Hepatitis C and other Chronic Liver Disease Etiologies in Primary Care Practices

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Background: Little is known of the prevalence of chronic liver disease (CLD) in general, and hepatitis C in particular, in primary care patient populations. We conducted a cross-sectional study among primary care practices in Waterbury, CT to estimate CLD prevalence and its attributable causes among patients seeking primary care and to explore primary care practitioners' (PCPs) CLD-diagnosis documentation and referral habits. **Methods:** All 46 PCPs located within the Waterbury city limits were invited to participate. Patient charts were selected from each participating practice's active patient roster according to a simple weighted, random sampling scheme. Demographic and clinical data, substance use history, diagnosis of CLD, and referrals to gastroenterologists were recorded. A diagnosis of CLD was assigned using standard definitions for probable and possible CLD. Standard criteria were used to assign CLD etiologies where appropriate. **Results:** Of the 46 Waterbury PCPs, 31 (67%) participated, comprising 11 practices (7 group, 4 solo). A total of 1,610 charts (range 65-608 per practice) were screened. The median patient age was 42 years

(range 18-96); 39% were male. A total of 60 patients met our definition for CLD, making the overall prevalence in our sample 3.7% (95% CI: 2.8-4.7%). The age, gender, and racial distributions of CLD cases were similar to the remaining 1,550 screened patients. Sufficient clinical data were available to assign an etiology for CLD in 38 (63%) cases. Of these, 18 (30%) had fatty liver and 15 (25%) had hepatitis C. Hepatitis B, alcohol-related liver disease, autoimmune hepatitis, hemochromatosis, and primary hepatic malignant disease each accounted for 2%. Of the 28 (47%) patients documented as having CLD by the PCPs, 12 (43%) were referred to gastroenterologists in a median period of 14 months after diagnosis (range 0-64 months). Hepatitis C was the most common etiology for which CLD patients were referred to gastroenterologists (6, 50%). Of the 48 patients who were not referred to gastroenterologists, 17 (35%) had fatty liver and 9 (19%) had hepatitis C. **Conclusions:** In our study of a primary care patient population, we found a CLD prevalence of 3.7% and 0.9% of patients had recognized hepatitis C. However, these figures most likely reflect minimum estimates because not all patient charts contained sufficient clinical information to determine if a CLD diagnosis was appropriate, including testing for chronic hepatitis C virus infection. Fatty liver and hepatitis C were the most common etiologies for CLD. More than half of CLD cases were not documented as such or referred by the PCP, indicating the possibility of under-diagnosis and limitations in access to subspecialized care for CLD patients. This is especially important in cases of hepatitis C, where curative therapy is available.

Intestinal Anaerobic Bacteria in Early Rheumatoid Arthritis

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The etiology of rheumatoid arthritis (RA) has remained unknown. Recently, increasing attention has been paid to the normal intestinal flora as a potential source of etiological agents. Clinical studies have indicated that changes in the intestinal flora, due to fasting or diet, may accompany reduction of disease activity in RA. Changes in the flora reflect improvement of the patients when they are divided into high and low-responders. Based on analysis of bacterial fatty acids, evidence has been presented that composition of the intestinal flora in the early RA is different from that of non-RA controls. The difference was due primarily to anaerobic bacterial species. The present study was designed to compare the fecal microbiota of the patients with early RA with the microbiota of the control patients using 16S rRNA oligonucleotide probes, detecting a variety of anaerobic bacteria in the normal intestinal flora. Fecal samples of 25 early, disease modifying antirheumatic drugs naive RA patients and 23 control patients suffering from non-inflammatory pain were investigated. The contribution of five bacterial groups was determined by using whole cell hybridization with seven fluorescently labeled 16S rRNA-targeted oligonucleotide probes. These probes cover one third to a half of the total bacteria in the human intestine. Patients with early RA had significantly less bacteria belonging to the *Bacteroides, Prevotella* and *Porphyromonas* genera than the controls (4.7% vs. 9.5%, p=0.00005). The finding was confirmed with a probe specific for bacteria of the *Bacteroides fragilis* group (1.6% vs. 2.6%, p=0.02). The samples of RA patients and the controls did not differ significantly when five other oligonucleotide probes were applied. They were detecting bacteria in the genera *Atobium, Coriobacterium, Collinsella, Bifidobacterium* and *Fusobacterium*, and in the *Eubacterium rectale-Clostridium coccoides* group. We conclude that the content of anaerobic bacteria in the intestinal flora of the patients with early RA is significantly different compared with the controls. The number of bacteria belonging to the *Bacteroides-Prevotella-Porphyromonas* group was, on the average, in RA patients only half that of the controls. If this finding can be confirmed, together with a recent suggestion that certain *Bacteroides* species are required for fortification of the barrier function in the intestinal epithelium, it adds further evidence to the hypothesis that intestinal bacterial flora plays a role in the etiopathogenesis of RA.

Postdiarrheal Hemolytic Uremic Syndrome in New York State

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Objectives: To estimate the number of Hemolytic Uremic Syndrome (HUS) cases in New York State exclusive New York City; to assess the sensitivity of the Communicable Disease Surveillance System in New York State for HUS; and to describe the epidemiologic and clinical features of HUS cases. **Methods and Materials:** Medical records for patients with HUS as a primary or any secondary discharge diagnosis (ICD-9-CM code 283.11) from the Statewide Planning and Research Cooperative System (SPARCS) between January 1998 and December 1999 were reviewed and matched with the postdiarrheal HUS cases that were reported to the Communicable Disease Surveillance System for the same period. Capture- recapture method was used to estimate the total number of postdiarrheal HUS cases and to evaluate the sensitivity of HUS reporting to the surveillance system. Cases identified in SPARCS were matched to the surveillance cases by last name and date of birth. Data abstracted from medical records were analyzed to describe the epidemiologic and clinical characteristics of HUS patients. **Results:** From January 1998 to December 1999, a total of 36 confirmed postdiarrheal HUS cases were reported to the surveillance system. From 246 discharges coded as HUS in SPARCS, 54 cases were identified as confirmed postdiarrheal HUS after chart review. The estimated total number of reportable HUS cases in 1998-99 was 65 (95% CI: 59, 70) and the surveillance sensitivity was 55% (39% in 1998 and 67% in 1999). From the medical record review of the 54 confirmed cases, the highest rate of HUS was observed among children in the 3-10 year age group with a rate of 1.4 per 100,000. Females were more likely to develop HUS than males (RR=2.0, 95% CI: 1.0, 4.0). The median length of hospital stay was 11 days. Death occurred in 5 (8%) cases. 93% of the cases had an acute or bloody diarrhea (75% of them bloody). Stool samples were tested for any pathogen in 84% of the patients and E. coli was isolated in 68% of the tested samples. Renal dysfunction was present with protein- or hematuria in 50 (79%). The mean serum creatinine was 4.2 mg/dl, and mean blood urea nitrogen (BUN) was 74 mg/dl. Thrombocytopenia (platelet <150,000/ml) was present in 90% of the patients, and 76% had hemolytic anemia with microangiopathic changes on peripheral blood smear. Hemodialysis was necessary for 30% of the cases and anemia was treated with blood transfusion in 60% of the cases. **Conclusions:** The 55% sensitivity of the communicable disease surveillance system for HUS indicates that the incidence of disease is higher than suggested by the number of HUS reports received. Since HUS is a leading complication of E. Coli 0157:H7 infection, it is important to check hospital discharge reports to ensure complete reporting.

Outbreak of *Cryptococcus neoformans* var. gattii in a Restricted Zone in British Columbia

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Background: Cryptococcus neoformans var. gattii (CNVG) is a human and animal pathogen which is distinct from the more common C. neoformans var. neoformans (CNVN). It more commonly causes disease in immunocompetent individuals. The prevalence of CNVG has been shown to be highest in geographically restricted areas in tropical and subtropical regions. The incidence of CNVG in endemic areas like Australia is approximately 1 case per million per year. A specific association between CNVG and particular species of eucalyptus trees has been identified. Infection has not been known to be endemic in Canada, where there are few eucalypts. Moreover, an outbreak of CNVG infection has not previously been described. Since January 1999, 38 patients with cryptococcal disease have been identified on the east coast of Vancouver Island, giving an estimated incidence of 27 cases per million per year. **Methods:** Clinical histories for the 38 patients with pulmonary disease or meningitis due to CN were reviewed over the past 36 months. Epidemiological features were collected and analyzed for each case. Microbiological isolates were retrieved and classified as CNVG or CNVN by serological methods. Geographic Information Systems (GIS) technology was used to map the distribution of cases. Environmental samples were collected from the gardens of the cases' homes as well as the surrounding areas. **Results:** All of the patients in the outbreak were diagnosed with laboratory confirmed (culture and/or histopathology) cryptococcal lung disease and/or meningitis. Of the 38 cases, 64% had no evidence of underlying immunodeficiency per se, although 25% were taking steroids in doses exceeding 20mg per day. 82% were smokers. None of the patients were HIV positive. Of the 15 microbiological isolates, 14 were identified as CNVG, and one as CNVN. GIS mapping revealed a distribution of cases confined to a single biogeoclimatic zone. Environmental samples have not yielded a source for the outbreak as yet. **Conclusions:** We report the emergence of CNVG disease in a temperate region not previously known to harbour this fungus. This unique outbreak of cryptococcosis in predominantly immunocompetent hosts and companion animals allows for further elucidation of the epidemiology of CN infections. A seroepidemiological case-control study examining possible exposures and reservoirs, molecular typing of the clinical isolates, and an investigation into animal cases are all ongoing.

Tuberculosis Gene Deletion Typing, Not YATM ("Yet Another Typing Method")

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Yves-Olivier Goguet de la Salmonière, Charlie Kim, Mary Sloan Siegrist and Peter Small

Molecular epidemiology is useful in assisting classical epidemiology. It allows better outbreak tracking, understanding of transmission dynamics, and helps tuberculosis management such as cross-laboratory contamination investigation or hospital organization improvements. Many different typing methods for M. tuberculosis exist, but few are frequently used. RFLP typing with the IS6110 marker remains the gold standard; although it is time consuming. Spoligotyping is also appreciated for its simplicity, rapidity and discriminatory power for some strains.

Recently, a new approach for genetically analyzing strains has been developed using a whole genome microarray for detecting genomic deletions (Kato-Maeda et al., 2001, 11:547-554). This technique has now been applied to over 100 strains of MTB, but cannot be applied for large typing studies because of the prohibitive cost and the technical complexity of this approach. So far, more than fifty different DNA deletions have been detected by hybridizing DNA from clinical strains with the "DNA chip," representing the genome of H37Rv. More deletions will be identified as more strains are analyzed. By using the deletions detected as markers in a reverse line blotting method, we created a new typing method that is both straightforward and inexpensive, even affordable for some developping countries. This approach will be easily standardized, encouraging international collaborations. We have developed MTB membranes that can interrogate 43 of these regions simultaneously. Preliminary data suggest that this simple reproducible method promises to be helpful for different typing purposes while also providing biological information. Given the nature of the markers used, it will yield reliable phylogenetic information. In addition this technique generates information about genome genes content that provides a new way of correlating genotype with the biological properties of individual strains.

47 Foodborne and Waterborne Illness I

Monday, March 25, 3:00 p.m.
Centennial Ballroom IV

Outbreak of Viral Gastroenteritis and an Ill Baker Who Should Have Known Better: Novel Application of Email for Rapid Investigation

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Introduction: On 18 January 2001, a Dutch municipal health authority received a report that more than 200 of about 850 government staff developed vomiting and diarrhea within 24 hours of a reception in a restaurant. An investigation was conducted to determine the source of the outbreak and to implement control measures. **Methods:** The restaurant provided a food list and information about restaurant staff who were ill. Food-inspection service staff visited the kitchens, took food samples, and implemented general hygiene measures. Fecal samples were requested from both restaurant and government staff who became ill. An electronic questionnaire was emailed to all government employees to ascertain the number who became ill and the foods they had consumed. A case was defined as an employee attending the reception who developed vomiting or diarrhea (>2 times/24h) within 72 hours. Data on returned questionnaires were analyzed as a case-control study. **Results:** Of 550 (response approximately 65%) government staff who returned questionnaires, 231 met the case definition (attack rate [AR] among respondents = 42%). The occupational physician estimate of the total number of cases was around 240 (estimated overall AR = 28%). Viral etiology was suspected since 76% of cases reported vomiting and diarrhea and recovery generally within 2-3 days. An additional 5 of 8 food handlers reported onset of illness after the reception. Food and fecal samples were negative for common bacterial pathogens, but 24 (62%) of 39 fecal samples were positive for Norwalk-like virus (NLV) by RT-PCR; all the NLV-positive specimens contained the same genotype, which had not previously been identified. A rapid assessment of 150 questionnaires within 6 hours demonstrated that all 39 cases had eaten at least one roll, compared with 103 of 111 controls (p=0.11). Further analysis with all 550 questionnaires failed to indicate a significant association of disease with any particular roll, but did show

a strong association with increasing number of rolls eaten (p<0.001). Additional investigation found that the baker had had diarrhea and had vomited in the bakery sink while baking and slicing the rolls. A fecal sample from the baker was positive for the outbreak strain of NLV. Strict hygiene measures were implemented in the bakery. **Conclusions:** This investigation shows that contaminated bread was the probable cause of this large outbreak of NLV illness and underscores the ease with which food can be contaminated. Use of email and electronic questionnaires allowed for rapid data collection, and identification of the vehicle and source of the outbreak. Awareness of food handlers and food health authorities of the transmissibility of NLVs needs to be improved. Of interest, 10 outbreaks in the subsequent 6 months in the Netherlands were attributed to this strain, suggesting that this outbreak may have been a seeding event.

Challenges in the Interpretation of Classical and Molecular Epidemiology Results; Two *Calicivirus* Outbreaks Due to Oysters; Denmark at New Year 2000

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Objective: Oysters are a recognized source of foodborne *Calicivirus* outbreaks. We evaluated sequencing of the *Calicivirus* polymerase gene as a typing method to compare strains between patients and oysters causing outbreaks in Denmark, 2001. **Background:** We investigated two *Calicivirus* outbreaks. January 3, 2001, two incidents of gastrointestinal illness were reported. Two and five persons were ill, and the attack rate was 100% among individuals who ate oysters. Oysters from several origins were on the Danish market at that time, but the patients incriminated a single batch of imported oysters (recalled January 4). From January 3 to 16, 297 cases of oyster-associated illness were reported from all over the country; one patient was hospitalized. In an epidemiological study, we estimated the attack rate among exposed to be 80%. Late in February, two restaurants reported gastrointestinal illness among 6 and 3 patrons, following the consumption of oysters; two patients were hospitalized. The attack rate was 90%. The oysters were imported from the same producer, but were not from the same batch as the one causing the New Year outbreak. **Testing:** Nested Reverse Transcriptase PCR for the polymerase of *Calicivirus* were positive in 6 of 15 oyster samples from the implicated batches. None of the employees at the importer's facility reported being sick prior to handling the implicated batch. One of 18 environmental samples taken on the premises was positive using RT-PCR. Stools samples from 17 patients were available; *Calicivirus* was detected in 13 patients using electronic microscopy and RT-PCR with JV12 and JV13 primers. The analysis of 285 bp of the polymerase gene from patients' samples revealed various strains, different from those in oysters. In one incident, two patients sharing the same meal shed different strains. In one patient, different strains were found in the same sample. Other patients, who independently ate oysters from the same batch, were infected with similar strains. Finally, a patient-strain from the New Year outbreak had 100% similarity with a patient-strain from the February outbreak, although the oysters were from a different batch. **Discussion:** By using classical tools of epidemiology, we concluded that the disease was associated with consumption of contaminated oysters. However, sequencing data demonstrated a wide heterogeneity of strains circulating in the outbreaks. This suggests that sewage contamination of the sites where the oysters were harvested or stored was the likely cause. Our observations indicate that molecular typing is not sufficient to link exposure (food item) to patient material, nor does differences between strains preclude such a link. To better understand why a given patient harbors one strain rather than another, and under which conditions *Calicivirus* mutate and re-combine, we recommend examining different strains from the same sample. Part of EU project QRLK1 99 594

Coordinating Environmental Public Health Practice with Epidemiology and Laboratory Analysis: A Waterborne Outbreak of "Norwalk-like Virus" in the Big Horn Mountains of Wyoming

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Background: In February 2001, the Wyoming Department of Health received reports of acute gastroenteritis among persons who had recently been on a snowmobiling vacation in the Big Horn Mountains. Initial interviews and laboratory testing suggested that exposure to a "Norwalk-like virus" in drinking water from a lodge was responsible for the illness. **Methods:** Environmental health specialists and epidemiologists from several state and federal agencies coordinated an investigation of environmental risk factors and system failures. The environmental assessment of the three lodges in the area included food service operations, water supply systems, and sewage disposal. A retrospective cohort study was conducted among 82 persons identified from guest registers to identify risk factors associated with illness. Stool and water system samples were collected for laboratory analysis. **Results:** Statistical analysis from the retrospective cohort study suggested that illness was associated with water consumption at one lodge (RR=3.3, 95% C.I.=(1.4, 7.7)). A chi-square test for linear trend showed that risk of illness increased significantly with the number of glasses of water consumed (p=0.0003). The consumption of individual food items was not statistically associated with illness. Reverse transcriptase-polymerase chain reaction (RT-PCR) testing on 13 stool samples yielded 8 positives for "Norwalk-like virus" (NLV) genogroup II, with 3 distinct sequence types detected. Fecal contamination of one of three operating wells was also found and one of the samples tested positive for NLV genogroup II. The environmental assessment of the property revealed that an inadequately installed sewage system was delivering effluent into shallow soil with poor filtering capacity. This effluent likely contaminated drinking water of an overloaded water system. **Conclusion:** This event represents the largest waterborne outbreak ever reported in Wyoming. It illustrates the potential for waterborne transmission of viral gastroenteritis and the advantages of coordinating environmental public health practice with traditional epidemiologic and laboratory investigations. It is essential that personnel representing each of these entities participate fully in outbreak investigations and that environmental health specialists receive training in systems analysis and sampling methodologies. Outbreak investigations should address all of the systems of a facility including food service, water supply, and sewage systems.

Sesame-Seed Paste Caused an International Outbreak Due to *Salmonella* Typhimurium DT104 – The Investigation in Norway

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Background: The incidence of domestically acquired salmonellosis is generally low in Norway. The last three years up to 12 annual sporadic domestic cases due to *S.* Typhimurium definitive phage type 104 with R-type ACSSuT (DT104) have been diagnosed. By April 2001, the Norwegian Institute of Public Health

(NIPH) had received notifications of an unusual cluster of cases with DT104. Oriental names were over-represented among cases. **Methods:** Isolates from patients were characterised by standard antimicrobial drug assays and phage typing methods at the Reference Laboratory of Enteropathogenic Bacteria (RLEB). A case was defined by the isolation of DT104 from a person living in Norway while being ill. Descriptive epidemiological analyses were undertaken. Meanwhile, the Swedish Food Authority detected DT104 from helva, a Turkish sesame-seeds paste with different flavours. This enabled a more directed case-control study to investigate the association between cases and helva. The cases were matched with controls for age, sex, region and "ethnic background." The questionnaire contained colour pictures of helva products and other food items from a shop to ease the communication. We collected data from 18 cases and 20 controls. The data were analysed by stratified exact logistic regression. **Results:** The first case recorded in Norway had onset on 3rd November 2000, months before the positive batch from Sweden was distributed for retail sale. By July 31st, 28 cases had been reported in Norway. Twenty-two cases (79%) belonged to minority ethnic groups from Eastern-Mediterranean countries. On average, 3.1 cases per month were recorded. The median age was 23 years. In the case control study, consumption of helva the week before onset was associated with illness (OR_e = 8.8, 95% CI: 1.2-394). DT104 was later also isolated from helva leftovers from two patients and from two retail sale packages, all from the same factory in Turkey. **Discussion:** Because the Norwegian notification system records place of acquisition, we were able to discover this outbreak of domestic DT104, a rare infection in Norway, and launch an investigation. The pictures of food items in the questionnaire partially solved language barriers. The association between disease and helva consumption was clear. The group of ethnic minorities was more likely to be infected because of food habits, but none of the six cases with Norwegian names had consumed helva. This number is however within the range of what could be expected from sporadic cases. Related outbreaks were reported from Sweden, Australia, Germany and the UK.

Changing Epidemiological Patterns of *Salmonella* serotype Enteritidis in Barbados: Implications for Tourism and Trade

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Objective: To determine the etiology, sources and risk factors for *Salmonella* Enteritidis (SE) infections in Barbados, to compare its epidemiology with that of SE infections in Trinidad and to develop preventive measures. **Methods:** Retrospective (1996-1998) and prospective (August 1998-November 2000) descriptive epidemiological studies were conducted to determine the occurrence, distribution and potential risk factors for SE infections in Barbados. To determine the etiology for SE infections, a matched case control study of 30 cases and 60 age- and neighborhood-matched controls was conducted between February 1999 to November 2000. Standard written questionnaires were used for the prospective and case control studies, administered through face to face interviews. SE outbreaks were also investigated. *Salmonella* isolates were serotyped and phagetyped using standard methods. Data was analyzed in Epi Info version 6.04c software. Findings: The isolation rate per 100,000 population of SE increased from 1.1 in 1990 to 10.0 in 1999. Children < 10 years were most susceptible to SE infections (44 % cases, 39 infections per 100,0000). No distinct seasonal pattern was observed in the occurrence of SE cases. SE infection was found to be associated with the consumption of undercooked eggs (matched odds ratio [mOR]=43.5, 95% confidence interval [CI]=6.79-1737,p<0.00001) and undercooked chickens (mOR 8.23, 95%CI =1.57-73.6, p<0.01). In particular soft boiled eggs (mOR = 29.0, p<0.0001), scrambled eggs with soft yolks (mOR=8.39, p<0.001) and caesar salad (mOR =10, p<0.001) were the main implicated undercooked egg-containing foods. Three hotel SE outbreaks, involving visitors and 6 family outbreaks were investigated. Caesar salad, soft boiled and scrambled eggs, and undercooked chickens were implicated. Of the 60 isolates phagetyped, PT8 was most prevalent (33 cases, 55%), followed by PT4 (19 cases, 32%), PT2 (6 cases, 10%), PT24a (1 case) and PT11 (1 case) Ten cases (17%) were hospitalized , and 2 died (case fatality rate 6.7%). **Conclusion:** This is the first reported analytical study of SE infections in Barbados. It highlights that in Barbados, the consumption of undercooked eggs and undercooked chickens are the major vehicles for SE infections, unlike our previous findings in Trinidad. SE PT8 and PT4 predominate. This is the first time that undercooked chicken has been associated with SE infection in the Caribbean, and it is also the first time that PT2 has been identified in the Caribbean. The findings of this study have important implications for public health, food safety, trade and tourism in Barbados. It has demonstrated the increasing impact of SE infection in local and visitor population which requires a "Farm to Table" for effective prevention and control.

Health Impact of the Salmonella enterica Serotype Enteritidis Phage Type 4 Epidemic

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Background: In the 1980s Salmonella enterica serotype Enteritidis emerged as a major foodborne pathogen. Rising levels of human disease were linked to a developing panzootic in poultry. During the 1990s the UK Government and industry introduced a range of measures to reduce contamination in chicken meat and eggs, culminating in a flock vaccination program starting in 1996. We examined the impact of S. Enteritidis phage type (PT) 4 and the effect of control measures on human health in England and Wales. **Methods:** We refined the United States Centers for Disease Control and Prevention (CDC) method for quantifying the impact of food-related disease to correct for imported disease and to describe trends. We estimated the number of illnesses, presentations to primary care physicians (presentations), hospitalizations, days of care in hospital (days) and deaths due to indigenous foodborne S. Enteritidis PT4 (IFSE4) over 20 years. **Results:** Between 1981 and 2000 IFSE4 infection resulted in an estimated 586000 illnesses, 418000 presentations, 18000 hospitalizations (104000 days) and 1300 deaths in England and Wales. In 1981 there were 750 illnesses, 540 presentations, 20 hospitalizations (130 days) and 2 deaths. Infection rates rose to reach a plateau between 1990-7. In 1993 there were 59000 illnesses, 42000 presentations, 1800 hospitalizations (10400 days) and 130 deaths. Annual rates of IFSE4 infection have fallen by over 70% since 1997. In 2000 there were 15000 illnesses, 11000 presentations, 470 hospitalizations (2800 days) and 30 deaths. The fall in IFSE4 has meant 88000 less illnesses, 63000 less presentations, 2700 less hospitalizations (16000 less days) and 190 fewer deaths in three years. **Conclusion:** In the last 20 years no single strain of foodborne pathogen has impacted on human health in England and Wales in the way that S. Enteritidis PT4 has done. However our analyses suggest that the introduction of flock vaccination has had a major effect in rapidly reducing the burden of disease attributable to this pathogen. The refinements that we have made to the CDC method for measuring the impact of food-related disease enable both the impact of pathogen emergence and the effectiveness of interventions to be objectively assessed.

48 Antimicrobial Resistance I

Monday, March 25, 3:00 p.m.
Centennial Ballroom I

Antibiotic Susceptibility and the Mechanisms of Macrolide Resistance in Invasive Group B *Streptococcus*, Minnesota, 1998 and 2000

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Background: Group B Streptococcus (GBS) is the leading cause of invasive neonatal infections in the U.S. Intrapartum antibiotic prophylaxis with penicillin or ampicillin is recommended to prevent neonatal disease. For women allergic to β-lactam antibiotics, clindamycin (C) or erythromycin (E) is recommended. Although resistance to penicillin has not been confirmed, resistance to macrolides and lincosamides is well described. In GBS, resistance is typically conferred either by methylation of the 23S ribosomal subunit (*erm*) or by efflux pumps (*mef*A, *mef*E). Methylation usually results in cross-resistance to macrolides, lincosamides and streptogramin B (MLS phenotype) while the efflux mechanism confers resistance only to macrolides (M phenotype). Few studies have evaluated MLS resistance mechanisms in GBS. Our objectives were to determine the prevalence of E and C-resistance and to characterize the resistance mechanisms among invasive GBS isolates. **Methods:** Invasive GBS infection is reportable in Minnesota. Cases are reported to MDH through a statewide active surveillance system. Surveillance includes collection of epidemiologic data and submission of isolates to MDH for antimicrobial susceptibility testing by broth microdilution. Resistant strains were evaluated by PCR and isolates were tested for inducibility of the MLS phenotype for the *mef* and *erm* genes. **Results:** Among the 101 isolates tested in 1998, 21 (21%) were E-resistant and 8 (8%) were C-resistant. Among the 220 isolates tested in 2000, 50 (23%) were E-resistant and 27 (12%) were C-resistant. All C-resistant strains were E-resistant. Sixty-four of the 71 E-resistant GBS isolates were evaluated by PCR. Of the 20 1998 isolates, 7 with an MLS phenotype contained *erm*B (3) or *erm*TR (4). One MLS resistant strain failed to yield products with the primers tested. Twelve 1998 isolates had M phenotype; all contained *mef*E. Of the 44 year 2000 isolates, 18 had M phenotype and 26 had MLS phenotype. All 44 isolates contained the *erm*B gene. E minimum inhibitory concentration values were higher in *erm*B-containing strains ($p<0.02$). Twelve MLS phenotype isolates tested were of the constitutive MLS type, while 15 of the M phenotype (by broth microdilution) isolates from 2000 were of the inducible MLS type. Three M phenotype isolates, all of which contained *mef* as well as *erm*B, failed to induce MLS resistance. **Conclusion:** Although there was no increase in E-resistance in invasive GBS between 1998 and 2000, there was a trend towards increased C-resistance. This was accompanied by an increase in the prevalence of the *erm*B gene in both MLS and M phenotype isolates. The reason for this shift in resistance determinants in not known, but could be a consequence of selective pressure by use of these antibiotics. E and C resistance have important implications for prophylaxis and treatment of GBS disease; these susceptibility patterns need to be monitored.

Multi-Drug Resistant *Neisseria gonorrhoeae* with Decreased Susceptibility to Cefixime, Hawaii, 2001

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Background: Gonorrhea, the second most commonly reported communicable disease in the United States, increases HIV transmission and causes pelvic inflammatory disease, which can lead to ectopic pregnancy and infertility. Over the years, *Neisseria gonorrhoeae* (GC) have readily acquired resistance to various antibiotics, including sulfanilamide, penicillin (pen), tetracycline (tet), spectinomycin (spec), and ciprofloxacin (cipro). **Report:** We report on 3 patients in Hawaii who were diagnosed with multi-drug resistant GC that also had markedly decreased susceptibility to cefixime (cfx). Patient A, a 36 year old white male, presented in 2/2001 with urethritis and was treated with cfx 400 mg and azi 1 gm. Subsequently, his culture grew GC which was spec sensitive, but resistant to pen (Minimum Inhibitory Concentration [MIC] of 8.0 mg/L), tet (MIC 8.0 mg/L), and cipro (MIC 8.0 mg/L), and had decreased susceptibility to azi (MIC 0.25 mg/L) and cfx (MIC >0.125 mg/L). The patient returned in 4/2001 with urethritis and was treated with spec 2 gm and doxycycline 100 mg BID x 7 days. His second culture grew GC with the same antibiogram as his first. A test-of-cure performed 3 weeks later was negative. Patient A reported having 2 female sex partners, both of whom visited Hawaii from Japan. One sex partner could not be located; the second, Patient B, presented in 5/2001. Patient B was a 27 year old Japanese female who reported having yellow vaginal discharge since 2/2001, having only Patient A as a sex partner, and having sex with Patient A once in 2/2001 and once in 4/2001. She was treated with ceftriaxone 125 mg and azi 1 gm. Her culture grew GC which was spec sensitive, but resistant to pen (MIC 4.0 mg/L), tet (MIC 2.0 mg/L), cipro (MIC 16.0 mg/L), and had decreased susceptibility to azi (MIC 0.25 mg/L) and cfx (MIC 0.25 mg/L). Patient C was a 30 year old Pacific Islander male who presented in 3/2001 with urethritis and was treated with cfx 400 mg and azi 1 gm. His culture grew GC which was spec sensitive, but resistant to pen (MIC 4.0 mg/L), tet (MIC 8.0 mg/L), and cipro (MIC 8.0 mg/L), and had decreased susceptibility to azi (MIC 0.125 mg/L) and cfx (MIC >0.125 mg/L). A test-of-cure performed 3 months later was negative for GC. Patient C reported having one female sex partner who could not be located. These first reports of multi-drug resistant GC with decreased susceptibility to cfx in the United States are worrisome because their existence and spread may further limit treatment options for GC.

Shigella dysenteriae Serotype 1 in West Africa: Intervention Strategy for an Outbreak in Sierra Leone, 1999-2000

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Background: Bacillary dysentery has been a disease affecting poor and crowded communities throughout history, and continues to be a major cause of morbidity and mortality in developing countries. In the past two decades, large outbreaks due to *Shigella dysenteriae* serotype 1 (Sd1) have been reported in Central and Southern Africa. In November 1999, a Médecins Sans Frontières team based in the south eastern part of Sierra Leone (Kenema dis-

trict) reported an increased number of cases of bloody diarrhoea. We describe the investigation of the outbreak and report the outcome of cases treated with a 5 day regimen of ciprofloxacin. **Methods:** A case was defined as a person living in this region, presenting blood in the stools, observed by a health worker, from December 1999 to March 2000. Microbiological confirmations at Institut Pasteur, Paris, were performed for the early cases. Mobile teams visited the affected area and referred patients at high risk of death from dysentery (children less than 5 years old, adults 50 years of age or older, malnourished older children and adults) to medical facilities for isolation and a 5 day treatment of ciprofloxacin. Other patients received Oral Rehydration Salts and were referred to isolation centres if needed. Hygiene advice was given. **Results:** A total of 4,218 cases of dysentery was reported in Kenema district from December 1999 to March 2000. The overall attack rate was 7.5%. The attack rate was higher among children under 5 years compared to the rest of the population (11.2% vs 6.8%). The case fatality ratio was 3.1% (131/4,218), also higher for children under 5 years (6.1% vs 2.1%). Most deaths occurred at the beginning of the outbreak. The strain isolated was resistant to common antibiotics (amoxicillin, amoxicillin + clavulanic acid, tetracycline, trimetoprim-sulfamethoxazole and choramphenicol), and was sensitive to nalidixic acid, ciprofloxacin and ceftriaxone. 583 patients considered at higher risk of death were treated with ciprofloxacin in isolation centres. The treatment compliance was 99.7% and the case fatality ratio was 0.9% (5/583). Discussion: This is the first time a large outbreak caused by Sd1 has been reported in West Africa. The disease is not yet well known by local health care workers and health authorities of the region should be warned of the potential epidemic risk. In this setting, with poor medical facilities, a 5-day ciprofloxacin regimen was highly effective in the most severe bloody diarrhoea cases and the case fatality ratio was less than that observed with nalidixic acid treatment during previous outbreaks in Central Africa. Treatment with ciprofloxacin should be restricted to isolation units and directly observed in order to delay emergence of resistance.

The Acquisition of Ciprofloxacin Resistance in Travel-Associated and Home-Acquired *Campylobacter jejuni* Infection: A Case-Case Comparison

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Aim: To determine factors independently associated with the acquisition of a ciprofloxacin resistant *Campylobacter jejuni* infection. **Background:** Campylobacter enteritis is usually an unpleasant but self-limiting disease. Management is typically limited to maintaining fluid balance. Where antimicrobial therapy is indicated the treatments of choice have tended to be erythromycin or ciprofloxacin. However, the emergence of resistance against fluoroquinolones, and ciprofloxacin in particular, has become a major public health problem worldwide. **Methods:** Human *campylobacter* isolates referred from laboratories within a sentinel surveillance system (population ~12.5 million) were speciated and sub-typed. Antimicrobial resistance was determined by an agar dilution method supported by minimum inhibitory concentrations for ciprofloxacin and erythromycin. Epidemiological information, captured by self-completion postal questionnaire, was linked with the typing data using the patients' surname and date of birth. The exposures of cases infected with a ciprofloxacin resistant *C. jejuni* infection ('cases') were compared with those infected with a sensitive strain ('controls') using single risk variable analysis and logistic regression. The analysis was restricted by travel status to control for the confounding effect of foreign travel. **Results:** Nineteen percent of strains were resistant to ciprofloxacin. Over half (55%) of the campylobacter infections acquired abroad were resistant to ciprofloxacin, compared with 10% of UK strains (relative risk 5.31; 95% Confidence Interval (CI) 4.69-6.02; P<0.001). Amongst travel-associated cases of *C. jejuni* infection, ciprofloxacin resistance was independently associated with the consumption of chicken (Odds Ratio (OR) 2.45; 95%CI 1.28-4.70; P=0.007) and bottled water (OR 2.09; 95%CI 1.15-3.81; P=0.016) in the two weeks prior to illness. Indigenous cases who were infected with a ciprofloxacin-resistant strain of *C. jejuni* were more likely to report the consumption of pre-cooked cold meats (OR 2.13; 95%CI 1.44-3.13; P<0.001) than cases infected with a sensitive strain.**Conclusions:** The risk of acquiring antimicrobial resistant *campylobacter* infection was strongly associated with foreign travel. Restricting our analyses by travel status revealed different sets of risk exposures for acquiring a resistant *C. jejuni* strain, suggesting that different intervention strategies might be required. Case-case comparisons proved to be a useful tool for the generation of hypotheses for *campylobacter* infection from surveillance data.

Prevalence and Consequences of Fluoroquinolone-Resistant *Campylobacter* Infections: NARMS 1997-2000

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Background: *Campylobacter* causes 2.4 million infections each year in the United States. Fluoroquinolones (e.g., ciprofloxacin) commonly are used in adults with *Campylobacter* and other infections. Fluoroquinolones also are used in livestock and poultry. Human infections with fluoroquinolone-resistant *Campylobacter* have become increasingly common and are associated with consumption of poultry. These, and other data, prompted FDA to propose withdrawal of fluoroquinolone use in poultry in 2000. **Methods:** In 1997, the National Antimicrobial Resistance Monitoring System (NARMS) for Enteric Bacteria began monitoring antimicrobial resistance among *Campylobacter* in the Foodborne Disease Active Surveillance Network (FoodNet) sites; by 2000, the number of sites had increased to 9. Additionally, a case-control study of sporadic *Campylobacter* infections was conducted in 7 FoodNet sites between 1998-1999. Isolates collected from individuals with *Campylobacter* infections were forwarded to CDC for speciation using hippurate test and PCR, and susceptibility testing to ciprofloxacin using the E-test. **Results:** NARMS tested 1202 *Campylobacter* isolates from 1997-2000; 1145 (95%) were *C. jejuni*, 44 (4%) *C. coli*, 7 (0.6%) *C. upsaliensis*, and 6 (0.5%) other *Campylobacter* species. Fourteen percent of isolates (163/1202) were ciprofloxacin-resistant (MIC ≥ 4 µg/ml); 13% (155) of *C. jejuni* isolates, 16% (7) *C. coli*, and 0.6% (1) *C. upsaliensis*. Among 775 patients in the FoodNet *Campylobacter* case-control study, 11% (85) had ciprofloxacin-resistant infections. Among 421 persons with a *Campylobacter* infection who did not take a strong antidiarrheal medication (e.g., Imodium, Lomotil, or prescription), persons with ciprofloxacin-resistant infections had a longer duration of diarrhea than persons with ciprofloxacin-susceptible infections (8 vs 7 days, p=0.05). Of these 421 persons, 126 (30%) took fluoroquinolones and no other antimicrobial agent for their illness. Among the 126 persons who took fluoroquinolones, the mean diarrhea duration was longer in patients with ciprofloxacin-resistant infections than in patients with ciprofloxacin-susceptible infections (8 vs 6 days, p=0.04). **Conclusions:** NARMS surveillance data illustrates emerging fluoroquinolone resistance of *Campylobacter* in humans. Persons with ciprofloxacin-resistant *Campylobacter* infections have a longer duration of diarrhea than persons with ciprofloxacin-susceptible *Campylobacter* infections. Fluoroquinolones commonly are used to treat human infections; additional efforts are needed to protect the efficacy of fluoroquinolones.

High Prevalence of Antibiotic Resistance in Enterotoxigenic E. coli (ETEC); Minnesota 2000 - 2001

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Background: Enterotoxigenic *E. coli* (ETEC) is a leading cause of morbidity and mortality worldwide. It is the primary cause of traveler's associated diarrhea, and can acquired from imported produce. Antibiotics, such as ciprofloxicin (CIP), trimethoprim-sulfamethoxazole (SXT), and doxycline (DOX) are often prescribed to travelers for self-administration in case of illness. Recent studies have shown a high incidence of CIP resistance among cases of *Campylobacter jejuni*, another travel-associated diarrheal agent. Limited information is available about antibiotic resistance in ETEC, the more common cause of traveler's diarrhea. **Methods:** The population examined were patients presenting with diarrhea at a large HMO serving a predominately urban population, and at a hospital serving a predominately rural population during 2000 and 2001. Travel, antibiotic use, exposure histories, and demographic data were collected by case interviews. Samples were cultured on SMAC agar, and colony sweeps were examined using a CYBR-green PCR assay. Three primer sets were used for detection of the LT gene (eltB) and the ST alleles STa1 (estA1) and STa2-STa3 (estA2 and estA3), and isolates were biochemically identified. Fifty-five isolates of ETEC were tested for susceptibility to a standard antibiotic battery, which includes CIP, SXT, and tetracycline (TE) using NCCLS disk diffusion protocols. **Results:** Thirty-two of the 55 patients (58.2%) reported travel outside the U.S. One of 55 (1.8%) isolates were resistant to CIP, 14/55 (25.5%) to SXT; and 27/55 (49.1%) to TE. The single case with a CIP resistant isolate had traveled to Thailand, and had been treated with multiple, unspecified medications. Travel and antibiotic use histories were available for 13/14 (92.9%) cases with SXT resistance. Reported travel included South America (2), Mexico (3), India (1), Central America (2), Europe (1), and no travel (4). None of these cases (0/13) reported SXT use. Ten patients were <18 years old, and of those 3/10 (33%) had isolates resistant to SXT. Two patients treated with TE prior to illness had TE-resistant isolates. Temporal trends were not observed in any of the 12 antibiotics tested. The sources of domestic acquisition were not determined. **Conclusions:** This study examined cases of ETEC acquired in MN and in foreign countries. The prevalence of resistance to CIP continues to be very low, but should be further monitored due to increasing use of this drug. The prevalence of SXT resistance was high, and likely global in nature. The prevalence of DOX resistance, represented by TE, was very high. These data, when taken with *C. jejuni* susceptibility data, suggest that current recommendations for treatment of traveller's diarrhea need to be re-evaluated.

49 International Health Panel

Tuesday, March 26, 7:30 a.m.
Regency Ballroom VI/VII

50 Antimicrobial Resistance II

Tuesday, March 26, 8:30 a.m.
Grand Hall East

Board 1. High Frequency of Metronidazole and Clarithromycin Resistance in *Helicobacter pylori* isolates from Alaska Natives

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Background: *Helicobacter pylori* (*H. pylori*) infection is common (75% seroprevalence of IgG antibodies) among Alaska Natives (AN). In this population, it is a major cause of gastritis and peptic ulcer disease, and may be associated with rates of gastric cancer that are over twice the national average. Elsewhere in the United States, *H. pylori* cure rates are high (85-95%) and reinfection rates are low (< 5% over a 2-year period); however, preliminary data from an ongoing study in Alaska indicate markedly lower eradication rates (60-70%), and higher reinfection rates (16.3% at 2 years) among AN. **Methods:** We analyzed *H. pylori* data from CDC's sentinel site surveillance in Alaska to determine: 1) the rate of culture positivity of biopsy specimens from AN adults undergoing routine upper endoscopy, and 2) the susceptibility of *H. pylori* isolates to metronidazole, clarithromycin, tetracycline and amoxicillin. We cultured clinical specimens obtained from biopsies of AN patients undergoing upper endoscopy from 7/99 through 7/01 at medical facilities located in Anchorage, Bethel, and Dillingham. Susceptibilities of all culture-positive *H. pylori* isolates were determined by Agar dilution. **Results:** Of 643 biopsy specimens obtained from 435 AN patients, 302 (47%) were culture positive, representing 222 (51%) patients. Females were more likely to be culture-positive compared to males (173 (49%) of 355 vs. 129 (45%) of 288, OR 1.2, p = .35). Mean age of culture-positive and culture-negative patients was 50 years. AN living in Western Alaska were more likely to test positive by culture when compared to those who lived in other regions of Alaska (86 (67%) of 129 vs. 216 (42%) of 514, OR=2.8, p < .001). 46% of isolates had a minimum inhibitory concentration (MIC) of > 8 µg metronidazole/ml, 33% had an MIC of > 1 µg clarithromycin/ml, 2% of isolates had an MIC of > 1 µg amoxicillin/ml and no isolates were resistant to tetracycline (> 2 µg tetracycline/ml). Resistance to metronidazole (MtzR) and clarithromycin (ClaR) varied by region (ranges, 39-46% and 24-46%, respectively). Females were more likely than males to show MtzR (56% vs. 33%, OR=2.9, p < .01) and ClaR (36% vs. 29%, OR=1.4, p = .22). No difference in mean age was observed for MtzR (mean age resistant 48.5 yrs vs. mean age sensitive 51.2 yrs, p = .21) or ClaR (mean age resistant 50.3 yrs vs. mean age sensitive 49.7 yrs, p = .65). **Conclusions:** Rates of resistance to metronidazole and clarithromycin are elevated among AN when compared with the rest of the United States. A high prevalence of infection with *H. pylori* in AN, combined with a high frequency of antibiotic resistance in *H. pylori* isolates could result in high rates of treatment failure among AN.

Board 2. Trends in the Use of Azithromycin/Clarithromycin and the Quinolones for Selected Infectious Diseases in Ambulatory Care Settings in the US, 1993/94-1999/2000

L. F. McCaig, C. W. Burt

National Center for Health Statistics, CDC, Hyattsville, MD

Background: The increased use of antibiotics has coincided with the emergence of antimicrobial resistance. With thousands of Americans taking antibiotics because of the recent anthrax outbreak, there is a renewed urgency to monitor antibiotic prescribing. We examined data from the National Ambulatory Medical Care Survey (NAMCS) and National Hospital Ambulatory Medical Care Survey (NHAMCS), annual national probability surveys of office-based physicians and hospital emergency departments (ED's) and outpatient departments (OPD's), respectively, in the US to describe trends in the prescribing of specific antibiotics for selected infectious diseases seen in ambulatory care settings and to provide a baseline in the use of ciprofloxacin. **Methods:** Data were analyzed from the 1993-2000 NAMCS and NHAMCS and were weighted to produce national annual estimates. Two years of data were combined to provide more reliable estimates. Each year, ~2500 physicians and ~500 hospitals were in the NAMCS and NHAMCS samples, respectively, and data were collected on ~25000 visits in each setting. A drug prescribing rate was calculated which was defined as the number of antimicrobial drugs prescribed divided by the number of visits. Rates for the quinolones (including ciprofloxacin), azithromycin/clarithromycin, and the erythromycins were calculated for all 3 settings combined (i.e., physician office, OPD, and ED) for sinusitis, bronchitis, pneumonia, and urinary tract infection (UTI). **Results:** From 1993/94-1999/00, the azithromycin/clarithromycin prescribing rates for sinusitis, bronchitis, and pneumonia in ambulatory care settings in the US increased on average by 128%, while there was a corresponding decrease in the erythromycin prescribing rates of about 65%. The quinolone prescribing rate for the 3 respiratory diseases combined (sinusitis, bronchitis, and pneumonia) and for UTI increased by 123% and 58%, respectively. The overall ciprofloxacin prescribing rate increased by 23%, (from 6.1 prescriptions per 1000 visits to 7.5). **Conclusions:** The shift from the use of narrower spectrum antibiotics (erythromycins) to broader spectrum drugs (azithromycin/clarithromycin) raises concern and the appropriateness of their use need to be assessed. Establishing a baseline of prescriptions for ciprofloxacin prior to the anthrax outbreak of 2001 is important to allow for the detection of unusual patterns of prescribing subsequent to the bioterrorist attack. It is expected that ciprofloxacin prescriptions will continue to rise in 2001.

Board 3. Ecological and Human Health Impacts of Agricultural Use of Antimicrobials

S. J. DeVincent

Alliance for the Prudent Use of Antibiotics (APUA), Boston, MA

In 1999, APUA instituted its Facts about Antimicrobials in Animals and the Impact on Resistance (FAAIR) project. The specific objectives of FAAIR have been to:

- Review and analyze scientific evidence pertaining to antimicrobial use in agriculture
- Increase public awareness of related human health issues
- Foster communication among stakeholders concerning benefits and risks
- Influence policy makers to implement measures for improved use
- Develop an ecological perspective on the issue of antimicrobial resistance

To meet these goals, APUA convened a Scientific Advisory Panel of nationally-recognized experts to examine evidence relevant to policy debates on this issue. The Panel developed a comprehensive report, *The Need to Reduce Antimicrobial Usage in Agriculture: Consequences of Use on Ecological and Human Health.* This report considers concerns expressed by stakeholder groups as well as comments made by outside reviewers from government and industry.

The FAAIR Report begins with analyses of the extent of antimicrobial use in food animal production and plant agriculture. It then addresses the origin, spread, and persistence of resistance genes. There is a review of the epidemiological evidence for a link between the use of antimicrobials in food animals and the incidence of infection due to resistant foodborne pathogens in humans. The final sections of the report deal with risk assessment and evidence that the agricultural use of antibiotics imposes a burden on human health.

Some key findings of the FAAIR Report include:

- Use of antimicrobials in agriculture creates selective pressure for the emergence of antimicrobial resistance in bacteria of food animals.
- These resistance determinants contribute to an environmental reservoir of resistance. They can be transmitted to humans through the food supply or by contact with the animals or their environment.
- This increase in resistance can result in human health consequences.

The report includes a series of Conclusions and Policy Recommendations intended to improve public policy on the agricultural use of antimicrobials. In this section, the Panel suggests practical strategies to encourage more appropriate use of antimicrobials in agriculture and to preserve the effectiveness of these drugs for the treatment of human disease.

Board 4. The Economics of Appropriate Antimicrobial Use in Treating Acute Pharyngitis in Adults

K. Roy, M. I. Meltzer, R. E. Besser, J. T. Weber

Centers for Disease Control and Prevention, Atlanta, GA

Background: Although viruses are the most common cause of pharyngitis in adults, antimicrobials are prescribed in 76% [Gonzales, et al., JAMA 1997] of all cases. Such inappropriate use of antimicrobials may exacerbate the growing problem of antimicrobial resistance. **Objective:** To conduct an economic evaluation of both recommended and practiced treatment strategies. The evaluation balances the consequences of untreated Group A β-hemolytic streptococcal (GABHS) pharyngitis, which causes 5-15% of all cases, against decreases in inappropriate antimicrobial use. **Methods:** A decision tree, with a societal perspective (direct, indirect, and productivity costs included), was used to determine the most cost-effective (lowest $/case correctly diagnosed and treated) strategy from the following options: 1) Prescribe antimicrobials to all patients with sore throat; 2) Current practice of prescribing antimicrobials to 70-100% of patients based on physician's discretionary use of clinical criteria and diagnostic tests; 3) Use Centor's (1980) clinical decision rules [to treat patients if > 3 symptoms, not treat if < 2 symptoms, and treat after further diagnostic tests if 2-3 symptoms] and diagnostic tests that use both rapid antigen testing (RAT) and throat culture (TC) for negative RAT [Note: TC involves delays in optimal treatment while waiting for results]; 4) Use clinical decision rules and RAT only; 5) Use clinical decision rules and TC only; 6) No prescription and no tests. Values for the input variables were obtained from published literature, existing databases and expert opinion. Reductions in probabilities of antimicrobial prescription (PR_{script}) were calculated but no valuation was placed on such reductions. Sensitivity analyses were conducted to determine when one strategy would be changed for another. **Results:** The most cost-effective strategy depended upon the probability of GABHS (PR_{GABHS}) in the community. If 0% < PR_{GABHS} < 5% - choose no prescription and no tests (PR_{script} = 0%); if 5% < PR_{GABHS} < 30% - choose clinical decision rule plus RAT (PR_{script} = 18-32%); if 30% < PR_{GABHS}<50%choose clinical decision rule plus RAT and TC (PRs_{cript} = 34-46%); if PR_{GABHS} > 50% - choose treat all (PR_{script} = 100%). **Conclusions:** Among healthy

adults with acute pharyngitis typically antimicrobials should be only prescribed after employing decision rules and RAT (strategy 4). Compared to current practice (strategy 2), this will reduce the probability of antimicrobial prescription from 70% to 23%; while the proportion of infections not treated remain the same (4-5%) for both strategies. Only if the probability of GABHS is >50% should antimicrobials be prescribed indiscriminately to all without appropriate laboratory test(s). These results support recently published guidelines for treating acute pharyngitis in adults.

Board 5. Comparison of Animal and Human Multidrug-Resistant Isolates of *Salmonella* Newport in Minnesota

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Background: Multidrug resistance, including resistance to ceftriaxone, has been emerging among human clinical *S.* Newport isolates submitted to the Minnesota Department of Health (MDH) since 1999. Of 56 *S.* Newport isolates submitted during 1999-2000, 13 (23%) were resistant to ≥ 5 antimicrobials, and 12 were resistant to ceftriaxone. The objective of this study was to evaluate antimicrobial resistance and molecular subtype characteristics of clinical *S.* Newport isolates from animals from a veterinary diagnostic laboratory in Minnesota and to compare them with human clinical *S.* Newport isolates in Minnesota. **Methods:** *S.* Newport isolates from clinically ill or dead animals submitted to the Minnesota Veterinary Diagnostic Laboratory from January 2000 through September 2001 were forwarded to MDH. Animal isolates were subtyped by pulsed-field gel electrophoresis (PFGE) and tested for antimicrobial resistance at MDH using the same methods used to test human clinical isolates submitted to MDH through routine surveillance. Antimicrobial resistance testing was done by disk diffusion; Etest for ceftriaxone was done on isolates with intermediate susceptibility by disk diffusion. **Results:** Isolates from 33 animals (all from different farms or homes) were tested, including 22 cattle, 5 swine, 2 horses, 1 deer, 1 dog, 1 owl, and 1 iguana. Of the 33 isolates, 25 (76%) were resistant to > 5 antimicrobials, and 24 had resistance to at least ampicillin, chloramphenicol, streptomycin, sulfamethoxazole, and tetracycline (R-type ACSSuT); these isolates were recovered from cattle (n=19), swine (n=2), a horse, a dog, and a deer. Of the 24 ACSSuT isolates, all were also resistant to cephalothin (Cf), 23 to ceftriaxone (Cro), 20 to kanamycin (K), and 19 to gentamicin (Gm). Nineteen of 33 animal isolates (58%) were resistant to 9 antimicrobials (R-type ACSSuTCfCroKGm), including 16 isolates from cattle. PFGE subtyping of the 33 animal isolates yielded 16 subtype patterns. Nine PFGE subtypes represented 16 cattle isolates that were at least penta resistant; 5 of these 9 subtypes have been associated with clinical illness in humans in Minnesota. Isolates belonging to this group of 5 PFGE subtypes were also recovered from horses (2 isolates), a pig, a dog, and a deer. **Conclusions:** Clinical animal isolates of *S.* Newport submitted to the Minnesota Veterinary Diagnostic Laboratory during 2000-2001 were highly multidrug-resistant; over one half of isolates were resistant to 9 antimicrobials, including ceftriaxone. Cattle were the primary host from which multidrug-resistant strains of *S.* Newport isolates were recovered. PFGE subtyping revealed indistinguishable subtypes between human and animal (particularly cattle) isolates. Future studies to determine specific risk factors for infection with multidrug-resistant *S.* Newport in humans should include investigation of cattle as a potential reservoir.

Board 6. Antimicrobial Susceptibility Among Enterotoxigenic *Escherichia coli* (Etec) and *Shigella* sp. Isolated from Rural Egyptian Children with Diarrhea.

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Antibiotic susceptibility testing (AST) was conducted on 1,203 ETEC and 193 *Shigella* sp. isolates collected from 875 rural Egyptian children. Children were enrolled in one of three prospective diarrhea studies conducted near Alexandria from 1995 through 2000. For each study subject, twice weekly home visits were conducted and a stool sample and rectal swab were collected if a 'loose, liquid, or bloody stool' was reported. Rectal swabs were inoculated into Cary-Blair transport medium, and along with the stool sample, placed in an ice chest, and transported to a field laboratory. Aliquots of stool were inoculated into Buffered-Glycerol-Saline tubes and all clinical specimens were transported thrice weekly to the microbiology labs at NAMRU3 in Cairo. Standard laboratory procedures were used for the isolation and identification of ETEC, *Shigella* sp., *Salmonella* sp., and *Campylobacter* sp. AST was conducted by the disk diffusion method and interpreted according to NCCLS guidelines. Some of the antibiotics tested include, ampicillin, amikacin, aztreonam, cefepime, ceftriaxone, ceftazidime, gentamicin, nalidixic acid, ciprofloxacin, tetracycline, and sulfamethoxazole/trimethoprim (SXT). The overall rates of resistance for ETEC and *Shigella* in our study population were: ampicillin (62.6% & 55.4%), SXT (51.0% & 44.6%) and tetracycline (40.3% & 75.1%), respectively. Over the length of the study, ETEC demonstrated slight statistical increases in resistance to SXT, while demonstrating minor decreases in resistance to ampicillin, tetracycline, and multi-drug resistant isolates. Among *Shigella*, there was a slight statistical increase in resistance to SXT, while all other drugs generally showed a decrease or had no discernible change in resistance over the study. Little resistance (~1%) among ETEC and *Shigella* were noted for all other antibiotics. In this region of the Middle East, antibiotic resistance to commonly available antibiotics was quite high, but overall demonstrated a slight statistical decrease during the six-year period, with the sole exception of SXT. This study also suggests that *in vitro* resistance to newer antibiotics is very low, possibly reflecting limited use among the general population in this rural area.

Board 7. Advantages of a Coordinated System of Independent Global Surveillance Databases: A Report from the Global Advisory on Antibiotic Resistance Data (GAARD)

J. Stelling[1], **K. U. Travers**[2], R. Jones[3,4], L. Miller[5], D. Sahm[6], B. Souder[2], T. O'Brien[2,1], S. Levy[2,4]

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Background: Though antimicrobial resistance (AMR) is recognized as a serious public health threat, a coordinated global AMR surveillance system is not in place. Despite a demonstrable role in AMR control, independent surveillance program data have not been systematically compared, suggesting the utility of a coordinated approach.

Methods: Aiming to serve as a comprehensive global information resource for AMR surveillance, GAARD analyzed data submitted by three major surveillance programs: the Alexander Project, SENTRY, and The Surveillance Network (TSN). Data, from 1997-1999, were derived from reference-quality minimum inhibitory concentration (MIC) systems. APUA, coordinated the

analysis as project manager, and identified issues important to further collaborative projects.

Results: SENTRY, Alexander, and TSN provided MIC data for 4248, 1306, and 12,960 S. pneumoniae isolates, respectively. Comparison was complicated by recent changes in interpretive criteria. Also, the use of differing dilution ranges, isolate sources, and sampling and testing methods among the programs required careful consideration.

Conclusion: The coordination of AMR surveillance programs requires significant expertise and cooperation to handle inevitable protocol discrepancies. Susceptibility testing against sufficiently broad ranges of antibiotic dilutions facilitates program integration. GAARD exemplifies the capabilities inherent in well-integrated longitudinal collaborative surveillance efforts that will substantially guide future international AMR interventions.

Board 8. Resistance to Penicillin in U.S. *S. pneumoniae* Isolates Collected from 1997-1999: A Report from the GAARD Project

J. Stelling[1], **K. U. Travers**[2], R. Jones[3,4], L. Miller[5], D. Sahm[6], B. Souder[2], T. O'Brien[1,2], S. Levy[2,4]

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Background: GAARD was created to supplement the significant public health benefits of independent antibiotic resistance (AMR) surveillance programs. Coordination and comparison of methods and data strengthen problem-solving capacity and consequent AMR control efforts. **Methods:** GAARD member organizations Alexander Project, SENTRY, and The Surveillance Network (TSN), reported penicillin susceptibility data from U.S. isolates of S. pneumoniae from 1997-1999 to the project manager, APUA. Alexander and SENTRY reported data for consecutively collected isolates sent to central laboratories for testing, while TSN reported data collected directly from hospital laboratory information systems. The MIC and categorized susceptibility data were analyzed longitudinally for trends associated with time period and surveillance system. **Results:** Over the three-year period, the annual proportions of *S. pneumoniae* isolates not susceptible to penicillin were 29%, 28%, 32% in SENTRY; 34%, 34%, 41% in Alexander; and 50%, 47%, and 44% in TSN. SENTRY and Alexander data suggested a trend toward higher non-susceptibility in 1999; that trend was statistically significant in the Alexander data ($p<0.02$). Significantly higher non-susceptibility was noted overall among TSN isolates ($p<0.001$). **Conclusion:** GAARD surveillance data documented potentially important trends toward greater penicillin resistance in U.S. *S. pneumoniae* isolates. The program-specific differences in susceptibility may be due to different sampling methods, network sizes, and institution type. These conclusions have greater public health importance given the collaborative analysis of the joint data.

Board 10. Ability of Proteolytic Inhibitor E-aminocaproic Acid to Amplify Antimicrobial Action of Antibiotics Against Emerging Infectious Diseases Agents

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We have shown previously that proteolysis inhibitors demonstrate antiviral and antimicrobial activity towards dangerous infectious agents such as influenza virus, herpes simplex virus, adenoviruses, toxoplasmosis, etc. The scope of the present work is the study of the proteolysis inhibitor E-aminocaproic acid

(E-ACA) influence on the sensitivity of emerging diseases agents (*Francisella tularensis* and *Vibrio cholerae*) to various antibiotics. We have studied the antimicrobial action of 18 representatives of 10 antibiotics classes combined with addition of 5 % of E-ACA to the nutrition medium. Standard discs containing needed quantity of antibiotics under testing. Two strains of *Francisella tularensis*: vaccine strain 15 (FT 15) and virulent strain 29 (FT 29) and three strains of *Vibrio cholerae*: strain 569 (VCC 569), El-Tor strain 754 (VCEl 754), Non-1 strain 146/11 (VCNon-1 146/11) were used as the infectious agents. We have discovered that all studied infectious agents are resistant to E-ACA action taken apart from antibiotics. It was discovered that FT 15 strain was resistant to carbenicillin and ofloxacin. Lysis zones around the discs containing these antibiotics were totally absent. Addition of E-ACA leaded to the increase of FT 15 sensitivity towards antibiotics. Diameter of inhibition zones were equal to 16 mm in the case of carbenicillin and to 28 mm in the case of ofloxacin. FT 29 was totally non-sensitive to cefotaxim and ceftriaxon. Addition of E-ACA caused the effect of FT 29 becoming highly sensitive to these antibiotics. E-ACA addition has transformed VCNon-1 146/11 strain resistant to cefatoxim, ceftriaxon, erithromycin, norfloxacin and tetracyclin into highly sensitive one to these antibiotics. Zones of growth hindering for VCNon-1 146/11 due to the mentioned antibiotics combined with E-ACA were in the range of 11 to 25 mm. It was shown that E-ACA addition increased this strain sensitivity to canomycin, ofloxacin and lomefloxacin. Addition of E-ACA solution caused the sensitivity increase of VCC 569 to ampicillin, gentamycin, sizomycin, vancomycin, canomycin. This strain was totally resistant to erithromycin. After E-ACA addition the growth hindering zone diameter was increased up to 28 mm. Strain VCEl 754 became much more sensitive to the antibiotics of penicillin class, aminoglycosides, norfloxacin and tetracyclin after combined application of E-ACA. Analysis of the experimental results has shown that various strains of emerging diseases infectious agents become more sensitive to known groups of antibiotics being applied in combination with E-ACA. Addition of this preparation being tested and classified as non-toxic one in great majority of countries leads to great enhance of efficacy of antibiotics antimicrobial therapy in laboratory testing cycle. The use of E-ACA as the promotor of antibiotics antimicrobial action could be recommended for clinical trial.

Board 11. Epidemiology of Community-onset Methicillin-resistant Bloodstream Infection with Staphylococcus aureus in Connecticut, 2000-2001

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Background: A previous Connecticut (CT) study demonstrated that community-onset (CO) bloodstream infection with methicillin-resistant *Staphylococcus aureus* (MRSA) is an important public health problem. Starting in 2000, laboratories were required to report all bloodstream MRSA isolates in CT residents. In 2001, the system was expanded to include all invasive (sterile site) MRSA isolates. The objectives of the surveillance system are to determine the incidence, epidemiology, trends and risk factors for CO-MRSA. **Methods:** A case of CO-MRSA was defined as a person with an isolate of MRSA obtained as an outpatient or no later than 2 days after admission to a hospital and who was not a resident of a long-term care facility (LTCF) or a hemodialysis patient. A standardized medical record review was done for all CO-MRSA. Patients were further classified as either a) healthcare associated (HA) if they had a hospital admission, outpatient surgery, previous MRSA infection, or resided in a LTCF in the past year, or b) community-acquired (CA). In addition, they were independently classified as either having an underlying illness (UI) predisposing to SA infection or not. Individuals identified as CA-MRSA are being interviewed using a standard questionnaire to determine if other risk factors exist. **Results:** In 2000, 676 reports of MRSA

bloodstream isolates were identified; 128 (19%) were CO-MRSA. Medical record review for year 2000 is complete on 117 (91%). Overall incidence of CO-MRSA was 3.8 per 100,000 population. The rate of CO-MRSA was highest in individuals over 65 years of age (14.9), residents of towns >100,000 in size (4.9), blacks (4.7) and males (4.4). Only one case was <18 years old. For 2001 as of December 1, 220 additional persons with CO-MRSA were identified, of whom 164 (75%) had bloodstream isolates. The projected year 2001 rates for all invasive CO-MRSA and for bloodstream cases are 7.0 and 5.3 per 100,000, respectively. Medical record reviews have been completed for 240 (69%) cases of CO-MRSA from years 2000 and 2001 combined. Of these, 205 (85%) were both HA and had UI, 5 (2%) were HA only, 29(12%) appeared to be CA with UI, and 1 was CA with no UI. Of the 210 HA cases, 180 (86%) had been hospitalized and 126 (60%) had undergone surgery. UIs were present in 233 of the cases; status of one case was unknown. The most common UIs were heart disease (44%) and diabetes (39%). HIV was present in 5%; underlying injection drug use was present in 6%. **Conclusions:** CO-MRSA is common and appears to be increasing in CT. The epidemiology is similar to that found in a previous pilot study. Rates are highest among those over 65 years and residents of urban areas. Most CO-MRSA is healthcare-associated. Invasive community-acquired MRSA in persons without underlying conditions is rare. Continued surveillance and examination of risk factors in those with apparent community-acquired MRSA is needed.

Board 12. Trends in Invasive Pneumococcal Disease, Connecticut, 1996-2000

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Background: Since 1995, the CT ABCs project has conducted statewide active population-based surveillance for invasive pneumococcal disease (IPD), monitored antimicrobial resistance and, since 1998, serotype trends. Our objectives were to assess the 5 year trends in rates of IPD, antimicrobial resistance and serotypes covered by vaccine by demographic subgroups.

Methods: Case data was obtained by medical record review. IPD isolates were sent to a reference laboratory for antimicrobial testing and to CDC for serotyping. Rates of IPD were determined per 100,000 population-specific groups. Vaccine coverage of serotypes was determined based on the 7-valent vaccine (PCV) for 0-4 year olds and the 23-valent vaccine (PPV) for >4 year olds. **Results:** Over 5 years, the rate of IPD decreased from 24 to 20.3 cases per 100,000. Between 1999 and 2000, when PCV was introduced for infants, the largest drop in rates was in the <2 year age group (23%). Comparing 2000 rates to the 1996-99 average, rates in <2 year olds decreased most in Hispanics (31%) and whites (22%) but less in blacks (7%). Blacks <2 years still have the highest rate of IPD (250 cases/100,000). Penicillin-resistant IPD (PRSP) increased from 11% to 13.6% of isolates over 5 years. Percentage (%) that were resistant increased for all antimicrobials, except for vancomycin (still 0%). The largest increases in % resistant were for erythromycin (5.2 to 15%), amoxicillin (4.3 to 12%), cefotaxime (3.4 to 7.2%), and meropenem (2.1 to 6.4%). Percentage resistant to erythromycin (ERSP) increased in both penicillin susceptible (2.2% to 4.8%) and non-susceptible isolates (19.2% to 52.7%). The % of isolates that are ERSP increased in all age groups. The % that were ERSP and that were PRSP were significantly lower in blacks than whites (5.4% vs. 10.8%; 8.4% vs. 13.5%, p 17 years old. At least 86% of serotypes in CT IPD isolates have been covered by PCV (children) or PPV (adults). No distinct age-specific decrease in % of isolates with serotypes covered by vaccines was seen from 1998-2000. When resistant were compared to susceptible isolates for % vaccine coverage, ERSP were less likely than ESSP isolates to be covered (77% vs 88%, p<.00001), unlike PRSP compared to PSSP isolates (92% vs 88%, p>.05) **Conclusions:** In CT, overall IPD rates may be decreasing. Distribution of PCV may already be having an effect on IPD incidence in infants, but use among blacks may be lagging. Antibiotic-resistant IPD is progressively increasing, especially erythromycin resistance. Fluoroquinolone resistance may be emerging. The association between erythromycin resistance and having a lower percentage of serotypes contained in the vaccines needs further exploration.

Board 13. Erythromycin Resistance Among Invasive Group A Streptococcal Infections in the United States, 1999

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Background: Group A streptococcus (GAS) is a common cause of both invasive and noninvasive infections. Although GAS has remained universally sensitive to penicillin, macrolides are often used as alternate therapy. Resistance to erythromycin and other macrolides has risen to high levels in many countries outside of North America (20% to 60%). We sought to determine percent of erythromycin resistance among invasive isolates in geographically diverse regions of the United States using CDC's Active Bacterial Core Surveillance (ABCs) system. **Methods:** ABCs conducts active laboratory- and population-based surveillance for invasive GAS infections. Bacterial isolates obtained from invasive GAS infections identified by participating ABCs sites (CA, CT, GA, MD, MN, NY, OR) in 1999 were tested for resistance to penicillin, ampicillin, erythromycin, clindamycin, vancomycin and cefotaxime by broth microdilution. According to NCCLS guidelines, strains with mean inhibitory concentrations (MIC) of 0.5 mg/ml and > 1.0 mg/ml to erythromycin were defined as intermediate (EryI) and resistant (EryR), respectively. Emm typing was performed on isolates using standard methods. **Results:** In 1999, 772 cases of invasive GAS were identified; 547 (71%) isolates were available for antimicrobial susceptibility testing. Of these, 6.4% (n=35) were EryR and four were EryI. Significant variation in % EryR was noted among sites: 0% (GA), 2.8% (CT), 3.9% (MN), 5.5% (MD), 7.7% (NY), 13.7% (CA) and 13.8% (OR). Upon comparison of patients with EryR to patients with EryS isolates, no significant differences were noted for the following variables: sex, race, hospitalization, outcome, and type of infection. Age > 18 years was associated with having an EryR infection (P=0.028); persons age 35-49 years had the highest % EryR (10.3%). Emm typing was completed on 521 (95%) of the available GAS isolates. EryR was identified among 12 of the 50 different emm types identified but was most common in types emm114 (13 of 16 strains), emm83 (4 of 7 strains), and emm58 (4 of 8 strains). Twelve of 16 emm114 isolates were from GAS cases in CA and OR; nine (75%) were EryR. The remaining four emm114 strains, found elsewhere (MD=1, MN=3), were EryR. **Conclusion:** Erythromycin resistance among invasive GAS isolates shows significant geographic variation, with the greatest resistance noted in ABCs sites located in two states. Resistance is more common in certain emm types; predominance of resistant strains of emm 114 in the western U.S. could be due to expansion of a resistant clone, although local antibiotic use is likely also a factor.

Board 14. Rapid Detection of Methicillin-Resistant Staphylococcus aureus by Real-Time PCR Using LightSpeed Probes

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The emergence of methicillin-resistant *Staphylococcus aureus* (MRSA) has become an important cause of nosocomial infections and is associated with increased morbidity, mortality and hospital costs. Furthermore, the lack of rapid methods for identification of MRSA often leads to empirical treatment of *S. aureus* infections with vancomycin which can lead to the development of vancomycin-resistant enterococci, another important antimicrobial-resistant pathogen. Here we describe a simple 40-minute real-time PCR method for detection of the methicillin resistance gene, mecA, in MRSA using LightSpeed probes. LightSpeed probes are dual-labeled peptide nucleic acid probes with a fluorescent dye and quencher molecule bound to the opposing termini. Upon hybridization, the fluorophore and quencher are spatially separated and the LightSpeed probe becomes fluorescent. The test is performed as a homogeneous sealed tube assay, where the formation of amplicons is detected on-line by an increase in fluorescence. The performance of the test was initially established using seven reference strains representing both MRSA and MSSA and showed 100% accurate discrimination. Evaluation using 16 clinical isolates showed 81% (13/16) agreement with antimicrobial susceptibility testing. Discrepancies are being examined further.

Board 15. Antimicrobial Susceptibility and Serotype Patterns of Invasive Group B *Streptococcus* Isolates from Georgia, Minnesota, New York and Oregon, 1996- 2000

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Background: Maternal carriage of Group B *Streptococcus* (GBS) poses a risk for vertical transmission to neonates. Intrapartum GBS chemoprophylaxis recommendations implemented in the 1990's reduced invasive early-onset neonatal disease by 65% (1.7 to 0.6 per 1000 livebirths during 1993-1998). Nonetheless, GBS remains the leading cause of neonatal invasive disease and is an important pathogen for peripartum women and nonpregnant adults. Identifying susceptibility and serotype trends is critical for guiding chemoprophylaxis recommendations and vaccine formulation. **Methods:** Active population-based surveillance for GBS was conducted in four states during 1996-2000. Case-patients were defined by isolation of GBS from a sterile site; analyses were performed on perinatal (neonates and pregnant women) and adult case-patients. Isolates were tested for susceptibility by broth microdilution and serotyped. Preliminary **Results:** Of 3,399 case-patients; 1,043 (31%) had susceptibility data and 1,638 (48%) were serotyped. No isolates were resistant to penicillin, vancomycin, cephalothin, or cefazolin. Clindamycin resistance was found in 110 (11%) and erythromycin resistance in 196 (19%) isolates. Comparing 1996-1998 with 1999-2000, erythromycin resistance increased from 16% to 21% (p=0.025) and clindamycin resistance from 8% to 12% (not significant). Perinatal isolates were commonly serotype III (40%), Ia or Ia/c (27%) and V (17%). Adult isolates were most often serotype V (30%). Serotype V was associated with clindamycin or erythromycin resistance among perinatal (p<0.001 for both) and adult isolates (clindamycin, p=0.009; erythromycin, p=0.02). **Conclusions:** Clindamycin and erythromycin are alternatives to penicillin for intrapartum prophylaxis in penicillin-allergic women; however, resistance to both was found. Cefazolin or vancomycin may be preferable alternative agents. Clindamycin or erythromycin resistance was associated with serotype V. Vaccine strategies should consider predominant serotypes and/or serotypes associated with resistance.

Board 16. Phenotypic and Genotypic Comparison of Salmonella Strains Collected from Humans and Swine in North Carolina

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Background: Multiple antimicrobial resistant *Salmonella*e are an emerging problem at the global scale. In the ICEID 2000 symposium, we reported that multi-drug resistance with distinct pentaresistant pattern was common among *Salmonella enterica* isolates collected from swine in North Carolina. We found that 36.2% of 484 *Salmonella* serovar Typhimurium (including Copenhagen) isolates from swine were of phage type DT104, which commonly exhibits pentaresistance (R-type ACSSuT). Provided this phage type has been increasingly reported from human outbreaks in most parts of the world and the state of North Carolina is one of the leading in pork production, there has been a growing concern that clinical *Salmonella* isolates identified from humans in the swine producing counties would more likely be similar or identical strains as that of the swine. **Methods:** In order to test this hypothesis, we compared frequency of resistance as well as the genotypes of isolates collected from swine and humans. We received 179 isolates from the North Carolina Public Health Laboratory between the year 2000 and 2001. We tested antimicrobial susceptibility of isolates for 12 antimicrobial agents using Kirby-Bauer disk diffusion method. To discern similarity between human and swine isolates, we used genotyping by Pulsed Field Gel Electrophoresis (PFGE). **Results:** Antimicrobial susceptibility tests revealed that 81% of the isolates from human clinical samples did not exhibit resistance to any of the antimicrobial agents tested. On the other hand more than 85% of isolates from swine were resistant to at least one antimicrobial agent. Among Typhimurium isolates from human, 6% exhibited consistent pentaresistance pattern as that of DT104. We found higher frequency of multi-drug resistance among serovar Heidelberg isolates from humans ranging between 4 and 19% per antimicrobial agent. Serovar Heidelberg often exhibited either no resistance or only tetracycline resistance among isolates collected from swine. None of the human isolates were found to be resistant to ciprofloxacin, amikacin and gentamicin. However, 2% of the isolates showed reduced susceptibility to a third generation cephalosporin, ceftriaxone. None of the swine isolates exhibited resistance to third generation cephalosporins or ciprofloxacin. PFGE comparison of isolates with similar resistance pattern showed disparity of fingerprints (with less than 75% pearson pairwise correlation) between human and swine isolates. **Conclusion:** Our findings so far, do not warrant that human clinical isolates are similar to those commonly found in swine. Rarely, similar fingerprints have been noticed. The common finding of disparity in resistance pattern as well as DNA fingerprints may imply that there could be other common reservoirs of human infection more important than the swine-human transmission cycle.

Board 17. Detection of a Class I Integron in Multi-Drug Resistant *Salmonella niakhar*

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In the United States, *Salmonella enterica* serotype *niakhar* is a rarely isolated serotype of *Salmonella*. Between 1997 and 2000, the animal arm of the National Antimicrobial Resistance Monitoring System — Enteric Bacteria (NARMS) at USDA-ARS

in Athens, GA assayed for antimicrobial resistance a total of 22,383 *Salmonella* isolates from various animals (swine, cattle, chickens, turkeys, cats, and dogs). Isolates originated from on-farm studies, veterinary diagnostic laboratories, or raw product collected from federally inspected slaughter and processing plants. Only 5 (0.02%) of these isolates were identified as *niakhar* (designated A-E). Of the five, B - D isolates were isolated in the Midwest (dairy cattle), A and E were isolated in the Southern United States (dairy cattle and dog). Antimicrobial resistance testing indicated that isolates A, B, and E were susceptible to all antibiotics tested; whereas isolate C was only resistant to ampicillin. Isolate D was resistant to ampicillin, chloramphenicol, ciprofloxacin, kanamycin, nalidixic acid, streptomycin, sulfamethoxazole, tetracycline, and trimethoprim/sulfamethoxazole. Class I integrons (*intI1*) in *Salmonella* are known to harbor multiple resistance genes. Using PCR primers to the 5'conserved segment of *intI1*, a 568-bp fragment was amplified from isolate D. The integron from this isolate was localized to a ~ 12 kb *XbaI* fragment using PFGE. Further characterization of all isolates is ongoing. This is a first report of ciprofloxacin resistant *Salmonella* from NARMS as well as the first identification of *intI1* in *Salmonella niakhar*.

Board 18. Assessment of the Etest™ System for Determination of Antibiotic Susceptibilities of *Bacillus anthracis* Strains Representative of World-Wide Diversity

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Twenty-five *Bacillus anthracis* strains representative of the geographic diversity of this pathogen were evaluated for resistance to nine clinically relevant antibiotics using the Etest™ system (AB Biodisk, Solna, Sweden) by standard methods. Relative susceptibility and minimum inhibitory concentrations (MIC) were determined for azithromycin, cefotaxime, cefotaxime/clavulanic acid, ciprofloxacin, erythromycin, gentamicin, penicillin, tetracycline, and vancomycin. Initial analysis of these 25 isolates revealed that the level of resistance to azithromycin was consistently 4-12 times greater than that previously noted (Turnbull et al., unpublished results) ranging from 1.5 to 12 mg/L with a median range of 4 to 6 mg/L. All strains were susceptible to cefotaxime, cefotaxime/clavulanic acid, ciprofloxacin, and erythromycin, in good agreement with prior reports using different methodologies. Of the remaining antibiotics, sensitivity to penicillin was greater than previously reported with over 90% of the strains having MICs between 0.012 to 0.032. One of these strains, ASC 32, previously reported as penicillin resistant had a markedly higher MIC to this antibiotic (24 mg/L) than did the other strains but this value was less than that reported in a study be Lightfoot and co-workers (64 mg/L). The MICs for gentamicin ranged from 0.019 to 0.5 mg/L while those for vancomycin ranged from 0.75 to 3.0 mg/L. We propose that the Etest™ method provides an effective, simple alternative to the disk-diffusion and broth dilution methods for the direct quantification of *B. anthracis* susceptibility. The relevance of our findings to the therapeutic uses of different antibiotic classes in human clinical cases will be discussed. Further studies are underway to assess the susceptibility of these and other selected strains to additional antibiotics.

Board 19. National Department of Defense Surveillance for *Streptococcus pneumoniae*: Update on Antibiotic Resistance and Serotype Distribution

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Background: *Streptococcus pneumoniae* is commonly associated with pneumonia, bacteremia, meningitis, and otitis media. Recent emergence of antibiotic resistant *S. pneumoniae* is a growing concern among military and civilian health practitioners. Surveillance for antibiotic resistance and serotype distribution among pneumococcal isolates can provide critical information for the effective use of antibiotics and vaccines. **Methods:** *S. pneumoniae* clinical isolates were systematically collected from seven large military hospitals between August 1997 and May 2001. Antibiotic susceptibility testing was completed with E-test gradient strips. Isolates were serotyped by latex agglutination with diagnostic antisera and confirmed with the Quellung test. Basic demographic and clinical information was available from existing sources in the health care centers. **Results:** Three hundred four isolates were evaluated for antibiotic resistance. One hundred seven (35.2%) had intermediate or high-level resistance to penicillin. Seventy-three (24.0%) of the isolates had multi-drug resistance to penicillin and any two of the following: erythromycin, sulfamethoxizole/trimethoprim, or ceftriaxone. All isolates were sensitive to levofloxacin and vancomycin. To date, we have successfully serotyped 250 of the 304 isolates, and 20 different serotypes were identified. The most common were serotypes 14(27.6%), 9V(13.6%), 19F(10.4%), 6B(12.0%), 4(9.2%) and 23F(8.8%). Serotypes 18C and 4 were significantly more likely to be penicillin sensitive ($p=0.017$, and $p\leq0.001$, respectively), while 9V was more likely to be penicillin resistant ($p=0.045$). Serotype 4 was significantly more likely to be multidrug sensitive ($p=0.003$) while serotypes 19F and 23F were more likely to be multidrug resistant ($p=0.004$, and $p=0.045$, respectively). **Conclusions:** Antibiotic resistance is present in a significant proportion of *S. pneumoniae* isolates obtained from military healthcare beneficiaries. Furthermore, data indicate a significant penicillin resistance in serotype 9V and significant multi-drug resistance in serotypes 19F and 23F. Those serotypes found to be resistant are included in the 23-valent pneumococcal vaccine; this may have important public health ramifications. Continued surveillance of these trends is critical to assure success in future treatment of the diseases caused by this pathogen.

Board 20. Penicillin-Resistant *Streptococcus Pneumoniae* in New York State: Population Variability

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Background: *Streptococcus pneumoniae* (SPN) is the leading bacterial cause of a number of diseases including pneumonia, meningitis, otitis media, and bacteremia resulting in high morbidity and mortality in the U. S. The prevalence of drug resistant SPN strains has increased since resistance was first reported in the early 1990s. Drug resistant, invasive SPN disease became reportable in New York State in July 1995. In 1999, all invasive pneumococcal infections became reportable in the 15 Albany and Rochester counties that comprise the Active Bacterial Core (ABC) component of the NYS Emerging Infections Program (EIP). The purpose of this report is to characterize populations at risk for invasive disease and, more specifically, those at risk for penicillin-resistant SPN. **Methods:** Confidential case reports were completed for all culture-confirmed invasive cases among residents of the NYS EIP during the period 1999-2000. Isolates were tested locally for penicillin resistance and results were coded according to NCCLS guidelines. In this analysis, intermediate and fully resistant cases were collapsed into a single 'resistant' category. Patient information included demographic characteristics, length of hospitalization, outcome, and underlying medical conditions. **Results:** During the two-year period 1999-2000, 831 invasive SPN cases were reported in the NYS EIP for an annual incidence rate of 19.9/100,000. Eight cases with 'unknown' susceptibility results were excluded from the analysis. Of the remaining 823 cases, 658 were classified sensitive

(15.8/100,000 per year), and 165 resistant (4.0/100,000). Females had slightly higher rates of infection compared to males (21.1 vs. 18.7/100,000 per year) and a higher percent resistant (22.3% vs. 17.3%), but these differences were not significant. The difference in overall incidence rates between blacks and whites was highly significant (44.5 vs. 17.9/100,000; OR=2.48, p<.00001) but there was no difference in the percent resistant between the two groups (20% resistant within each race). Younger (< 5 years; 69.1/100,000) and older (> 65 years; 58.2/100,000) individuals were at significantly greater risk for infection (OR=4.25, p<.00001 and OR=4.27, p<.00001 respectively) compared to all other age categories but there were no significant differences in the percent resistant by age. **Conclusions:** Although both age and race were shown to be independent risk factors for invasive pneumococcal disease, this analysis did not identify any significant risk factors for infection with penicillin-resistant strains. Identification of risk factors associated with drug-resistant SPN infection will continue to gain importance as the prevalence of these strains rises.

Board 21. Prevalence of Antimicrobial Resistance of *Salmonella* in Chickens and Pigs in Thailand: Reflection of the Overuse of Antimicrobial Drugs

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Background: The estimated prevalence of human Salmonellosis in Thailand is 76-1,053 cases per 100,000 population. Likely sources of infection include food of animal origin such as chicken and pork, which are a favorite protein diet of the Thai population. **Methods:** Fecal samples from 563 native-chickens, 1,645 farm-broilers, 114 native-pigs, and 722 farm-pigs were tested. All *Salmonella* isolates were tested for antimicrobial susceptibility using an agar dilution technique. **Results:** *Salmonella* was found in 8.9 % (50 isolates) of the native-chicken samples, 5.3 % (87 isolates) of the farm-broiler samples, 6.1 % (7 isolates) of the native-pig samples, and 3.1 % (24 isolates) of the farm-pig samples. The results showed that *Salmonella* isolates from native-chickens and native-pigs had a lower percentage of antimicrobial resistance than *Salmonella* isolates from farm-broilers and farm-pigs (Table 1). Table 1 Percentage of antimicrobial resistance of *Salmonella* isolates from feces of native-chickens, farm-broilers, native-pigs and farm-pigs in Thailand.

	% Resistance of *Salmonella* Isolates from Feces			
Antimicrobial Testing	Native-Chickens	Farm-Broilers	Native-Pigs	Farm-Pigs
Ampicillan	0.96	24	0	75
Chloramphenicol	0	13.3	14.3	16.7
Kanamycin	0	13.3	14.3	25
Nitrofurantoin	0	11.7	0	4.2
Tetracycline	10.2	29.4	0	95.8
Nalidixic acid	33.3	59.2	28.6	45.8
Ciprofloxacin	0	0	14.3	20.8
Furazolidone	4.8	49.7	28.6	4.2
Sulfamethoxazole	9.3	16.2	0	70.8
Sulfamethoxazole + Trimethoprim	9.3	12.8	0	6.7

Conclusion: Native-chickens and native-pigs are raised in rural areas, consume natural feed, and are rarely given antimicrobials as growth promoters or for disease prevention; this could explain the lower prevalence of antimicrobial resistance among these samples. Farm-broilers and farm-pigs, however, are raised intensively and usually given antimicrobials as growth promoters or for disease prevention. Since 2001, Thailand has fully adopted "Recommended International Code of Practice for Control of the Use of Veterinary Drugs (CAC/RCP 38-1993)" and implemented "Good Farm Practices" in all industrial food-animal farms. Additionally, the Ministry of Public Health has established food-safety plans, which address all major national food-safety problems. Related governmental sectors understand that food safety requires the integration of all stakeholders rather than any individual organization; therefore, co-operation among stakeholders is improving. However, the insurance of "Safe from Farm to Table" is still a challenging task that requires hard work from all related agencies. To help reduce the burden of foodborne diseases and implement prudent use of antimicrobials in food-animals, a strong collaboration of all stakeholders involved in the food chain, including both government and private agencies (i.e. veterinarians, farmers, food microbiologists, epidemiologists, etc.), is essential.

Board 22. The Use of Pulsed Field Gel Electrophoresis and Automated Ribotyping to Monitor the Increased Prevalence of a Multidrug Resistant Salmonella serotype Newport in Massachusetts Associated with Cows

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A strain of multidrug resistant *Salmonella* serotype Newport (MDR *S.* Newport) has recently emerged in the United States, first appearing in Massachusetts in April 1999. This strain is characterized by resistance to at least ampicillin, cephalothin, chloramphenicol, clavulanic acid, streptomycin, sulfamethoxazole, tetracycline and ceftriaxone. Between January 1999 and December 2001, 167 human and 17 bovine isolates were identified as *S.* Newport at the Massachusetts State Laboratory Institute (SLI). The rate of MDR among *S.* Newport isolates received at SLI rose from 23% in 1999, to 49% in 2000 and to 54% in 2001. All 17 bovine isolates were MDR, whereas 66 of the human isolates were MDR suggesting a possible bovine reservoir for this particular strain of *S.* Newport. Automated ribotyping discriminated *S.* Newport from other serotypes and correctly identified MDR *S.* Newport as one of two dominant ribotypes. There were 71 pulsed field gel electrophoresis (PFGE) patterns of *Xba*I digests of *S.* Newport in both MDR *S.* Newport (n=8) and other *S.* Newport (n=63). The dominant PFGE pattern in the MDR *S.* Newport isolates was MA-JJP0034. Thirteen of 17 the bovine and 43 of the 66 human isolates displayed this pattern. Thus, both typing methods were helpful in identifying the MDR strain of *S.* Newport; however, automated ribotyping was particularly useful in rapidly identifying the serotype and PFGE in detecting associations that aided epidemiologic investigations.

Board 23. Comparison of Two *Campylobacter* Isolation Methods and Their Effect on Antimicrobial Resistance Patterns

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Introduction: *Campylobacter* spp. are fairly ubiquitous in the environment but their fastidious nature make detection and isolation in the laboratory difficult and time consuming. As part of the National Antimicrobial Resistance Monitoring System (NARMS), we routinely isolate *Campylobacter* from chicken carcass rinses. We developed a new *Campylobacter* isolation method and compared it to our conventional isolation method routinely used in our ARS laboratory. **Methods:** In the conventional method (CM), Bolton enrichment broth (BB) was inoculated with a cotton-tipped applicator soaked in the carcass rinse while in the new, or spin, method (SM), 10 mL of the carcass rinse was pelleted, the

supernatant was decanted and the pellet was resuspended in BB. For both methods, broths were incubated at 42°C for 48 h under reduced atmosphere, streaked to Cefex agar, and incubated at 42°C for 48 h. Typical *Campylobacter* isolates were picked and confirmed by PCR. **Results:** Using the SM, 92/331 (27.8%) rinses were positive for *Campylobacter* while only 356/2564 (13.9%) rinses were positive using the CM. Isolates were tested for resistance to azithromycin (Az), ciprofloxacin (Ci), chloramphenicol (Cl), clindamycin (Cm), erythromycin (Em), gentamicin (Gm), nalidixic acid (Na), and tetracycline (Tc). No isolates were resistant to either Cl or Gm. The total percent *C. jejuni* isolated by the SM (n=48) that were resistant to Az (4.2%), Ci (22.9%), and Na (22.9%) was higher than total percent *C. jejuni* isolated by the CM (n=217): 2.8%, 17.5%, and 19.4%, respectively. Conversely, resistance to Tc was 33.3% from the SM versus 49.3% from the CM. For *C. coli*, the total percent resistant to Az (13.6%), Ci (18.2%), Em (13.6%), and Na (18.2%) from the SM (n=44) was lower than those from the CM (n=139): 22.3%, 25.2%, 22.3%, and 29.5%, respectively. Resistance to tetracycline was also reversed with more (61.4%) isolates resistant from the SM versus the CM (54.0%). Preliminary analysis of the isolates recovered from the same sample by both methods (21/331; 6.3%) does not indicate any resistance differences between methods. **Conclusions:** The increase in recovery from the SM versus the CM suggests that total numbers of *Campylobacter* are low within the sample and/or there may be a tendency for more fit bacteria to survive and propagate in one method over the other, most likely by concentration of numbers. Additionally, we have observed more particulate material in the pellet which may have a higher association with *Campylobacter*. The difference between methods for both recovery and resistance data when isolates are not recovered from the same sample clearly demonstrates that outcome is affected by methodology and must be considered when analyzing data from different studies.

Board 24. Comparison of Antibiotic Susceptibility Patterns of Enteric Pathogens Between Local Populations and U.S. Travelers to Thailand from 1995 through 2000

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Antibiotic resistance among enteric pathogens is of a critical concern and influences the effectiveness of treatment for patients suffering from traveler's diarrhea (TD). The Armed Forced Research Institute of Medical Sciences (AFRIMS) routinely tests enteric pathogen isolates from patients for antibiotics susceptibility (AS) patterns during the course of conducting research on TD in South East Asia. We reviewed our databases for the years 1995 through 2000 to compare the AS patterns of isolates from U.S. adults traveling to Thailand to isolates collected from studies done by AFRIMS in Thailand with local populations. We compared the differences of resistance in bacterial isolates to ampicillin (AMP), tetracycline (TCN), trimethoprim-sulphamethoxazole (SXT), ciprofloxacin (CIP), and azithromycin (AZM). **Percentage of antibiotic resistance among enteric pathogens isolated from U.S. adults traveling to Thailand compared to isolates from Thai local populations.**

		Bacterial Pathogen [% Resistance (n=)]					
Antibiotic	Isolate source	*Campylo-bacter*	*E.coli* (non-ETEC)	ETEC	*Salmonella* non-typhi	*Shigella*	*Vibrio*
AMP	Thai	24(25)	**47(900)**	57(345)	**27(996)**	**39(379)**	
	US	40(210)	**22(82)**	51(73)	**20(184)**	**13(16)**	**58(12)***
TCN	Thai	**41(27)**	**54(899)**	**41(345)**	**54(995)**	91(379)	
	US	**92(266)**	**85(82)**	**67(73)**	**80(184)**	100(16)	0(12)
SXT	Thai	**85(26)**	49(900)	48(345)	**37(996)**	92(379)	
	US	**99(264)**	38(82)	47(73)	**23(184)**	88(16)	17(12)
CIP	Thai	**78(876)**	1(900)	1(344)	0(996)	0(379)	
	US	**91(329)**	4(82)	0(73)	0(184)	0(16)	0(12)
AZM	Thai	**6(839)**	**17(101)**	**14(58)**	2(190)	**0(76)**	
	US	**2(328)**	**4(82)**	**3(71)**	8(143)	**33(3)***	0(12)

Bolded numbers denote a statistical difference of p<0.05 between the isolate sources. * While a statistical difference exists between sources, would disregard due to small "n" for U.S. isolates. Overall, widespread resistance is noted for enteric isolates to AMP, TCN, and SXT as well as for *Campylobacter* to CIP. With the exception of SXT, *Vibrio* appears to continue to be susceptible to these antibiotics. AZM has the least percentage of resistance of these antibiotics. Differences in the AS patterns between the two sources of isolates are noted especially to TCN. Higher percentages of resistance from U.S. isolates may be a result of the widespread prophylactic use of doxycycline by the U.S. military against malaria when deployed to Thailand. Interestingly, Thai isolates appear to have higher percentages of resistance to AZM, though still a relatively small percentage. A consistent difference is noted among pathogens only for *Campylobacter* where U.S. isolates had a higher percentage of resistance than Thai isolates. More research on *Campylobacter* is needed to explore this phenomenon. Reporting of results from research studies and surveillance systems throughout Asia will be increasingly important for tracking changes in AS patterns and making recommendations for the clinical treatment of TD.

Board 26. Comparison of Antimicrobial Resistance Patterns in *Campylobacter* Species Isolated from Broiler Chickens in 1999 and 2000

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Introduction: Antimicrobial resistance has been increasing in many bacteria. The National Antimicrobial Resistance Monitoring System — Enteric Bacteria (NARMS) was established to monitor for emerging resistance in food borne and commensal bacteria of human and animal origin. **Methods:** The animal arm of NARMS conducted antimicrobial susceptibility testing on *Campylobacter* species isolated from broiler chicken carcass rinses collected at federally inspected slaughter and processing plants in 1999 (*C. jejuni* n=77; *C. coli* n=19) and 2000 (*C. jejuni* n=90; *C. coli* n=16). All isolates were tested for susceptibility to eight antimicrobials: azithromycin, ciprofloxacin, chloramphenicol, clindamycin, erythromycin, gentamicin, nalidixic acid, and tetracycline using the E-test (AB Biodisk) as per manufacturer and NARMS protocol. Data were analyzed by dividing the US into regions representing the Northeast (Region 1; R1), Southeast (Region 2; R2), Central North (Region 3; R3), Central South (Region 4; R4), and West (Region 5; R5). More isolates of *C. jejuni* were available than *C. coli* in R2 and R4 (representing regions with the highest broiler production) for both years. For *C. jejuni*, total numbers by region for 1999 and 2000, respectively, were R1 - 14 and 9, R2 - 32 and 39, R3 - 4 and 6, R4 - 25 and 29, and R5 - 2 and 7. For *C. coli*, total numbers by region for 1999 and 2000, respectively were R1 - 2 and

1, R2 - 9 and 10, R3 -3 and 0, R4 - 3 and 5, and R5 - 2 and 0, respectively. **Results:** In both years, all isolates were susceptible to chloramphenicol and gentamicin. Resistance to other antimicrobials varied by year and district; however, isolates were more resistant to tetracycline than any other antimicrobial. For *C. jejuni*, total numbers of isolates resistant to ciprofloxacin were 9 for 1999 and 10 for 2000. Multiple resistance (defined as resistance to 2 or more antimicrobials) among *C. jejuni* varied between regions for both years. Total number of *C. coli* resistant to ciprofloxacin decreased from 1999 (5) to 2000 (1). For both years, multiple resistance was highest in R2 for *C. coli* isolates. **Conclusions:** Regional distribution indicates that a majority of the isolates originated from the Southeast (R2) and Central South (R4) which correlates with the major poultry production areas. The relatively low numbers of isolates from R1, R3 and R5 confound analysis of the data. Collectively, there appears to be little variation among resistance patterns throughout the regions with the exception of multiple resistance in *C. coli* as multiple resistance was observed in all 5 regions for 1999 and while only in R2 and R4 in 2000. Continued monitoring and increasing total numbers of isolates tested is warranted.

Board 27. Multiple Resistance Among *Salmonella* Isolates of Animal Origin from The National Antimicrobial Resistance Monitoring System -Enteric Bacteria 1997-2000

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Introduction: Developing antimicrobial resistance to new and older drugs is of global concern. However, the growing trend of multiple resistance involving both new and older drugs will exacerbate the problem. The National Antimicrobial Resistance Monitoring System — Enteric Bacteria (NARMS-EB) was established to monitor emerging resistance in food borne and commensal bacteria of human and animal origin. **Methods:** As part of the animal arm of NARMS, *Salmonella* isolates were submitted from raw product collected at slaughter and processing plants (designated SI) or from feces or tissue samples collected from diagnostic submissions (designated DI) from chickens (CH), cattle (CL), swine (SW) and turkeys (TK) for 1997 through 2000. Antimicrobial susceptibility testing was conducted using the SensititreTM System (Trek Diagnostics, Inc.) as per manufacturer's directions. Antimicrobials were selected and configured in a 96 well custom made panel. Results were analyzed by year, type (SI or DI), source (CH, CL, SW, TK), and serotype. Total percent pan-susceptible and resistance to only 1 antimicrobial were combined for this analysis. Multiple resistance was defined as resistance to ≥ 2 antimicrobials. **Results:** Overall, SI from CL, SW, and TK were more susceptible than DI regardless of year. For CH isolates, however, multiple resistance was 34% in 1997 and 1998 and 33% in 1999 and 2000 among SI while multiple resistance among DI was 23%, 40%, 26%, and 26% for 1997-2000, respectively. Regardless of type, turkey isolates had more multiple resistance than CH, CL, or SW. The least multiple resistance was observed among CL samples collected from SI. The most common resistance pattern from all sources was to Streptomycin, Sulfamethoxazole and Tetracycline. Resistance to more antimicrobials was observed among DI. Analysis within source by year was variable and no trend among sources was detected. The top 5 serotypes also varied widely between sources by year. **Conclusions:** These data indicate that multiple resistance is less in CL, SW and TK SI when compared to DI. This is not unexpected as diagnostic submissions are often made after an animal is ill or dead, and depending upon source, may have been treated for prior illness. The data observed for CH isolates was not expected. It is possible that this reflects submission of samples from earlier periods in production prior to extended exposure or use of antimicrobials or variations in serotype. The most common multiple resistance pattern for all isolates is to older drugs. However, when multiple resistance included newer drugs, resistance was also observed to the older drugs. Molecular analysis of multiple resistant cassettes will assist in further analysis of the data. While multiple resistance does not appear to be significantly changing among SI, analysis by serotype and region will provide the additional detail which is necessary to determine if trends are emerging.

Board 29. Alternative Antibiotics with Specific Anti-Staphylococcal Activity

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The development of multiple resistance of *Staphylococcus aureus* towards clinically relevant antibiotics was the reason to analyze the effectiveness of patented antibiotics towards *S. aureus* back to the year 1948. The number of patents covered by this analysis exceeds 600 and the number of antibiotics 1100 (1).

The effectiveness of the respective antibiotics is expressed as 'Therapeutic Index' (TI) according to the formula TI = LD50 /MIC, which calculates the toxicity of antibiotics towards microorganisms *in vitro* (MIC = minimal inhibitory concentration in ppm) and the toxicity towards animals *in vivo* (LD50 = that dose causing death of 50% of test animals in mg/kg/body weight). The toxicity data of antibiotics towards animals have been determined on several administration routes, and therefore, it was distinguished between oral, intraperitoneal (ip) and intravenous (iv) 'TIs'. The TIs (iv, ip) of vancomycin were used as reference and only such antibiotics are listed among results which show higher TIs than the reference compound itself.

To select antibiotics with anti-staphylococcal activity having different chemical basic structures than antibiotics used in the therapy of *S. aureus* infections, antibiotics belonging to the following groups were excluded from this analysis: tetracyclines, beta-lactams, macrolides, aminoglycosides, ansa-type antibiotics and quinolones. In a second attempt the selected antibiotics were checked for occurrence of microbial resistances and positive compounds were also excluded.

The selected antibiotics on the basis of iv toxicity data are nosiheptide, platomycin B, diumycin A, moenomycin, pholipomycin, thiostrepton, siomycin, platomycin A, and FR-900451. On the basis of ip toxicity data danomycin, nosiheptide, thermorubin, thiostrepton, siomycin, platomycin B, A-82846-A, diumycin A, enduradicin, A-47934, and thiopeptin A1 are selected. On the basis of oral toxicity data chlorobiocin, pactamycin, resistomycin Bayer, actinomycin C complex, carriomycin, cervinomycin A2 monoacetate, cervinomycin A1 triacetate, AM-5344-A2, macromomycin, aflastatin A, T-2636-C and amicetin showed promising results. The data on the selected antibiotics indicate that a greater number of compounds exist being more effective against *S. aureus* than vancomycin. Their usefulness as clinical therapeutics depends on further factors, such as the failure of cross-resistance to therapeutically relevant antibiotics, satisfactory bioavailability, and absence of side effects.

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51 Syndromes and Diagnosis II

Tuesday, March 26, 8:30 a.m.
Grand Hall East

Board 30. Surveillance for Patients with Acute Meningitis in Egypt

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Background: Acute meningitis is an important cause of morbidity and mortality in Egypt. Surveillance for patients with meningitis is a high priority to determine the etiology and design prevention strategies. In June 1998, a project to develop enhanced surveillance for patients with meningitis and encephalitis was implemented in diverse areas of Egypt. This report describes clinical and epidemiological features of bacterial meningitis from this network during the first 3 years. **Methods:** Clinical and laboratory training was conducted to optimize recovery of bacterial pathogens and standardize collection of clinical information. **Results:** Of the 6868 patients evaluated between June 1998 and August 2001, 691 (10.1%) had culture-confirmed bacterial meningitis. The etiology of disease included 244 patients (35%) with *S. pneumonia* (SP), 129 (19%) with *H. influenzae* (HI), 125 (18%) with *N. meningitides* (NM), 106 (15%) with *Mycobacterium tuberculosis* (MTB), and 87 (13%) with other bacterial causes of disease. The mean age of culture-positive patients was 13 years for patients with SP, 1.0 for patients with HI, 15 for patients with meningococcal disease, and 24 years for patients with MTB. The overall case fatality ratio was 25.5% and was highest among patients with MTB (46.2%), followed by HI (25.6%), SP (23%) and NM (16%). The mean interval from the onset of illness to date of hospital admission was highest among patients with TB meningitis (13 days) and was higher among patients who died (7 days) compared to patients who survived (4.6 days). Sensitivity to penicillin and ceftriaxone was 56%/94% (SP), 71%/90% (HI) and 14%/81% (NM-ampicillin used). **Conclusion:** SP is the leading cause of bacterial meningitis in Egypt followed by HI, NM and TB. The case fatality ratio for patients with all forms of meningitis is higher than what is reported in United States and European countries and could be due to delayed presentation and the emergence of antibiotic resistance.

52 Travelers' Health

Tuesday, March 26, 8:30 a.m.
Grand Hall East

Board 31. The Association of Enterotoxigenic *Escherichia coli* with Hospitalized Diarrheic Patients in Denpasar, Indonesia

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Infection caused by enterotoxigenic *Escherichia coli* (ETEC) poses a serious health problem among children and adults in developing countries. Colonization of the small intestinal mucosa by ETEC strains is mediated by antigenically specific fimbrae. The relationship between ETEC and hospitalized patients with acute diarrhea was examined in two hospitals in Denpasar, Indonesia. A total of 489 hospitalized patients with acute diarrhea were enrolled in this study and their stools were screened for enteric bacterial pathogens. Toxins, colonization factor antigens (CFAs), *in vitro* antimicrobial susceptibility and seasonal distribution patterns associated with ETEC were ascertained. The diagnosis of ETEC infection and CFA association were performed with GM-1 ELISA and Dot blot immunoassays. ETEC was isolated from the stools of 14.9% of the patients. The distribution of toxins among the ETEC strains was ST- 51 at 69.9% and LT and ST/LT with 28.8% and 1.3%, respectively. A high isolation rate of ETEC was found among children between 1 and 5 years. CFAs were identified in 28.8 % of the ETEC strains. A high prevalence of CFAs was found among the stools of patients with ST isolates. A high resistance to ampicillin, trimethoprim/sulfamethoxazole, chloramphenicol, tetracycline and cephalothin was observed among ETEC strains. All ETEC strains were susceptible to norfloxacin, ciprofloxacin and nalidixic acid. The results of this study document the association of ETEC bacteria among hospitalized patients with acute diarrhea in Denpasar, Indonesia. These data may help current research efforts on the development of CFA-based vaccines for humans against ETEC and provide additional information for future ETEC vaccine trials in Indonesia.

53 Blood Safety

Tuesday, March 26, 8:30 a.m.
Grand Hall East

Board 32. Hepatitis C Virus: Tainted Blood in Latin America

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The number of cases of transfusion-transmitted infectious diseases can be estimated from the number of blood donors, percentage of donors screened, and the prevalence rate of serologic markers in the donor population(1,2).We report here such information for 9 Latin American countries in 1993 (Chile, Colombia, Ecuador, El Salvador, Guatemala, Honduras, Nicaragua, Peru, and Venezuela, with 1,125,579 screened donors for all these countries); for 9 countries in 1994 (Colombia, Ecuador, El Salvador, Honduras, Nicaragua, Panama, Peru, Uruguay and Venezuela, with 976,670 screened donors); for 12 in 1995 (the same countries as in 1994 plus Argentina, Costa Rica, and Paraguay, with 1,929,124 screened donors); and for 13 in 1997 (the same countries as in 1995 plus Chile, with 2,326,685 screened donors for all these countries). Estimates were based on official national reports of the number of blood donors, percentage of donors screened, and prevalence of HCV by EIA in the donor population (1-3). The prevalence of HCV in the different countries varied from 0.5 to 9.4/1,000 donors during the study period. To calculate the potential number of tainted units of blood the following assumptions were made (1,2): 1) Reagents and blood bank procedures were of good quality and appropriate, 2) fractionation indices used were those published elsewhere (3); when data were not available, it was assumed that each blood donation was used for a single transfusion to one recipient; 3) The prevalence of HCV for the non-screened population was considered to be equivalent to that reported among the screened donors. We estimated that there were 6,675 tainted units of blood in 1993; 2,231 in 1994; 3,540 in 1995, and 797 in 1997. No country screened 100% of donors, and the percentage of screening varied from 25% to 57% in the 9 countries for which data

were available in 1993. Donors were not screened in Bolivia and Costa Rica in 1993, or in Paraguay in 1994. On the other hand, 4 and 6 countries, respectively, screened 100% of donors in 1995 and 1997. In those that did not, screening coverage varied from 25 to 99%. The number of tainted units per 10,000 blood donors decreased from 59 in 1993, to 23 in 1994, 18 in 1995 and 3 in 1997. Continuous collection of this type of information is essential for obtaining the support needed to expand blood donor screening. References: Schmunis GA, Zicker F, Pinheiro F, Brandling-Bennett D, 1998. Risk of transfusion transmitted infectious diseases in Central and South America. Emerg Infect Dis 4: 5-11. Schmunis G, Zicker F, del Pozo A, Segura E, 2000. Blood transmitted infectious diseases: Argentina 1995 through 1997. Transfusion 40: 1048-1053. 3. Pan American Health Organization. Third Meeting of the Task Force on Surveillance for Emerging and Re-Emerging Infectious Diseases, 1998. November 16-17. Mexico City, Mexico, PAHO/HCP/HCT/141/99.

Board 33. Detection of Viable *Chlamydia pneumoniae* in Peripheral Blood Mononuclear Cells Obtained from Healthy Blood Donors

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C. pneumoniae (Cpn) is an obligate intracellular bacterium associated with respiratory tract infections. Current studies suggest a possible involvement of Cpn in some chronic diseases, such as asthma, arthritis, and atherosclerosis. In particular, atherosclerosis is recognized as a chronic inflammatory disease and the involvement of Cpn in this disease has been strongly indicated. In this regard, current studies showed that Cpn antigens can be detected by PCR not only in atherosclerotic plaques but also in peripheral blood mononuclear cells (PBMCs) obtained from patients with coronary artery disease. However, the viability of these bacteria in the specimens is not known due to the difficulty of Cpn culture. Therefore, it is not clear whether the bacteria detected in specimens, particularly in PBMCs, can be a potential risk factor for the diseases associated with Cpn infection. In the present study, we examined the prevalence of Cpn in PBMCs from healthy blood donors by PCR assay specific for Cpn as well as by Cpn antigen detection with FITC-conjugated anti-Cpn antibody. Furthermore, the cultivation of PBMCs for detection of viable bacteria using RT-PCR and determining increased numbers of Cpn was also performed. The PBMCs of healthy blood donors were found positive for Cpn in a significant number (8.9 %; 21 positive/237 tested) as determined by both PCR and staining for Cpn. When a highly sensitive PCR protocol, established in our laboratory, was utilized for detection of Cpn in blood specimens, the prevalence of Cpn in the blood obtained from healthy donors increased significantly. Culture *in vitro* of PBMCs obtained from health donors resulted in an increase of Cpn numbers as well as message levels of Cpn genes determined by staining with specific antibody and RT-PCR, respectively. These results clearly indicate that Cpn detected in the PBMCs are viable and can proliferate. The demonstration of the presence of viable Cpn with growth potential in blood of healthy donors reveals a potential risk factor carried by a significant number of healthy people, as well as the possibility of transmission of this pathogen through blood transfusions.

Board 34. Comparaison by PFGE of *S. marcescens* Strains Isolated from Post Transfusional Infections

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We are reporting the analysis by PFGE of 32 strains of *S.marcescens* isolated to investigate of nosocomial infections (gynecology and surgery wards) . The strains prove from blood culture of patients have presented a post transfusion hypothermia, from surface groups and pockets of blood, some of which were administered to some of these patients. All these cases happened in the same period (on one month). A study of antibiotic sensitivity shows a same profile of all, and identical at there of the wild strain (cephalosporinase low level). The pulsed field gel electrophoresis, after restriction with XbaI, reveal 3 different groups according (A, B and C) to migration profil. Nevertheless the pulsotype A represent the majority (30/32=93.73%). For one patient we had: the same strains isolated from blood culture and pocket blood that was transfused for this patient. This presume that this patient was contaminated by the transfusion, and for all specimens the same source of contamination was determined. If infection is a rare complication of blood transfusion, this is often fatal. Bacterial control at different steps of blood construction would have to be made.

54 Detection of Novel Agents

Tuesday, March 26, 8:30 a.m.
Grand Hall East

Board 35. Group I Intron as Therapeutic Target : Screening of Chemotherapeutic Agents Lodging Amino Groups Against *Candida albicans*

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Earlier *in vitro* studies have shown that certain antimicrobial antibiotics act as potential inhibitors of group I intron self splicing mechanism. Some of these agents act as competitive inhibitors, while some lodging amino groups bind strongly to unique regions of the RNA. Moreover the presence of the catalytic RNA in the essential genes of the pathogens, and their absence in humans suggest that group I introns can be a potential target site for such agents, especially if they are properly oriented and delivered to their target site.

The above reports were an initiative to take up the *in vitro* screening of certain aminoglycoside antibiotics such as streptomycin, amikacin, tobramycin, gentamycin, kanamycin; antimicrobial antibiotic - tetracycline; antitumour agents like mitoxantrone and mitomycin C, against ATCC 10261 and three clinical strains of *Candida albicans*. This pathogenic fungus is a normal commensal organism causing mild, superficial infections in an immuno competent host but capable of causing life threatening systemic, disseminated disease in a compromised patient, for which self splicing group I introns have been identified in the 25S rRNA gene, denoted as Ca.LSU. Disc diffusion, growth curve analysis, broth macro dilution, RNA isolation and fluorescent microscopic studies were carried, and the results indicated that tetracycline, amikacin, streptomycin, mitoxantrone and mitomycin C had inhibited remarkably the multiplication of *Candida albicans*. Mobility shifts were observed in the band corresponding to 25S rRNA isolated from aminoglycosides and tetracycline treated candida and degra-

dation in antitumor agents treated ones, suggesting the interactios of drugs with RNA. Marked changes in the morphology of the ovoid cells and hyphae were observed in the drug treated cells stained with EtBr viewed under Nikon fluorescent microscope at 100X magnification.

These interpretations may suggest that detailed molecular analysis as well as drug delivery system of the above drugs through liposomes/epitopes would further aid in reacting with respective target sites of RNA of *Candida albicans*.

REFERENCE:

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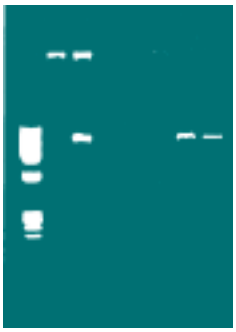
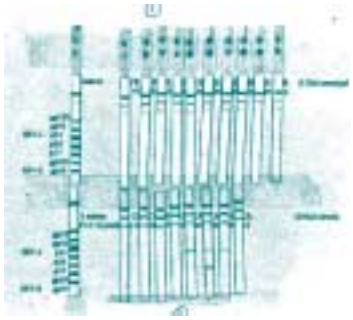
Board 36. Natural Infection by SIV in Indian Primates

J. S. Nandi

National Institute of Virology, Pune, INDIA

It is generally believed that the Asian primates, unlike the African primates are not naturally infected by SIVs. However serological and PCR based experimental evidence suggets that the wild Indian rhesus monkeys (*Macaca mulatta*) are naturally infected by putative SIV. Phylogenetically it is likely to be related to but distinct from the known African SIVs. The relevant data are presented and discussed.





Board 37. Stealth-Adapted Viruses and Viteria: Insights into Virus Construction, Replication and Potential Therapies Based on DNA Sequence Analysis of an African Green Monkey Simian Cytomegalovirus-Derived Stealth Virus

J. Martin

Center for Complex Infectious Diseases, Rosemead, CA

Stealth-adaptation is a mechanism that allows cytopathic viruses to evade immune elimination through the deletion of genes coding the major antigens targeted by the cellular immune system. A prototype stealth-adapted virus, repeatedly cultured from a patient with chronic fatigue syndrome (CFS), was cloned and partially sequenced. The virus has a fragmented, genetically unstable, genome. It has retained numerous viral sequences that can be aligned to various regions of the genome of human cytomegalovirus (HCMV). Where the comparison can be made, the sequences match much more closely to those of African green monkey simian cytomegalovirus (SCMV), indicating an unequivocal origin from SCMV. Kidney cells from cytomegalovirus seropositive African green monkeys were, until recently, routinely used to produce live poliovirus vaccine. The SCMV-derived stealth-adapted virus has five adjacent, but divergent, open reading frames that potentially code for molecules related to the US28 CC chemokine receptor protein of HCMV. In addition, the virus has acquired cellular sequences from infected cells, including a set of three divergent genes that potentially code for proteins related to the putative oncogenic CXC chemokine known as melanoma growth stimulatory activity (MGSA/Gro-alpha). The amplification of chemokine and chemokine receptor related genes in the prototype SCMV-derived stealth-adapted virus, supports current experimental therapeutic approaches based on chemokine suppression. Interestingly, the MGSA-related genes generally lack introns and were, therefore, presumably assimilated into viral DNA from cellular RNA through reverse transcription. The virus has also acquired genetic sequences from various bacteria. This finding has led to the secondary designation of this type of novel microorganism as viteria. Molecularly heterogeneous viruses, inducing similar cytopathic effects in culture (and when examined; non-inflammatory vacuolating cellular damage in brain and tissue biopsies), have been cultured from numerous patients with severe neurological, psychiatric, immunological and neoplastic diseases. In controlled, blinded, studies, cytopathic effects were recorded in 9% of healthy individuals donating blood for transfusion; in contrast to the positive results recorded in virtually all blood samples from patients with various illnesses. The differing clinical manifestations in infected patients may reflect the assimilation of different cellular and other sequences in various stealth-adapted viruses. Stealth-adapted viruses (and viteria) pose a major threat to Public Health. Further information is available on the internet at www.ccid.org

Board 38. New Rickettsiae and Ehrlichiae Detected in Ticks from Thailand and Vietnam

P. Parola[1,2,3], J. P. Cornet[4], J. P. Gonzalez[4], H. V. Thien[5], D. Raoult[3], R. S. Miller[2], **S. R. Telford, III**[1], C. Wongsrichanalai[2]

[1]Harvard School of Public Health, Boston, MA, [2]Armed Forces Institute of Medical Sciences (AFRIMS), Bangkok, THAILAND, [3]Unite des Rickettsies, Marseille, FRANCE, [4]Institut de Recherche pour le Developpement, Mahidol University, Bangkok, THAILAND, [5]Bao Loc General Hospital, Bao Loc, Lam Dong Province, VIETNAM

Background: To date, 2 spotted fever group (SFG) rickettsia have been identified in ticks in Thailand including (i) the Thai tick typhus *Rickettsia* (TT-118, suggested to be a strain of *Rickettsia honei*, which is an emerging pathogen prevalent on Flinders Island, Australia) and (ii) a new rickettsia of unknown pathogenicity (“*R. thailandii* sp. nov.’ Kollars et al. 2001). Their role as agents of human disease is not known. Ehrlichioses of veterinary importance are well-known to occur in Thailand, mainly canine ehrlichiosis due to *E. canis* and transmitted by the brown dog tick *Rhipicephalus sanguineus*. Although human ehrlichioses have been suspected to occur in Thailand based upon on serological data, ehrlichiae that are recognised as human pathogens have not yet been identified from patients or in human-biting ticks. Accordingly, we analysed ticks collected from peridomestic or other common animals for evidence of rickettsial and ehrlichial infection.

Methods: Between September and December 2001, around 500 ticks were collected in the central part of the Thai-Myanmar border (Sangkhlaburi District, Kanchanaburi Province, Thailand) by flagging vegetation, and from animals or people. Ticks included 8 species from 5 different genera. Thirty specimens collected in Vietnam were also included in this study. The DNA of each tick was extracted and rickettsial DNA was detected by PCR using RpCS.877p-RpCS.1273r which amplify an informative fragment of the citrate synthase gene. Ehrlichial DNA was detected with EHR16SR-EHR16SD primers which amplify a fragment of the 16S rRNA gene of ehrlichiae; larger portions of the 16S rRNA gene were subsequently amplified from tick DNA samples that were found to be positive, using the universal primers fD1 and rp2. All amplicons were sequenced and analysed by routine phylogenetic procedures.

Results: Five new ehrlichial genotypes were identified from ticks infesting peridomestic animals, including (i) Bm52 and Bm218 from Boophilus microplus collected on cattle in Thailand, (ii) Hh317 and Hh324 from *Haemaphysalis hystricis* collected on

wild pigs in Vietnam, and (iii) Aj360 from *Amblyomma javanense* collected on pangolins in Thailand. Bm52, Bm218, Hh317 and Hh324 were assigned to the *Ehrlichia canis* genogroup and Aj360 to the *E. phagocytophila* genogroup. Two new SFG rickettsial genotypes were also detected from *A. testudinarium* and from a pool of *Dermacentor* larvae; other genes are now being studied to better characterize these new rickettsiae. We conclude that rickettsiae and ehrlichiae are common infections of peridomestic animals in Thailand and Vietnam; their role as agents of human infection, however, remains to be described.

55 Vaccines

Tuesday, March 26, 8:30 a.m.
Grand Hall East

Board 39. Spectrum of Gut Immunologic Reactions to New *Vibrio cholerae* and its Toxin

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Vibrio cholerae is a normal inhabitant of aquatic environments. However, contaminated supplies in some areas of the world have enabled some clones of the species to become pathogenic for humans. We chose to work on an epidemic isolate of *V.cholerae* WO7 which was devoid of *ctx, zot* and *ace* genes, but elaborated an extracellular factor that evoked fluid accumulation in rabbit ileal loop and elongated Chinese Hamster Ovary cells in culture. The characterization and sequencing of purified toxin revealed that this toxin was distinct from the known cholera toxins. The analysis of the nature of immune responses evoked by this *V.cholerae* WO7 in the gut of mice revealed striking differences as compared to those elicited by V. cholerae569B. Oral infection with both *V.cholerae* WO7 and 569B resulted in an increased number of CD4+ cells in spleen, peyer's patches and mesentric lymphnode compartments. Significant differences were seen in the expression of CD45RO on cells in different compartments with *V.cholerae* WO7 as compared to V cholerae 569B.Infection with *V.cholerae* WO7 resulted in enhanced expression of IL-2R on the peyer's patches and splenic lymphoid cells. Oral infection with V cholerae 569B yielded a Th2type of response at peyer's patch as well as splenic level with traces of Il-12 and IFN-γ. However *V.cholerae* WO7 infection resulted in release of Th1 type of cytokines at gut as well as at systemic level during early stages which subsequently transformed to Th2 type during later stages. Infection with both *V.cholerae* WO7 and 569B induced toxin specific IgA secreting cells at gut as well as splenic level which was potentiated by the release of cytokines like IL6 and IL-10 at the gut as well as splenic level. The abundant IgM responses seen during initial stages decline gradually followed by IgG1 during later stages. Although there was appearance of other IgG isotypes but the net outcome in both the groups aws persisting IgG1 at gut as well as splenic level along with IgA. This understanding of toxin specific T cells and their activation will provide further basis for development of strategies for prevention and control of cholera infections.

Board 40. Haemophilus Influenzae Type B (Hib): Alternative and Fractional-Dose Regimens of Hib Vaccines for the Prevention of Hib Meningitis and Pneumonia in Resource-Poor Countries

D. Seyoum[1], K. W. Johnson[2], N. L. Blum[3]

[1]The United States Pharmacopeial Convention, Inc., Rockville, MD, [2]Management Sciences for Health (MSH) [formerly with the USP], Arlington, VA, [3]The United States Pharmacopeia (USP), Rockville, MD

Background: Invasive disease caused by Haemophilus influenzae type b (Hib), including meningitis, pneumonia, sepsis and epiglottitis, is associated with high mortality and serious neurological sequelae in children under 5 years of age. Hib conjugate vaccines provide substantial protection against nonbacteremic pneumonia, particularly those cases with alveolar consolidation, pleural effusion or other signs of likely bacterial infection. Hib meningitis is near elimination from many developed countries following the introduction of Hib conjugate vaccines into childhood immunization schedules; however, Hib remains a major cause of meningitis and pneumonia in many developing countries. Although Hib conjugate vaccines have been successful, nearly eradicating Hib disease in countries where used routinely, they are relatively expensive, compared with the vaccines routinely used in the Expanded Program for Immunization (EPI).

Methods: Although Hib vaccination would be considered a cost-effective public health intervention, it may be cost-prohibitive to implement in resource-poor countries. Members of the USP Drug Information Expert Committees reviewed the published clinical trials on alternative and fractional-dose regimens for vaccination against Hib presented to them in the form of evidence tables. The evidence tables were based on evidence ratings. The main outcome of the study was safety, effectiveness, and cost of Hib vaccines can be within reach of developing countries that currently cannot afford these vaccines.

Results: Published clinical trials of alternative and fractional-dose regimens of Hib conjugate vaccines were analyzed based on their evidence ratings. The immunogenicity of fractional-dose and two-dose regimens of Hib conjugate vaccines was compared to the standard three-dose series to identify more economical vaccination schedules. This analysis included the following regimens: three full doses, three fractional doses consisting of one half or one third of the full dose, and a regimen of two full doses (at age 4 and 6 months).

Conclusions: Alternative and fractional-dose regimens of Hib vaccines are safe and effective and these alternative and fractional-dose regimens could bring the cost of Hib vaccines within the reach of countries that currently cannot afford them. Therefore, the members of USP Drug Information Expert Committees recommend that fractional doses of Hib conjugate vaccines may be used in countries that currently cannot afford the standard 3 dose-series.

Board 41. Human T Cell Proliferative Responses Induced by ChimeriVaxTM-JE, an Experimental Live-Attenuated Vaccine, and the Licensed Inactivated Japanese Encephalitis Virus Vaccine

S. Green[1], A. L. Rothman[1], J. Cruz[1], F. Guirakhoo[2], T. P. Monath[2], F. A. Ennis[1]

[1]University of Massachusetts Medical School, Worcester, MA, [2]Acambis Inc., Cambridge, MA

Japanese encephalitis (JE) virus is a significant cause of neurologic morbidity and mortality in Asia. Although an effective vaccine is available, it is relatively expensive, requires multiple doses and is reactogenic. ChimeriVaxTM-JE is a candidate second-generation live-attenuated vaccine based on the safe and efficacious Yellow Fever (YF) 17D vaccine in which the prM and E genes have been replaced with those of JE virus. We examined T cell proliferative responses in 36 subjects enrolled in a Phase I clinical trial of ChimeriVaxTM-JE. Subjects were stratified by immune

status to YF and each stratum divided into three groups: ChimeriVaxTM-JE 5 logs, ChimeriVaxTM-JE 4 logs, or YF-Vax® , the currently licensed YF vaccine. Blood specimens were collected pre-vaccination and on day 31 post-vaccination, and peripheral mononuclear cells were separated and cryopreserved. T cell proliferation assays were performed using inactivated antigens prepared as crude lysates of Vero cells infected with YF, JE Nakayama strain, JE SA14-14-2 or the ChimeriVaxTM-JE virus.

Neutralizing antibody responses to JE viruses were detected in all subjects who received either dose of ChimeriVaxTM-JE. Proliferation responses to inactivated JE antigens were detectable in a minority of subjects, all of whom were in the YF-immune group. In addition, less than half of the YF-naïve subjects who received either ChimeriVaxTM-JE or YF-Vax® developed T cell proliferative responses directed against YF or ChimeriVaxTM-JE inactivated antigens by day 31. In contrast, T cell proliferative responses directed against YF or ChimeriVaxTM-JE were detected in the majority of YF-immune subjects on day 0; responses to YF antigen declined in some of these subjects by day 31.

We also studied two subjects who received 3 doses of the licensed inactivated JE vaccine as a control. PBMC from these donors responded to JE antigens 3 and 30 days following the third immunization. Serial samples from one donor demonstrated persistent T cell proliferative responses as long as 235 days following the third immunization.

We conclude that T cell proliferative responses to JE viruses can be induced by immunization with ChimeriVaxTMJE or by the licensed inactivated JE vaccines. Studies of CD4+ and CD8+ T cell responses to JE following ChimeriVaxTM-JE are ongoing.

Board 42. The Use of Surface Antigens from Gram-negative Bacteria for Vaccines

V. N. Parkhomenko[1], E. D. Moroz[1], M. T. Parkhomenko[2]

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The aim of investigations was to develop the vaccines and immune serum that are effective under hospital infections caused by bacteria Escherichia, Proteus, *Salmonella* and Pseudomonas, especially in consequence of immunodeficiency. Antigens were obtained by J.E.Scott, W.Nimmich, investigated biochemical, on cell cultures Vero, HeLa and neurons, on white mousses using probit analysis of lethality curves, in IHA. Samples were grouped in four complex surface antigens (CSA) according to genera. Contents of CSA: polysaccharide from 6-9 kDa to 300 kDa with small impurities of nucleic acid. LD50 of CSA were from 2.21 to 3.26 mg. We tested by factor analysis the method of serum obtaining with titers of antibodies: *Salmonella* 1:2560, Escherichia 1:2560,Pseudomonas 1:1280, Proteus 1:2560. Rise of im-munity were after vaccination of rabbit: increase of IgM, IgG and of bacteri-cidal, opsonic and cytotoxic neutralizing activity of serum, higher phagocytosis of bacteria by polymorphonuclear and macrophage cells, enlargement of T-helper and B lymphocytes. Protective action of serum was investigated on nor-mal and compromised white mice. For reduction of immunity the mice were X-rayed. LD50 for normal and LD*50 for X-rayed animals were determined for all strains. Immune serum (1:960) against Escherichia defended the normal mice from death under injection 4 LD50 and compromised mice under injection of 3 LD*50 *E.coli* K1. Immune serum (1:960) against spp. Proteus defended the normal mice from death under injection of 4 LD50 and X-rayed mice under in-jection 3 LD*50 P.mirabilis. Immune serum (1:1920) against P.aeruginosa de-fended the mice from death under injection 4 LD50 and x-rayed mice under in-jection of 4 LD*50 P.aerugiosa O2. Immune serum (1:1260) against *Salmonella* defended the normal mice from death under injection 5 LD50 and x-rayed mice under injection of 3 LD*50 S.typhimurium. LD50 and LD*50 differed in 3,7 - 5,2 times. Thus antibodies against surface antigens of Escherichia, Proteus, Salmo-nella, Pseudomonas can significantly increase efficiency of macroorganisms re-sistance.

Board 43. Randomized, Placebo-Controlled Field Trial of an Autoclaved Leishmania amazonensis Vaccine Plus BCG Adjuvant Against New World Cutaneous Leishmaniasis

R. X. Armijos[1,2], M. Weigel[3,2], A. Hidalgo[1], W. Cevallos[1], J. Correa[1]

[1]Universidad Central del Ecuador, Quito, ECUADOR, [2]Fundacion Internacional "Biociencias", Quito, ECUADOR, [3]Virginia Tech, Blacksburg, VA

The randomized, placebo-controlled study evaluated the safety, immunogenecity, and efficacy of an autoclaved-killed, whole cell *L. amazonensis* vaccine (Leishvaccin) against cutaneous leishmaniasis (CL) in an endemic tropical Ecuadorian population. Vaccine group subjects (n=1009) received two intradermal doses of vaccine plus a BCG adjuvant administered two months apart. Control group subjects (n=986) received two doses of an inert placebo administered in the identical manner. No serious adverse effects were recorded in either vaccination group. Significantly more vaccine than control group subjects converted to a positive leishmanin skin test (LST) two months after the second vaccination dose (74.4% vs. 14.7%; X^2= 438; P= 0.000001). The incidence of parasitologically confirmed CL at follow-up months 0-26 was not significantly different. Likewise, the cumulative incidence of CL was similar in the vaccine and control groups (2.0% vs. 1.3%; X^2= 1.1; p > 0.05). PCR analysis identified *L. Viannia* as the subgenus responsible for infecting 91% of the vaccine and 100% of control group subjects. It also confirmed the presence of *L. Viannia* and *L. Leishmania* DNA within the same lesion of the remaining vaccine group subject. The lack of vaccine efficacy observed for the vaccine differs from that reported for another candidate based on *L. (V) brazilensis, L. (V) guayanensis*, and *L. (L) amazonensis* and tested in an adjacent population (*J Infect Disease* 177:1352-7). It is possible that a *L. amazonensis*-based vaccine may not adequately protect against infection caused by species belonging to the *L. Vivannia* subgenus. Supported by Special Programme for Research and Training in Tropical Diseases (UNDP/WB/WHO/TDR) #TDR 970191.

Board 44. Field Trial of a Vaccine Against New World Cutaneous Leishmaniasis in an At-

Risk Ecuadorian Child Population: Protection During Months 13-60 of Follow-Up

R. X. Armijos[1,2], M. Weigel[3,2], L. Romero[1], M. de la Cruz[1]

[1]Universidad Central del Ecuador, Quito, ECUADOR, [2]Fundacion Internacional "Biociencias", Quito, ECUADOR, [3]Virginia Tech, Blacksburg, VA

In a previous work (*J Infect* Disease 177:1352-7), we reported on the results of a randomized, double-blinded, controlled Phase III study which evaluated the effectiveness of a phenol-killed whole parasite vaccine based on three *Leishmania* species plus BCG adjuvant in an at-risk child population living in an area of Ecuador endemic for cutaneous leishmaniasis (CL). Briefly, the results of the first study indicated that leishmanin skin test (LST) conversion was greater in vaccine compared to control group subjects (who received BCG only) one month after the second vaccination dose (85.8% vs.19.9 %; X^2= 282; p= 0.000001). CL incidence was significantly reduced in the vaccine compared to control group during the first 12-months of follow-up (2.1% vs. 7.6%; X^2= 8.95, P=0.0028). At the end of 12 months, the study was re-blinded to permit the additional 48-months of follow-up. The results revealed that CL incidence was significantly reduced in the vaccine compared to control group between months 13-18 (5.9% vs. 13.8%; X^2=8.8, p=0.003). In addition, at follow-up month 18, 67% of vaccine group subjects had a positive LST compared to only 36% in the control group (X^2=34.8, P= 0.001). However, by follow-up months 24, 30, 36, 42, 48, 54 and 60, the incidence of CL in the two vaccination groups was not significantly different (P > 0.05)

Likewise, at month 60 of the follow-up, the proportion of subjects in the vaccine versus control groups with a positive LST was not significantly different (40.8% vs. 32.5%, X^2=1.9, P > 0.05). The results suggest that the periodic administration of boosters may be necessary to maintain protection against New World CL in killed, whole-parasite vaccines. Supported by USAID-Ecuador #518-0058EXT.

Board 45. Adverse Event Reports Associated with a Mass Meningococcal Vaccine Campaign

A. Huang, **J. Iskander**, R. K. Pless

CDC, Atlanta, GA

Background: Mass vaccination campaigns are one strategy to control invasive meningococcal disease. Decisions to conduct a campaign are taken by public health authorities based on the epidemiology of disease. During early 1998 approximately 152,000 residents of Rhode Island were immunized with quadravalent meningococcal polysaccharide vaccine. Published reviews of the safety of this vaccine have found that serious adverse events were rare.

Methods: Reports to the Vaccine Adverse Event Reporting System (VAERS) temporally and geographically associated with the campaign were identified and analyzed in comparison to meningococcal vaccine associated VAERS reports overall. Biologic Surveillance data was used to calculate event reporting rates.

Results: A total of 47 reports were received. Only 5 (10.6%) were considered serious and there were no deaths. The reporting rate of 30.9/100,000 (3.3/100,000 serious reports) contrasts with the 7.0/100,000 overall reporting rate for meningococcal vaccine (rate ratio 4.4) in the VAERS database. Further, it was similar to the reporting rate seen in other mass campaigns with meningococcal vaccines.

Conclusions: Meningococcal and other mass vaccine campaigns may stimulate adverse event reporting above baseline levels. Planning for expected increases in adverse event reports during mass campaigns conducted over short periods of time will help alleviate undue concerns for the vaccine while highlighting the need for swift investigation.

Board 46. Implementation of a Large, Double-Blind, Placebo-Controlled Trial of the 23-Valent Pneumococcal Vaccine in Healthy Young Adults

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Naval Health Research Center, San Diego, CA

Background: *Streptococcus pneumoniae* infections are a significant cause of morbidity among U.S. military populations, especially trainees. With increasing antibiotic resistance, efforts to prevent pneumococcal infection must be pursued. A 23-valent pneumococcal vaccine has been available for nearly 20 years, but its value has not been well studied in healthy young adults. The US military was charged with performing a rigorous vaccine trial, although implementation of such a study was anticipated to be complex.

Methods: A sample size of 191,808 subjects was calculated using estimates of vaccine efficacy, percent coverage, and attrition. Collaboration with public health, academic, and other military institutions, as well as a vaccine manufacturer, Wyeth-Ayerst Pharmaceuticals, was essential for the design and initiation of the study.

Military site investigators were identified to help secure support from four U.S. Army, Navy, and Marine basic training sites. Research assistants (RAs) dedicated to the study were hired for daily maintenance; local investigators provide direct supervision. Trainees are enrolled during medical in-processing in basic training. The RAs brief the trainees as a group. Those choosing to participate complete consent forms and a brief information card. Vaccine or placebo injections are then administered.

RAs identify participants with radiographically confirmed pneumonia during basic training and collect laboratory specimens. Diagnostic tests include evaluation for *S. pneumoniae*, *M. pneumoniae*, *C. pneumoniae* and viral studies. All participants also provide survey information of respiratory symptoms at the completion of basic training. Cases of pneumonia and respiratory illness after basic training are captured with comprehensive medical information systems in the military.

Advanced software is used to design, scan, store, and interpret all written data.

Results: As of December 2001, the study is in its 14th month of enrollment and over 70,000 subjects have enrolled. Average participation rate is 70%. Radiographically confirmed pneumonia has been identified in 391 participants to date. Laboratory testing is ongoing.

The study has been well-received at all participating sites, and no adverse events related to study participation have been reported.

Conclusion: The US military provides a unique setting for the successful completion of a study of this magnitude. The large number of healthy young adults living and working in controlled environments, and the comprehensive medical databases available to the military, are attributes unique to the Department of Defense. Careful planning and coordination have resulted in successful implementation of this complex study. As one of the largest vaccine trials ever undertaken in military history, this work will better define the value of vaccinating healthy young adults against pneumococcal disease.

Board 47. Long Lasting Protection Against Canine Kala-azar Using The Fml-quila Saponin Vaccine In An Endemic Area Of Brazil(são Gonçalo Do Amarante, Rn)

C. B. Palatnik de Sousa, Sr., **G. P. Borja Cabrera**, N. N. Correia Pontes, V. O. da Silva, E. Palatnik de Sousa, W. R. Santos, E. M. Gomes, K. G. Luz, M. Palatnik, C. P. Palatnik de Sousa

Federal Univ. Rio de Janeiro, Rio de Janeiro, RJ, CA

Human kala-azar is an emergent zoonotic canid disease. The development of vaccines that could protect dogs form infection would reflect in the reduction of both canine and human cases of the disease. Naturally exposed dogs of an endemic area were vaccinated with the fucose mannose ligand (FML) antigen of Leishmania donovani in formulation with QuilA saponin. 100% of vaccinees were seropositive to FML and showed intradermal reaction to L. donovani lysate, 2 months after vaccination. The absorbency values and size of intradermal reaction were both significantly higher in vaccinees than in controls during a 3.5-year period (ANOVA, $p<0.0001$). Twenty five percent of the control animals (2 dogs on the first year and 6 dogs on the fourth year, respectively) and 5% of the vaccinees (1 dog during the fourth year) developed clinical and fatal disease by the end of experiment. This difference was significant ($c2= 3.93$, $p<0.05$). This means that 95% protection against kala-azar was achieved in vaccinees, after FML-QuilA vaccination (vaccine efficacy 80%). Leishmania infection was also confirmed, 3.5 years after vaccination, in saline controls that showed positive PCR for Leishmania DNA and FML-serology with no intradermal reaction. Higher seropositivities and intradermal reactions with no Leishmanial DNA were detected in vaccinees. The FML-QuilA vaccine induced a significant, long-lasting and strong protective effect against canine kala-azar in the field.

56 Vectorborne Diseases II

Tuesday, March 26, 8:30 a.m.
Grand Hall East

Board 48. Severe, Concurrent Lyme Disease, Babesiosis and Ehrlichiosis in a Healthy 23 Year-Old Connecticut Resident.

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[1]Waterbury Hospital, Waterbury, CT, [2]Connecticut Emerging Infections Program, New Haven, CT

Background: Lyme disease (LD), babesiosis, and human granulocytic ehrlichiosis (HGE) are emergent zoonotic diseases affecting residents in the Northeastern and Midwestern United States. The etiologic agents of each disease are perpetuated in a natural cycle between vertebrate reservoir hosts and the tick vector, Ixodes scapularis. The geographical and ecological overlap between HGE, LD and babesiosis suggests the potential for co-transmission, co-infection and co-morbidity. We describe the case of a Connecticut resident simultaneously infected with all three agents.

Case Report: A previously healthy, 23 year-old male presented to an emergency department (ED) after five days of headache, fever, sweats, myalgia, and fatigue. He recalled a tick bite about one week earlier. He was given the diagnosis of LD and treated with clarithromycin. Approximately two weeks later, the symptoms returned and he presented to our ED. Laboratory evaluation revealed leukopenia, thrombocytopenia, and a hematocrit of 41%. Liver function tests, and erythrocyte sedimentation rate were normal. LD serologies were sent. On evaluation, he was found to have tonsillar, cervical, and inguinal lymphadenopathy and splenomegaly that was confirmed by abdominal CT scan.

Five days later, the patient returned to the ED with acute left upper quadrant pain, and persistent fevers. Hematocrit was 29%. Repeat abdominal CT scan demonstrated increased splenomegaly and new left flank and pelvic fluid. The patient was admitted to the surgical intensive care unit with the presumed diagnosis of splenic rupture. Laboratory data were significant for leukopenia, thrombocytopenia, elevated LDH and AST, and decreased haptoglobin. The hospital course was remarkable for persistent high-grade fevers to 104.6° F. Lymph node biopsy showed follicular lymphoid hyperplasia and no evidence for malignancy. A peripheral smear showed intraerythrocytic ring forms consistent with Babesia. The patient was treated with clindamycin and quinine with rapid defervescence.

LD serologies from the previous ED visit were positive on both ELISA and Western Blot. After completing a course of clindamycin and quinine, the patient was started on a course of doxycycline. Serum samples were sent for HGE and Babesia microti serology. Indirect fluorescent antibody staining methods revealed an HGE titer of 1:4096 and a B. microti titer of 1:640. HGE-specific ELISA was confirmatory. Nine months later, repeat testing demonstrated a ≥ 4-fold decrease in antibody titer to both HGE and B. microti.

Conclusion: This patient had concurrent infection with three I. scapularis-borne diseases. The unexpected severity of illness in this otherwise healthy host can in part be attributed to the delay in diagnosis resulting from an atypical presentation and the possible immunosuppressive effects resulting from the interplay of the three diseases.

Board 49. Assessment of the Competence Of Field-Collected *Culex tarsalis* Mosquitoes to Transmit West Nile Virus Under Laboratory Conditions

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Based on testing of field-collected mosquitoes in the United States, ornithophilic mosquito species such as *Culex pipiens* are the primary enzootic vectors of West Nile virus (WNV). In Canada, *Cx. pipiens* has a discontinuous distribution. It is abundant in parts of British Columbia and from Ontario eastward but is absent from the prairie provinces (i.e., Manitoba, Saskatchewan and Alberta). The niche typically occupied by *Cx. pipiens* is filled on the prairies by the closely related species, *Cx. tarsalis*. Currently in Canada, the ranges of WNV and *Cx. tarsalis* do not overlap. However, since 1999 the range of WNV in North America has expanded dramatically. If WNV is introduced into the prairie provinces or western states it is anticipated that *Cx. tarsalis*, a proven vector of other related arboviruses (e.g., St. Louis encephalitis virus), might be an important vector. To assess the vector competence of *Cx. tarsalis*, females were collected at a site near Winnipeg, Manitoba, using CDC light traps, and allowed to feed upon groups of 3 or 4 white leghorn chicks (4-8 day old) that were syringe-inoculated subcutaneously 2, 4 and 6 days earlier with 0.1 ml of NY99 strain of WNV (titre-105 PFU/ml). To confirm chicks were infected, blood samples were collected immediately after mosquito feeding and tested for viral genome using standard RT-PCR. Female mosquitoes that fed on syringe-infected chickens were held for up to 22 days at 23.5 C (16 h Light: 8 h Dark), then re-fed on uninfected chicks. Sera were collected from mosquito-infected chickens 3 weeks post-feeding and tested for IgG and IgM antibodies against WNV using an in-house ELISA. Viral RNA was extracted from the bodies (non-disseminated infection) and legs (disseminated infection) of selected females that fed on syringe- or mosquito-infected chickens. WNV genome was then amplified using a real time RT-PCR assay. WNV RNA was detected in all but one syringe-inoculated chick and the amount of viral genome detected decreased with days p.i. In total, 38.9% (28 of 72) of *Cx. tarsalis* that fed showed evidence of infection (non- or disseminated infection) and WNV RNA was detected only in mosquitoes fed on the 2 day p.i. group of birds. In these mosquitoes, the infection (bodies only) and dissemination rates (bodies and legs) were 90.3 (range, 81.2-100%) and 77.4% (range, 68.8-87.5%), respectively. However, only 1 of 3 uninfected birds exposed to these mosquitoes developed WNV antibodies (titre, 1:32,000). The failure of all birds in this group to acquire WNV may be due to differences in virus titre in feeding *Cx. tarsalis* or because most mosquitoes did not feed to repletion when exposed to the uninfected chicks. Overall these results provide evidence that *Cx. tarsalis* is a competent laboratory vector of WNV and it may be capable of contributing to the enzootic amplification of virus should WNV be introduced into areas where this mosquito species is abundant.

Board 50. Comparison of the Effectiveness of Two Topical Paromomycin Treatments with Meglumine Antimoniate for New World Cutaneous Leishmaniasis

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The randomized, controlled study compared the therapeutic efficacy and safety of two topical paromomycin preparations with Glucantime (meglumine antimoniate) and with each other in 120 Ecuadorian patients. The two paromomycin treatment comparisons were double-blinded. Group 1 (n=40) received 15% paromomycin

plus 12% methylbenzonium chloride (PMBC) dissolved in a soft white paraffin base, applied twice daily for 30 days. Group 2 (n=40) was also treated for 30 days with 15% paromomycin plus 10% urea (PRU) dissolved in the same paraffin base. Group 3 (n=40) received 20mg/kg/day of IM Glucantime (GLU) for 10 days as per MPH convention. Post-treatment lesion redness, inflammation, and soreness were significantly more frequent in the two paromomycin groups compared to GLU group ($P < 0.05$); lesion burning was more frequent in the PRU than GLU group ($P < 0.05$). However, the frequency of treatment-associated side effects was not significantly different between the paromomycin groups. The 10-day treatment was completed by 90% of the GLU group while 72.5% and 75% of the PMBC and PRU groups completed their 20-day treatment regimes ($P > 0.05$). Six weeks after beginning treatment, 80.6% of the GLU (80.6%) were clinically cured compared to 48.3% and 40% of the PMBC and PRU groups ($X^2=12.6$, $P=0.002$). At 12 weeks, the proportion of clinically cured subjects in the GLU (91.7%), PMBC (79.3%) and PRU (70%) groups was similar ($X^2=5.1$, $P >0.05$). GLU-treated subjects clinically cured by 12 weeks had a faster mean healing time than the PMBC- and PRU-treated groups (29.5 ± 12.2 days vs. 43.1 ± 14.4 days vs. 43.5 ± 17 days; $F=8.9$; $P= 0.0001$). During the 12-month post-treatment follow-up period, infection reactivation was observed in 15.2% (GLU), 17.4% (PMBC), and 10.5% (PRU) of those subjects diagnosed as clinically cured by 12 weeks ($X^2= 0.6$, $P >0.05$). The results suggest that although healing time is longer, topical paromomycin may be an acceptable therapeutic alternative in cases where Glucantime is not available or is medically contraindicated. Supported by: Pan American Health Organization-Washington (#HDP/HDR/RG/ECU/1218).

Board 51. RNA isolated from Mosquito Pools Inhibits West Nile Virus Real Time RT-PCR: A Case Study Using the Smart Cycler

S. Sakallah, D. Bolton, S. MacRae

NH Department of Health & Human Services, Concord, NH

In the period between August and November 2000, we tested 440 birds and 200 mosquito pools for West Nile Virus. The virus was detected in 7 birds, but none of the mosquito pools tested positive for the virus. Since these pools were collected in the areas where positive birds were identified, the possibility exists that some positive mosquito pools may have been missed due to inhibition of the RT-PCR reaction. Preliminary experiments were launched in the spring of 2001 to answer this question. Mosquito pools were spiked with a known amount of RNA that tested positive for WNV. The Ct values reported for these reactions were compared with that from the positive RNA. Real Time RT-PCR reactions (25 ul) were carried out using the TaqMan One Step RT-PCR kit (Roche) and a FAM-tagged probe. Thermal cycling was performed in the Smart Cycler (Cepheid) starting with 30 minutes at 50°C followed by 45 cycles of 15 seconds at 95°C and 1 minute at 60°C with fluorescence detection.

Our preliminary data show that the majority of mosquito pools tested (57 out of 66) exhibited some level of inhibition. Inhibition patterns could be grouped into 3 categories: minor (where Ct values increased by up to 3 cycles), significant (Ct increased by 3-5 cycles), and total (Ct = 0, i.e. signal disappeared completely). Thirty-seven pools exhibited minor inhibition, 18 showed significant inhibition and 2 pools were totally inhibited. The majority of these pools (42 out of 57) contained 1-4 mosquitoes each, 12 pools had 6-25 mosquitoes each, while 3 pools had 26-50 mosquitoes each. There was no apparent correlation between the number of mosquitoes in the pools tested and the level of inhibition observed. Furthermore, we found no clear link between mosquito genus or species and inhibition.

The cause of RT-PCR inhibition was not the focus of this study. One possible explanation however could be the presence of inhibitors in the blood mosquitoes feed on. Our results demonstrate the importance of internal controls in these tests to ensure the validity of the negative results. We are currently in the process of developing controls for WNV and related viruses.

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The cause of RT-PCR inhibition was not the focus of this study. One possible explanation however could be the presence of inhibitors in the blood mosquitoes feed on. Our results demonstrate the importance of internal controls in these tests to ensure the validity of the negative results. We are currently in the process of developing controls for WNV and related viruses.

Board 53. Selection and Characterization of Antigenic Variants of West Nile Virus Using Monoclonal Antibodies and Membrane Receptor Preparations Which Recognize the Putative Envelope Protein Receptor-Binding Domain III

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The flavivirus envelope (E) protein is the major outer membrane protein and plays important roles in attachment to and fusion with target cell membranes. In particular, domain III of this protein has been proposed to function as the likely receptor-binding domain and is an important target for virus neutralizing antibodies. Five monoclonal antibodies were prepared against a North American isolate of West Nile (WN) virus. Four of these antibodies were found to specifically bind to purified recombinant WN virus E protein domain III (derived from strain 385-99, an isolate from the 1999 outbreak in New York) in ELISA and Western Blot assays. The same four antibodies were also able to neutralize WN viruses representing both genetic lineages I (which includes the virus currently circulating in North America) and II, confirming the importance of E domain III in WN virus infectivity. However, neutralization of lineage II WN strains was significantly less effective than for lineage I viruses, suggesting differences in the pres-

entation of domain III epitopes between WN lineages. The fifth antibody did not neutralize any WN virus tested. In addition, a polyclonal rabbit serum prepared against the purified recombinant domain III was also able to neutralize WN strains of both lineages, albeit with better efficiency against lineage I strains. We are currently evaluating potential neutralization escape variants that were plaque purified in the presence of neutralizing antibodies to identify residues in domain III critical to neutralization of WN virus. We have also investigated binding of WN virus strains to mouse brain tissue membrane receptor preparations (MRPs). Several strains in both lineage I and II were identified that bound strongly to mouse brain MRPs and binding escape variants have been selected. One variant, derived from lineage II strain H-442, contained a single nucleotide substitution in the E gene encoding a Lys-Thr mutation at E332, a residue which lies on the upper, outside face of domain III in structural models of the WN virus E protein. Additional MRP binding variants are being characterized. The virulence of these antigenic variants for mice is being studied to assess the role of E protein domain III in the virulence phenotype of WN virus.

Board 54. Epidemic Chikungunya Virus Transmission in Western Indonesia Occurs Over a Foci of Endemic Transmission

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We present data confirming six recent episodes of epidemic Chikungunya virus (CHIK) transmission in Indonesia and suggesting one foci of endemic CHIK transmission. In April 2000, a countrywide CHIK surveillance program was initiated with the assistance of the Indonesian Ministry of Health to investigate anecdotal reports of CHIK transmission in Java and Sumatra. Forty-eight representative acute samples from five geographic regions were analyzed, 61% were CHIK IgM positive (+) and 42% were CHIK RT-PCR (+). Two isolates were recovered and a portion of the E2 gene was sequenced to confirm CHIK etiology. Ten percent of the samples were dengue IgM (+) and 14% were dengue RT-PCR (+). CHIK transmission has been confirmed by PCR and serology in a 6th region of Indonesia in December 2001, suggesting that CHIK transmission is far more widespread across Indonesia than previously thought. Evidence also suggests that Yogyakarta represents the first recognized foci of endemic CHIK transmission. CHIK transmission was documented in Yogyakarta during 1983, and again during 1998/1999. However, physicians there report that they regularly treat patients with CHIK-like illness. A case-control study was initiated in Yogyakarta in December 2000, to verify ongoing CHIK transmission. Of cases examined, 34% (85/248) were CHIK RT-PCR (+) and 30% were CHIK IgM (+). Three percent were RT-PCR (+) for dengue. Three cases were dually infected with CHIK and dengue viruses (two with dengue 2 and one with dengue 4). Of controls, 7% (5/75) were CHIK IgM (+). Dengue serology is pending. A longitudinal study was then initiated in Yogyakarta in June 2001 to estimate yearly CHIK attack rates. Preliminary serological testing established that 19% (156/800) of the volunteers were IgG seropositive for CHIK at enrollment. Fifty-two of the 156 seropositive volunteers were born after the 1983 CHIK outbreak. These 52 individuals did not report CHIK-like illness in the past five years and were not living in the area where CHIK transmission occurred in 1998/1999. For the population born after 1983, (age 17 and under) this equates to 0.8% of the cohort seroconverting on average per year. Based on these data, we hypothesize that endemic CHIK transmission occurs in Yogyakarta and elsewhere in Indonesia.

Board 55. Sentinel Chickens Appear to be Useful Monitors of West Nile Virus in Florida

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Flocks of sentinel chickens have been used in Florida since 1978 for monitoring activity of St. Louis Encephalitis (SLE) virus and Eastern Equine Encephalomyelitis (EEE) virus. Historically, seroconversions to SLE virus in sentinel chickens predates human cases in Florida. During 2001, flocks of 6 chickens each were placed in 31 counties; the number of flocks per county varied from 2 to 21.

Blood was collected weekly or biweekly from the chickens and sent to the Department of Health Laboratory in Tampa where sera were assayed by the Hemagglutination Inhibition test for total antibody to flavivirus and to alphavirus. SLE virus strain TBH-28 sucrose acetone processed suckling mouse brain was used for flavivirus antigen. We have previously determined this antigen cross-reacts with antibody to other flaviviruses (Dengue 1-4) in the HAI test. Sera positive for flavivirus antibody in the HAI assay were assayed for IgM antibody to West Nile (WN) virus. Sera with low P/N ratios in the Elisa and a sample of HAI negative sera were assayed by serum neutralization plaque reduction assay (SNPR) against WN and SLE viruses to confirm the etiology of infection.

Mosquitoes are active throughout the year in Florida, and transmission of SLE and EEE viruses has been detected during winter months. Testing is performed every week of the year, although many counties only maintain their flocks from May through December. This year approximately 23,000 sentinel sera were submitted for testing. The first detections of WN virus in birds, horses and chickens occurred within 2 weeks of one another, in late June early July, 2001. Over the following 5 months, 177 sentinels from 20 counties demonstrated antibody development to WN virus. Seroconversions to SLE virus were minimal. Sentinel seroconversions predated detection of virus in dead birds and/ or horses in 7 counties. In counties where chickens were not the first indicator of WN virus activity, seroconversions started on average 7.1 weeks after the first WN positive bird or horse was detected. Human cases were reported from 2 counties with sentinel chicken surveillance programs. In both counties, chicken seroconversions to WN virus predated the human cases.

Board 56. Northern Expansion of Human Babesiosis Infection in New York State

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[1]New York State Department of Health, Albany, NY, [2]Westchester County Department of Health, New Rochelle, NY, [3]Dutchess County Health Department, Poughkeepsie, NY, [4]Columbia County Health Department, Hudson, NY

Babesiosis is a protozoan tick-borne infection endemic in focal geographic locations throughout the United States. It is primarily transmitted by *Ixodes scapularis*, but occasional infections occur through blood transfusion or organ transplantation. In northeastern United States, human *Babesia microti* infections are endemic in areas of Massachusetts, Connecticut, Rhode Island and New York State (NYS). In NYS, locally acquired infections have been limited to Long Island, primarily the eastern portion. In 2001, four cases of babesiosis were reported in NYS residents who had not lived in, nor traveled to previously recognized babesia-endemic areas. None had a history of blood transfusion or organ transplantation. One patient resided in Westchester County, two resided in Dutchess County, and one in Columbia County. Three (75%) patients had significant exposure to tick habitat in their county of residence and had evidence of previous or concurrent Lyme dis-

ease. The fourth patient had a travel history outside of NYS, but it was to an area where locally acquired babesiosis has never been documented and she had reported a recent tick bite acquired in her county of residence. The mean age of the cases was 52 years with a range of 42-77. Three (75%) patients reported an acute febrile illness with onset during the summer months. One (25%) patient, an afebrile 77 year-old female presenting with increasing dyspnea, was hospitalized. Based upon the laboratory finding of hemolytic anemia in this patient, peripheral blood smears were reviewed and intraerythrocytic ring-forms/parasites were noted. Three weeks prior to her admission, the patient had been placed on a tapering dose of steroids, an antihistamine and asthma inhaler for coughing, wheezing and shortness of breath. In addition, severe aortic stenosis was identified. No other immunosuppressive conditions were noted. None of the other patients had any history of immunosuppressive conditions. All patients had intact spleens. Each patient had at least one laboratory specimen confirmed by NYS Department of Health Wadsworth Center. Peripheral blood smears were available on 3 patients; *B. microti* was identified on all smears. Indirect fluorescent assay (IFA) was conducted on specimens from 3 patients; all had titers ≥ 128. Two patient specimens were tested by PCR; one was positive. This is the first documentation of human babesiosis acquired in NYS outside of Long Island. However, all 3 counties where the patients reside have high incidence rates for Lyme disease and human granulocytic ehrlichiosis, both of which are also transmitted by *Ixodes scapularis*. The presence of *I. scapularis* and the occurrence of non-travel associated babesiosis in 3 counties north of New York City and east of the Hudson River suggests a northern expansion of *B. microti* and a corresponding risk of human babesiosis infection.

Board 57. Chagas Disease in a Domestic Transmission Cycle in Southern Texas, USA

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Chagas disease is caused by the protozoan *Trypanosoma cruzi* and is transmitted by insects in the Reduviidae subfamily Triatominae. In the United States, the disease exists almost exclusively as a zoonosis, with only five cases reported in humans. On January 6, 1998, the Texas Department of Health Zoonosis Control Division office in Harlingen, TX was contacted following the diagnosis of Chagas disease in a canine pet that died of acute cardiomyopathy, following the death of a previous pet canine, in September of 1997, with a similar diagnosis. Both animals were purchased as puppies and owned for four or five months before becoming ill. On April 8, 1999, following the death of a third dog at the same location, personnel from CDC, TDH and the Cameron County Health Department conducted an investigation of the premises that included inspection of the home, garage, and grounds. Blood was drawn from three additional canine pets and tested for antibodies to *T. cruzi*. Because the homeowner recalled finding bugs inside the house on at least one occasion, two adults living in the home were also tested. The same veterinarian who diagnosed the initial cases reported an additional dog, from a kennel approximately two miles from the first site, to have Chagas disease-like symptoms. This second site was also inspected and blood drawn from the symptomatic dog and three additional dogs from the same kennel. A total of three dogs from the first site and one dog from the second site tested positive. No humans tested positive. A follow-up serological study was completed through the Cameron County Animal Control. A total of 28 of 347 stray dogs (7.5%) tested positive for antibodies against *T. cruzi*, with titers ranging from 1:32 to 1:512. During inspection of the first site, a total of 31 adult and immature *Triatoma gerstaeckeri* were collected underneath concrete slabs of a patio and inside an adjacent garage. Upon dissection, 24 or 31 were positive for hindgut trypanosomes. Cultures were established and confirmed as *T. cruzi*. No bugs could be found at the second site. Triatoma gerstaeckeri is considered a sylvatic species, most frequently associated with pack rat burrows. While it occasionally invades domestic dwellings, it is not known to colonize these habitats. In this instance, colonization appears to have occurred, the evidence being the observation of large numbers of bugs, including immature stages. At the first site, six dogs either died or tested positive for *T. cruzi*, and 24 of 31 bugs contained hindgut trypanosomes. These observations demonstrate the existence of a domestic transmission cycle. To evaluate the potential for the occurrence of this problem in other locations besides Cameron County, we used a niche analysis model to predict the areas where *T. gerstaeckeri* is likely to be found. A broad distribution was predicted, extending from central Mexico north along the Texas-Mexico border, into the Texas panhandle and New Mexico.

Board 58. Diagnosis and Treatment of Southern Tick Associated Rash Illness: An Emerging Infections Network Survey

A. V. Bode, E. B. Hayes

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Lyme Disease (Ld) is endemic in areas of the Northeast and upper Midwest. For more than a decade, the Centers for Disease Control and Prevention (CDC) has received reports of patients with an erythema migrans (EM)-like rash, often following tick bites, from non-Lyme disease endemic areas in the South and southern Midwest. Studies in these areas have found no evidence ofBorrelia burgdorferi in the majority of these patients; rather, there is evidence that a newly described Borrelia species might be associated with this condition . The Emerging Infections Network (EIN) recently surveyed their members about the diagnosis and treatment of this "Southern Tick-Associated Rash Illness (STARI)." Of the 278 physicians queried in the South and Missouri, 188 responded. Of these physicians, thirty nine (21%) had seen 96 patients for an EM-like rash during the summer of 2000. Thirty two (82%) of these 39 physicians said they usually ordered Ld serology on such patients, and 12 (31%) said they always (1) or sometimes (11) obtained skin biopsies from these patients. Twenty-seven (69%) of the 39 said they always treated the patients with antibiotics; ten (26%) of the 39 said they sometimes treated with antibiotics. Several antibiotics were used to treat these patients. Doxycycline was prescribed by 33 physicians, amoxicillin by 15 physicians, ceftriaxone by 3 physicians and cefuroxime by 2 physicians. Optimal management of STARI will depend on further definition of its etiology and natural history.

Board 59. The Relevance of Geometric Morphometry in Distinguishing Cryptic Species of the "Prolixus Complex"

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Rhodnius prolixus is a vector of Chagas disease to humans, *R. robustus* is not, however they have long been two problematic taxa as to their species identities and distribution. Using both traditional and geometric morphometrics, we compared wing size and shape in both sexes of 64 *R. robustus* and 38 *R. prolixus* reared in the same laboratory during one generation. *R. robustus* specimens were collected from palm trees in the state of Mérida (Venezuela), and *R. prolixus* were collected from houses in the state of Cojedes (Venezuela). Even after one generation of living in the same laboratory conditions, the two lines showed distinct sizes, divergent

allometric trends, and significant allometry-free differences in shape. Due to the epidemiological importance of this question, a further comparison was performed using other samples from other geographic areas of Venezuela, on specimens already verified as distinct species after mtDNA sequencing. Thus, 15 wings of *R. robustus* collected in Venezuela were compared to 45 wings of *R. prolixus* also from Venezuela. The wings were described by 9 landmarks: the 6 landmarks already used by us before, and 3 landmarks located at the junction between corium and membrane. The same significant differences were observed, again poorly related to size variation, while other differences were revealed at the corium-membrane limit. Since the species compared were genetically the most related pair within the so-called "prolixus complex", one could expect that morphometrics would be an efficient tool for accurate species diagnostic. As an example, using a discriminant analysis on wing shape variation, we were able to assign to *R. robustus* one single, unknown specimen of Rhodnius which was collected in Bolivia. In that study, 7 landmarks were used for comparing the questioned specimen to 64 confirmed *R. robustus*, 20 *R. prolixus*, 52 *R. stali* and 36 *R. pictipes*. Thus, it appears that geometric morphometry provides a highly discriminating tool for morphological diagnosis of cryptic species in Triatominae.

Board 60. The Genetic Characterization of Snowshoe Hare Virus Strains from Across Canada

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Snowshoe Hare (SSH) virus is a mosquito-transmitted bunyavirus belonging to the California serogroup. SSH virus has been documented across Canada and has been associated with cases of meningitis and encephalitis in Quebec, Ontario, New Brunswick, and Nova Scotia. As part of a study to determine the genetic diversity of SSH virus in Canada, 69 different viral isolates collected from five provinces and two territories during the 1960s, 70s, and 80s were characterized by reverse transcriptase (RT)- PCR amplification and amplicon sequencing. Sequencing of amplified portions of the M and S genomic segments indicated that the isolates could be grouped into six distinct genogroups. G2 glycoprotein encoding regions exhibited nucleotide sequence divergence as high as 23 %; however, all but one isolate displayed 100 % amino acid sequence similarity within the G2 portion analysed. Nucleotide sequencing of amplicons generated from the nucleocapsid encoding region revealed less sequence variation compared to the M segment genomic portions analysed in this study. All isolates from Ontario displayed high RNA sequence homology (> 98 %) despite being collected over a 15 year time period. In contrast, phylogenetic characterization of SSH strains from the Yukon and Quebec revealed the existence of at least two distinct co-circulating genotypes within each province. A SSH "variant" isolated from a larval mosquito in Saskatchewan displayed significant divergence with respect to both nucleotide and amino acid sequence composition when compared to Canadian and American isolates. Despite the M and S segment amino acid sequence changes displayed by this isolate this virus did not appear to display any features consistent with being a serotypic variant. Phenotypic and genetic properties that may distinguish this strain from other SSH isolates will be the subject of future studies. This genetic variant provides further evidence for the extensive evolution that these RNA viruses may undergo during their transmission and amplification cycles and the high degree of genetic diversity that may exist among strains within the same serotype.

Board 61. Mosquito, Rodent and Tick Surveillance and Vector-Borne Disease Threats at Selected US Forces Korea Installations and Training Sites, Republic of Korea, 2000-2001

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Introduction: Vector-borne diseases are potential public health threat to US Forces Korea (USFK). Malaria, transmitted by *Anopheles* mosquitoes, is only one of several diseases that may impact on military readiness and operations. Other vector-borne diseases of primary interest include Japanese encephalitis, hantaviruses, scrub typhus, murine typhus, leptospirosis, ehrlichiosis and other potential tick-borne parasites. Surveillance systems provide USFK the capability to collect and assess data for of potential exposures and to rapidly deploy and implement appropriate countermeasures. While data collection in a combat situation may be difficult and hazardous, during armistice there are many opportunities for data collection analysis and prediction that are required to obtain health threat information critical to the protection of the fighting strength. **Methods:** 1. Mosquito surveillance is currently conducted at selected US military installations. Because the taxonomy of anophelines is not well understood, mosquitoes were reared for morphological and DNA studies for species determination. 2. Rodents were collected at selected installations and training sites and assayed for hantaviruses, scrub typhus, murine typhus and leptospirosis. 3. Ticks were collected by cloth tick drags at selected US installations and training sites and assayed by PCR or *Ehrlichia/Anaplasma, Ehrlichia chaffeensis*, and human granulocytic ehrlichiosis parasites. **Results:** 1. During 1999 and 2000, >26,000 mosquitoes were assayed for malaria sporozoite antigen. Positive mosquitoes were identified from CP Gary Owen and CP Bonifas, near the DMZ. Of ?4,300 *Cx. tritaeniorhynchus*, 12 isolations of Japanese encephalitis were made. Examination of progeny broods of anophelines showed that An. sinensis could not be differentiated from An. lesteri, based on current keys. It is also suspect that there are at least two types of *An. yatsushiroensis*. 2. Rodent surveillance indicated a very high prevalence of hantaviruses at selected training sites near the DMZ (range 0-61% for different trapping periods. Scrub typhus was also prevalent throughout the same area, extending south. Murine typhus was identified from house mice at Yongsan Garrison in Seoul. Leptospirosis was infrequently isolated. 3. More than 95% of all ticks collected were *Haemaphysalis longicornis*, the bush tick. PCR results showed a high incidence of *Ehrlichia/Anaplasma* positive ticks. In addition, tissues from rodents showed that >75% of all rodents examined were positive for Ehrlichia/Anaplasma by PCR. **Conclusion:** Surveillance of arthropods and rodents provides information that can be used for threat analysis and provide data for developing disease reduction strategies.

Board 62. Inferential Modeling of Factors Determining *Anopheles* Distribution and Predictions of Potential Ranges

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The distribution of malaria vectors has been reported based on mosquito collections, and factors influencing their distribution have been identified by various methods. These methods often employ statistical analyses to correlate the collections with a single, or combination of, environmental variable(s) such as temperature and rainfall. We have applied a powerful new technique known as ecosystem niche analysis to model the distribution of the six member species of the *Anopheles gambiae* complex throughout the African continent. In addition, as a species complex for which both

high resolution base data and distribution information is available, we analyzed the North American *A. quadrimaculatus* complex. Niche analysis utilizes a genetic algorithm to produce a set of expert rules describing the entire ecological nice occupied by an organism. Since our maps elucidate the presence of areas where suitable niches for *A. gambiae (s.l.)* exist, we describe regions where collections could be made to validate these predictions. In addition, because our predictions are based on the occurrence of known ecological niches, we have created distribution maps that predict the species' prospective worldwide ranges based on the occurrence of the explicit niches. Using these worldwide maps, we depict the effect of various scenarios of global climate change on the distribution of these human malaria vectors and its implications for broadening of the vector habitat and subsequent control of the disease. Finally, we transform the world distribution maps into world risk-maps, which illustrate the areas of potential vector establishment either through accidental or hostile release of a species. We draw upon past incidents — the establishment of *A. gambiae s.l.* in Brazil and Egypt — to show that establishment of malaria-infected *A. gambiae* (s.l.) among non-immune human populations has dire public health consequences, due to its superiority as a vector of human malaria, and should not be ignored as an emerging threat to global health.

Board 63. Dead Bird Clustering: An Early Warning System for West Nile Virus Activity

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Introduction: Since the 1999 West Nile (WN) virus outbreak in New York City (NYC), health officials have been searching for an early warning system that could signal increased risk of human WN infection, and provide a basis for targeted public education and increased larval and/or adult mosquito control. Birds and mosquitoes with laboratory evidence of WN virus preceded most human infections in 2000, but sample collection and laboratory testing are time-consuming and costly. We describe a methodology for detecting small area clustering of dead bird reports, present the results of its application to data from 2000, and review its utility in providing an early warning of West Nile virus activity in NYC in 2001.

Methods: All unique non-pigeon dead bird reports were geocoded, and categorized as "cases" if occurring in the prior 7 days, "controls" if occurring during a historic baseline, or censored. The most likely cluster area was determined using the spatial scan statistic, and evaluated using Monte Carlo hypothesis testing. Analyses were performed in a prospective simulation for 2000 and in real time during 2001.

Results: For the 2000 data, dead bird clustering was found in Staten Island on June 14, 2000, over 4 weeks prior to laboratory evidence of WN virus in birds and mosquitoes from this area. Clustering also occurred in other areas of the City prior to the detection of bird, mosquito, and human infections. The implementation of this system in 2001 led to intensified larval control on June 27, 2001 in eastern Queens, over three weeks prior to laboratory confirmation of bird, mosquito, and human infections from this cluster area. Dead bird clusters were identified around the residence of five of seven human infections, from 0-40 days (median 12) prior to the onset of illness, and 12-45 days (median 17) prior to human diagnosis.

Conclusions: Prospective geographical cluster analysis of dead bird reports may provide early warning of increasing viral activity among birds and mosquitoes, and of subsequent human infections.

Board 64. Risk Factors for Dengue Infection, East Maui Dengue-1 Outbreak – Hawaii, 2001

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Background: In September 2001, the Hawaii Department of Health reported a dengue outbreak in East Maui, the first recorded transmission of dengue in Hawaii since 1945. Entomologic surveys revealed Aedes albopictus as the only potential vector. A survey was undertaken to identify risk factors for illness at the individual, household, and community level.

Methods: We surveyed communities A and B in the affected area, with high (19.3%) and low (0.4%) incidence respectively, as determined by surveillance. A seroepidemiologic survey was conducted, inquiring about travel history, symptoms, and potential exposures to areas with observed high populations of mosquitoes. Recent infection was defined as the detection of anti-dengue IgM antibodies in persons without recent foreign travel, or IgG antibodies in persons under age 56 without history of foreign travel or immunization against Japanese encephalitis or yellow fever.

Results: Community A had 60 households and 135 residents, of which 39 (65%) and 90 (67%), respectively, participated, compared to 44 of 49 (90%) households and 207 of 229 (90%) residents in B. In A, 72 (80%) participants contributed serum samples, compared to 131 (63%) in B. Median household and lot size in A and B were 2 persons and 2.8 acres, and 4 and 0.8, respectively. There were 27 (38%) recent infections detected in community A and 5 (4%) in B. Univariate analysis indicated a significant association between recent dengue infection and living in a property large enough that the neighboring house is not visible (19 [79%] of 24 cases vs. 27 [16%] of 164 non-cases, Odds Ratio (OR)=19.28, 95% Confidence Interval [CI]=6.14-70.25), living in a house without window screens (10 [34%] of 29 cases vs. 6 [4%] of 160 non-cases, OR=13.51, 95% CI=3.93-48.05), living in a property with taller bushes (mean estimated height for case properties, 11 ft. vs. 6 ft. for non-cases, $p < 0.0001$), greater vegetation cover near the house (67% vs. 33%, $p < 0.0001$), living in a property with mosquito positive containers (23 [79%] of 29 cases vs. 73 [43%] of 171 non-cases, OR=5.11, 95% CI=2.04-14.37), and the use of pay phones (6 [19%] of 31 cases vs. 8 [5%] of 165 non-cases, OR=4.71, 95% CI=1.30-16.88). These conditions are also associated with infection within each community (except the payphone, only for A), but significance is lost with the reduction in sample size. Multivariate analysis is currently underway.

Conclusions: Our survey indicates a 2 to 10-fold greater incidence of dengue infection than detected by surveillance, and risk factors consistent with a mosquito vector (Ae. albopictus) that breeds in natural and artificial containers. Our findings suggest that community A's pay phone area was a focus for dengue transmission, and that interventions such as using repellent when outdoors, installing window screens, trimming vegetation, and eliminating potential breeding sites may reduce the risk of dengue infection.

Board 65. Detection of West Nile Virus Activity in the Commonwealth of Virginia's Avian Populations

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Division of Consolidated Laboratory Services, Richmond, VA

To identify the presence of West Nile virus (WNV) in the Commonwealth of Virginia, the Division of Consolidated Laboratory Services has implemented a real-time reverse transcription polymerase chain reaction (RT-PCR) assay to detect WNV in tissues of recently dead birds. Over 1,253 dead wild birds, were submitted by the Virginia Department of Health in 2001. These birds were primarily crows (75%), blue jays (16%), and raptors (6%) and were necropsied to remove kidney, brain, liver, and heart tissues. Qiagen QIAamp Viral RNA kits were utilized to extract RNA from kidney tissues. RNA extracts were analyzed with a one-step RT-PCR assay using the LightCycler System with FAM- and TAMRA-labeled probes and primers that have been previously reported (Lanciotti et al. J Clin Micro 38:11 and Briese et al. Lancet 355:9215). The LightCycler assay amplified WNV c-DNA and identified 212 positive tissue samples obtained from birds collected from 19 counties. Of those tissue samples that yielded positive results, approximately 98% were derived from crows and 2% were derived from blue jays. WNV positive dead birds were the first indicator of WNV activity in 19 of the 20 counties in Virginia with WNV activity. In one county a WNV positive horse was the first indicator of WNV activity and in that instance, only one recently dead bird had been submitted for testing prior to the seroconversion of the horse. These data suggest that real time RT-PCR using the LightCycler System is a sensitive, specific, and cost effective method for the detection of WNV activity in the environment.

Board 67. Surveillance for West Nile Virus Infection in Mosquitoes, Birds and Mammals in New York City, 1999-2001

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Local transmission of West Nile virus (WNV) was first detected in New York City (NYC) in 1999. Infected mosquitoes, birds, and mammals were detected in Queens, Brooklyn and the Bronx, with the largest number of human infections in Queens. In order to prevent a recurrence of WNV in 2000, a comprehensive surveillance and control plan was implemented by the New York City Department of Health. A network of adult mosquito traps and dead bird sightings were monitored citywide to detect the presence of the virus. In 2000, West Nile virus transmission was most intense on Staten Island, with positive mosquitoes and birds first detected during the first week in July. Of the 4800 mosquito pools tested 205 were positive. The virus was detected in 8 species, *Culex pipiens*, *Cx. salinarius*, *Cx. restuans*, *Aedes vexans*, *Ochlerotatus cantator*, *Oc. triseriatus*, *Psorophora ferox* and *Anopheles punctipennis*. Overall, 14,849 dead bird reports were received from the public of which 1083 birds were submitted for laboratory testing. Corvus brachyrhynchos was the most prevalent species, accounting for 133 out of 185 WNV positive dead birds. The 2000 outbreak resulted in 14 laboratory-confirmed human cases. Ten cases were from Staten Island, 2 from Brooklyn, 1 from Queens and 1 from Manhattan. The number of fatalities associated with NYC was reduced from 5 in 1999 to 1 in 2000. Other mammals infected with the virus were 3 horses, and 1 squirrel. In 2001, the preliminary results of surveillance activities resulted in 208 WNV positive mosquito pools out of 6226 submitted for testing. The species that tested positive were *Cx. pipiens*, *Cx. restuans*, *Cx. salinarius* and *Ae. vexans*. The public reported 5212 dead bird sightings, with 667 birds submitted for laboratory testing. Out of the 165 that tested positive for WNV, 121 were *Corvus brachyrhynchos*. Active and enhanced passive human surveillance resulted in 7 laboratory confirmed cases and no fatalities. Staten Island, Brooklyn and Queens had two cases each, and 1 case was from Manhattan. There was no evidence of other mammals being infected with WNV. The utility of mosquito and bird surveillance data from 2000-2001 as early predictors of human illness will be discussed.

57 Global Climate Change

Tuesday, March 26, 8:30 a.m.
Grand Hall East

Board 68. Climate, Weather, and the Outbreak and Spread of Infectious Diseases: A Strategy

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Complex interactions and feedbacks across biological and physical systems and/or simple structural threshold like responses that cascade throughout are characteristic of the manner in which ecological systems function. Yet, historically most efforts have been focused on attempting to describe such complex nonlinear responses as more readily tractable linear and even stationary processes. Albeit, to anticipate and avoid surprises, particularly in the area of human health, a more comprehensive understanding of the inner relationships between human health, the outbreak and spread of infectious diseases and their relationships to the weather and climate of the coupled land, atmosphere, oceanic and hydrologic systems must be established. This paper describes a methodology which will result in a predictive capability for the outbreak and spread of infectious diseases which are related to environmental factors and pose the greatest risk to US coastal populations, including the Great Lakes. The intrinsic and ultimate objectives of the proposed approach will be to: identify processes and biophysical gradients likely to generate non-linear responses and therefore unexpected behavior under future environmental conditions; comprehend when nonlinear responses are important to scaling issues temporally and spatially; quantify transform functions between forcings and responses for verifying and parameterizing predictive process models; develop new tools to study nonlinear responses and thresholds; formulate new hypotheses derived from mathematical treatment of model systems, such as spatial scale dependence of perturbations that can be tested using data dependent reconstructive methods; and employ this knowledge of the nonlinear system responses to better guide human health policy development for adaptive and mitigation strategies to future environmental weather events and climate variability. Data compiled from meteorological, oceanographic, hydrological, epidemiological, environmental, and ecological monitoring would be utilized by a multidisciplinary team in the analysis of the complex connections, likely non-linear and non-stationary, between weather events and climate conditions and the outbreak and/or spread of infectious diseases affecting human health.

58 Health Communication

Tuesday, March 26, 8:30 a.m.
Grand Hall East

Board 70. Disparities in Foodborne Disease Education Among Physician Specialties that Treat At-Risk Populations

S. M. Thomas, K. G. McCombs, S. Lance-Parker

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Background: Foodborne disease is a significant problem in the United States with an estimated 70 million cases each year. Immunocompromised and pregnant individuals are at higher risk of acquiring a foodborne disease and of having a more severe illness if infected. Research has shown that consumers are not well educated about food safety, but are concerned about infectious disease. Because of the higher risk of illness in immunocompromised and pregnant individuals and the inherent lack of food safety education, physicians whose specialties are intimately involved in the treatment or management of at-risk individuals are essential in the education of these populations about foodborne disease.

Methods: In 2000, Georgia, as a member of the Emerging Infections Program, conducted a survey targeting four physician specialties that treat immunocompromised or pregnant individuals. The specialties included obstetricians, oncologists and hematologists, infectious disease (ID) physicians, and nephrologists. The survey focused on physician's beliefs, knowledge, and practices concerning education of their patients about foodborne disease risk and prevention.

Results: Three hundred nine surveys were distributed to these four specialties; 87 of the 134 questionnaires returned were used in the analysis. No difference was found in the proportion of physicians surveyed that treat at-risk individuals among the four specialties, with 98% of physicians reporting that they treated at least some at-risk patients. The proportion of patients that requested information regarding foodborne disease also did not differ among the four specialties, with 80% of physicians reporting that their patients request information on food safety and foodborne disease prevention. Thirty-eight percent of physicians reported that their practice provides information about foodborne disease to patients. ID physicians' practices were more likely to provide information than both nephrology (p=0.001) and obstetric (p=0.004) practices, while oncology/hematology practices were more likely to provide information than nephrology practices (p=0.043).

Conclusions: There is a disparity in foodborne disease education of patients among the four different physician specialties. ID physicians and oncologists/hematologists are more likely to ensure that their patients receive education on foodborne disease risk and prevention. Physician specialty appears to have the greatest impact on whether a physician's practice educates patients about foodborne disease. This study highlights two physician specialties in Georgia that should be targeted for increased education about foodborne disease and its impact on at-risk individuals.

Board 71. Multi-agency Coordination: The Key for West Nile Virus Surveillance and Health Communication in Florida, January- December 2001

R. L. Oliveri, L. Conti, C. Blackmore, S. Wiersma

Florida Department of Health, Tallahassee, FL

A history of endemic eastern equine encephalitis and periodic outbreaks of St. Louis encephalitis in Florida resulted in interagency cooperation among local, state and federal government agencies, state university research centers and local mosquito control agencies. The identification of West Nile (WN) virus in the United States presented an opportunity to expand arbovirus surveillance and expand partnerships in Florida leading to the early detection of WN virus and subsequent public health response. The collaboration and commitment of the interagency partnership brought together a network of arbovirus expertise and experience resulting in an inclusive and comprehensive response.

A Florida West Nile Virus Interagency Workgroup developed and provided consultation on a state West Nile virus Surveillance and Response plan. This provided guidance to the Florida Department of Health in its efforts to detect WN virus and coordinate response. This group met weekly to discuss program data and initiatives and provide input into public health communications, which included 1) press releases with health alerts, weekly statewide public conference calls to disseminate and clarify arbovirus surveillance information; and 2) establishment of a statewide hotline and internet-based reporting site for dead-bird reporting and regular internet summaries and GIS maps of surveillance data on each agency website with links to other member sites, as well as national arbovirus information sites.

Novel approaches to data access included development of an internet-based web-board by the Department of Health to provide automatic and immediate notification of dead bird reports and test results and the use of the Department's weekly Epi Update. Health alerts and data summaries were published through the Bureau of Epidemiology's Epi Update, a weekly electronic newsletter targeting a broad public health audience. Through direct participation and communication, complex surveillance strategies were successfully implemented across several agencies to meet public health objectives. Direct accomplishments achieved through multiagency coordination included early virus detection, continuing data collaboration, consistent interagency public health messages, decreased interagency program competition, shared resources, and increased public participation in dead bird reporting and apparent behavior modification to reduce risk of mosquito bites.

Board 72. Marketing Strategy in the Development of a Sentinel Surveillance System.

J. C. Hagen, B. Parota

DuPage County Health Department, Wheaton, IL

The critical need for, and role of, local public health surveillance has become even more apparent in recent months. This surveillance must reside at the local level, where both obstacles and opportunities are clearly understood. This is true not only with currently publicized bioagents, but to emerging diseases, and to the health effects of environmental agents. Carefully chosen sentinel events or conditions become foundation stones to this system. The weakest link is the relationship between the heath care community and population-based public health. Soliciting and solidifying a mutually beneficial interaction is a complex mix of education, health promotion, and the innovative use of marketing. DuPage County Health Department has undertaken a process to design and implement an innovative marketing concept to enhance collection of necessary surveillance data from several sectors. Extensive input has been gained from staff and targeted professionals concerning methods for achieving marketing outcomes. Five specific marketing elements are: clear, precise sentinel conditions or events to be reported, provision of emerging disease workshops and training, rapid email/messaging or broadcast fax mechanisms, dedicated interactive website for surveillance system partners, and constant reporting back to those involved. Early results indicate an increasing interest and level of support for this sentinel surveillance system. The key has been to attract and involve the health care professionals so critical to success of the system. Recent events have identified gaps that exist in our system We must take advantage of this opportunity to better protect the health and lives of our residents.

Board 73. The Pedagogy of Emerging Disease: Teaching Medical Microbiology Using a Multifaceted Approach

R. D. Siegel

Stanford, Stanford, CA

The control of emerging infectious disease demands a cadre of physicians and allied health professionals well versed in the concepts of microbiology and infectious disease. Medical students and others often have difficulty in mastering this information. Several factors contribute to this difficulty: 1) the large number of organisms, 2) the variable clinical manifestations of infection even for a single organism, 3) the complexity of interactions between pathogen and host, 4) the rapid rate at which new genomic and virulence information is being acquired, and 5) the complexities and protean nature of epidemiology and treatment. In addition, students vary widely in the ways in which they learn most effectively.

In light of these considerations, we have developed a multifaceted approach to the instruction of microbiology and infectious disease. This course is aimed at clinical medical students but is also taken by graduate students and could be adapted to other pedagogic settings.

Students can choose from a wide variety of instructional modalities that best suit their learning needs. These modalities include: 1) live daily lectures, 2) clinicopathological case discussions, 3) demonstration laboratories, 4) video streamed web based lectures, 5) teaching assistant led discussions and reviews, 6) detailed course reader, 7) printouts and online versions of PowerPoint presentations, 8) recommended textbooks, 9) optional weekly problem sets, 10) online mastery quizzes of microbial taxonomy, 11) numerous practice tests in both final exam format and arranged by organ system, 12) Microbe — a multimedia microbiology teaching tool available on the web or on CD, 13) the Interactive Simulated Patient, 14) an email distribution list, 15) a course specific web site containing many of the above resources and well as links to numerous other microbiology related websites, 16) PDA resources in conjunction with the Stanford Palm Project, 17) a resource bank of slides and video tapes, and 18) numerous opportunities to interact with the infectious disease consult service on working rounds and grand rounds.

Overall, the course is organized into nine sections: an initial section on host-pathogen interactions and an intro to structure/function relationships of the major pathogenic groups. This is followed by seven sections organized by organ systems and taught using a syndromic approach. The sections are: respiratory, GI, skin, genitourinary, liver, CNS, and systemic. The final section of the course deals with special topics including: use of antibiotics and antibiotic resistance, nosocomial infection and hospital epidemiology, surgical infections, zoonoses, travel medicine, emerging infections, and biological weapons.

This presentation will elaborate on the more innovative and less obvious aspects of these teaching modalities. We will present a detailed description of the website and how it is utilized.

59 Influenza

Tuesday, March 26, 8:30 a.m.
Grand Hall East

Board 74. Scenario Analysis of Expected Number of Hospitalizations and Deaths Due to Pandemic Influenza in The Netherlands

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National Institute of Public Health and the Environment (RIVM), Bilthoven, NETHERLANDS

Introduction: Another influenza pandemic, following the 1918, 1957 and the 1968 pandemics, is likely if not inevitable. In a 'regular' influenza epidemic 5%-20% of the population is to become clinically ill; during a pandemic this percentage can mount to 30% or even 50%. A pandemic could cause substantial social disruption, insofar it would involve a large proportion of the population contracting a serious or less serious form of the illness. In order to minimize the effects of such a potential pandemic the Dutch Ministry of Health has drawn up an influenza pandemic preparedness plan. Within the scope of this plan, the Ministry asked us to calculate the expected number of hospitalizations and mortality during an influenza pandemic.

Method: As many uncertainties are involved in this type of studies, we have developed alternative scenarios and consulted experts to give their opinion on these scenarios and on the underlying model and assumptions. Various interventions are compared with the 'do nothing' scenario on their effect in terms of avoided hospitalization and mortality. Possible interventions are influenza vaccination, pneumococcal vaccination or therapeutic use of neuraminidase inhibitors.

Results: Age-specific attack rates and complication rates appeared to be crucial to the outcomes in terms of number of hospitalizations and deaths. In case of a pandemic with an overall attack rate of 30%, age-specific attack and complication rates, and health care as in a 'regular' epidemic, we estimated that influenza vaccination of risk groups and health care workers could prevent around 60% of hospitalizations and deaths, therapeutic use of neuraminidase inhibitors for each person with an influenza-like illness about 50%, and pneumococcal vaccination of risk groups for influenza about 26% of hospitalizations and 3% of deaths. However, it is unlikely that an influenza vaccine will be available in time. Treatment with neuraminidase inhibitors should start within 48 hours after first symptoms, which would be a logistic challenge, whereas pneumococcal vaccination can be given before a pandemic threat.

Conclusions: Our analysis makes assumptions explicit and shows gaps in knowledge and data. Describing and comparing the alternatives gives insight into the impact of the pandemic in terms of number of hospitalizations and deaths, the impact of the various possible interventions in terms of avoided influenza-related hospitalizations and deaths and in the crucial model parameters. Scenario-analysis will be helpful in policy making and planning of control measures on national and regional level. When there is an acute pandemic threat, the availability of the underlying decision support model provides the opportunity to update estimates of hospitalizations and mortality based on surveillance data from the pandemic source region. The model can also be used for other countries, using country-specific data.

Board 75. Assessment of Antiviral Drugs for Influenza A Prevention in Critical Occupational Groups

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Statement of Purpose: This review identified and evaluated important variables related to the use of antiviral drugs to protect large critical occupational groups when vaccination cannot be accomplished and influenza A outbreaks occur.

Statement of Methods Used: Four FDA approved drugs for influenza A (amantadine, rimantadine, oseltamivir, and zanamivir) were reviewed. Each drug's mechanism of action, prophylaxis efficacy, dosing, side effects, effect on humoral response to infection and vaccination, frequency of drug resistance, cost, shelf life, storage requirements, production capacity, and availability were reviewed. Information was obtained through literature search, search of selected websites, and interviews. Efficacy data were obtained from studies on healthy adults with laboratory proven influenza illness.

Summary of Results: All 4 drugs have 70-90% prevention efficacy. Major distinguishing features are: side effects, cost, and frequency of drug resistance. The lowest cost drug is amantadine ($1.00/5 days, Federal price). Its limitations are 30% drug resistance emergence and 10% occurrence of central nervous system (CNS) symptoms. Jobs that require high levels of CNS functioning may make this drug undesirable. Rimantadine is similar to amantadine but only 2% experience CNS symptoms. The cost is higher ($6.80/5 days) and drug resistance emergence is 30%. The neuraminidase inhibitor oseltamivir costs $32.30/5 days; 10% of patients experience nausea and vomiting but only 1.5% show drug resistance emergence. Zanamivir is not approved for prophylaxis but studies show it is efficacious and may have a low rate of drug resistance. It has cost limitations ($26.76/5 days) and occasionally has caused bronchospasm and airflow reduction in chronic respiratory disease patients.

Statement of Conclusions Reached: All 4 antiviral drugs have similar prevention efficacies. Only 3 are approved for prophylaxis. Shelf life, storage requirements, production capacity and availability are under study. Decisions for use will have to balance cost with risks associated with side effects and consideration of resistance emergence.

Board 76.

V. P. Lozitsky

Ukrainian Anti-Plague Institute, Odessa, UKRAINE

In this research we investigated the influence of molecular structure of macrocyclic pyridinophanes and their analogs on their anti-influenza and antiherpetic activity. This task was solved by means of elaborated 4D-QSAR approaches on basis of simplex representation of molecular structure. Such representation for biologically active substances allows to unify the description of spatial structure of compounds with saving of the complete stereochemical information. It enables easily to determine common fragments of spatial structure either promoting or interfering the concrete biological activity for researched molecules. On base of such approaches it is easily to realize molecular design of compounds with the given level of activity with the help of generation of the allowed combinations of such types simplexes, which determine researched property. Statistic characteristics for QSAR of PLS (Partial Least Squares) models are satisfactory (R=0,92-0,97; CVR=0,76-0,86). The molecular fragments that increase and decrease antiviral activity were defined and will be demonstrated. This information is useful for design and directed synthesis of novel antiviral agents. Several compounds with predicted high anti-influenza and antiherpetic activities were already synthesized. And their activities were confirmed experimentally.

This work was partially supported by INTAS foundation (grant INTAS 97-31528).

Board 77. Early Detection of Pneumonia and Influenza Excess Mortality in 13 Big Cities in Japan

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Background: There is a well-developed infectious disease surveillance system in Japan that enables timely information about the size of influenza epidemics. To know the real impact and severity of the circulating virus, mortality related to influenza is required. In this project, we tried to find early warning signs in influenza mortality. Formerly, influenza related mortality (if 'influenza' was listed in any row of the death certificate) reporting was requested from all Public Health Centers in the country. However, the number reported was about half of the primary cause influenza deaths reported to the vital statistics office. In this project, we chose 13 big cities covering one eighth of the total population throughout Japan.

Methods: We produced mortality curves for each city using pneumonia and influenza (P&I) mortality data (1987-1999). Predicted mortality curves were produced by stochastic frontier estimation. P&I mortality was reported from Public Health Centers weekly by electronic files. The result was compared with morbidity and viral surveillance data. Death cases are reported by the date of death, sex, age, cause of death (pneumonia or influenza) and place of death.

Results: Within the cities with completed mortality reports (Sapporo, Chiba, Kobe, Hiroshima and Kita-kyushu) no significant excess deaths were found during the 2000/2001 season. Reporting delays were different in each city. Sendai, Tokyo and three other cities seemed to have some missing data, and the rest had difficulty in complete reporting.

Conclusion: Low mortality observed during the season was explained by the low morbidity especially among elderly and because influenza B and A/H1N1 mainly circulated in Japan. In Japan, large excess mortality is found when drifted A/H3N2 appears and co-circulates with influenza B.

In Japan, death certificates are brought to ward offices, and then the records are transferred to the Public Health Center, which is responsible for electronic data entry. This process of transfer is not electronic; the main cause of delay exists here and some infrastructure changes should be made. Preliminary reports of death used in United States' 122 cities are not available in our country for legal and other reasons. Prompt reporting is essential if this system is desired for early warning purposes.

Board 78. An Empirical Research for Demand of Influenza Vaccination in the Elderly in Japan

Y. Ohkusa

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Purpose: This paper examine to analyze what determines the demand for vaccination in elderly as high risk group. Then, by using the estimation results, this paper evaluate how the law recommendation and/or subsidy affect their demand. **Methods:** Original data were obtained from two survey to the elders living with decendants and the elders living without decendants , conducted by the author. The survey contain the information about the elders, the household, experience of influenza during the last season, immunization during and hypothetical questionare about immunization for Conjoint Analysis. The three estimations are performed for actual behavior, Conjoint Analysis and Joint Estimation which are combine the first two estimation. **Results:** Among estimation results, cost, number of immunization, immunization in night or weekend, and law recommendation heavily affect their demand. Experience of influenza and immuzation in the last season, are one of the most important determinant. Moreover, the superior of the Joint Estimation is confirmed. **Conclusions:** The estimation results implies that about 8.9 million elderlys will demand for vaccination if no cost and with law recommendation. Conversely, it will reduce to be 3.2

million if cost is 6000 yen (about 50 dollars) and without law recommendation. The change from no cost to just 500 yen (about 4 dollars) depress the demand by 1.6 million elders. Law recommendation alone can push up 2.0 million elderlys.

Board 79. Forecasting the Geographical Spread of Influenza Epidemics by the Method of Analogies

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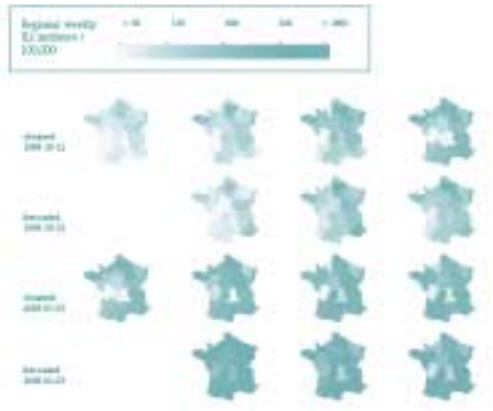
This work presents a method for prediction of the time and geographical spread of influenza epidemics, using a non parametric forecasting technique, the "method of analogies," previously proposed for forecasting weather by Lorenz (1). No statistical or modelling approach is currently considered a benchmark for forecasting the spread of an epidemic disease. Geographical mechanistic models have been proposed, but require extensive data on transportation flows (2). Statistical models for time series analysis demand assumptions that are rarely met, because the time series is neither stationary nor exactly periodic. The method of analogies does not require exogenous information for prediction, but uses retrospective data and a suitably chosen measure of proximity between contemporary observations and historical observations to approximate the dynamics of the epidemic. Incidence forecasts are based on the average evolution of past patterns, so-called 'neighbours', that most closely resemble contemporary observations.

We applied the method of analogies to forecast influenza-like illness (ILI) incidences in France and in the 21 administrative regions of France from a series of 807 consecutive weeks of ILI surveillance (16 epidemics) spanning 1984-2000 and recorded by the French Sentinel Network (3). Forecasts were made up to 10 weeks in advance. Parameters estimation was done by minimization of a cross-validation criterion based on the root mean square error of the predictions. The accuracy of the prediction was assessed by direct comparison of the distribution of observed and predicted incidences, and by estimating the Pearson correlation coefficient between observed and predicted incidences. The accuracy of the method of analogies was in turn compared with that of a linear auto-regressive models fitted to each series.

For the method of analogies, the correlation between observed and predicted regional incidences (see Figure) was above 0.62 (10-week ahead forecasts) and up to 0.81 (1-week ahead forecasts). Similar results were obtained for national incidences. This method yielded forecasts more accurate than those of linear AR models ($P<0.001$). However, the predicted incidences were slightly closer to the mean of the series than observed incidences.

The method of analogies is probably suitable for prediction of other communicable diseases, e.g. acute diarrhoea, as long as the disease displays recurring cycles. As any other prediction method, it also requires real-time collection of data to make prediction worthwhile. Finally, the method of analogies is a self-learning process, allowing its accuracy to improve with the length of the time series.



Board 80. Is Flu-Like Syndrome or Flu the Main Event of the Seasonal Illnesses in Patients Suffering From C Virus-Related Chronic Hepatitis (CCH), During IFN Treatment?

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Among side-effects of IFN therapy the so-called flu-like syndrome (FLS) is one of the most frequent and fearful experience that limits, in some ways, the patients (pts) quality of life (QOL) and the high dose-regimens, during their six- or twelve-month treatment period. On the other hand, influenza and other viral respiratory diseases (VRD) with their impact on general well-being sense casts shadows whether it should previously be managed with prophylaxis or eventually treated. Both circumstances overlap and sometimes it is difficult to distinguish between them, mainly facing illness mild expressions. Trying to clarify the VRD incidence in our setting we studied 246 (130 females) pts affected from chronic C hepatitis of which 124 (68 females) had undergone IFN therapy administered obviously in any year span (but at least started from 4 weeks). Were excluded pts with cardiovascular or pulmonary diseases, decompensated diabetics, sustained smokers, those older than 65 years and the vaccinated ones. On the base of clinical evidence coupled with specific serology there were discovered 48 cases of VRD including influenza, para-influenza and adenovirus infections in no treated pts, mostly evidenced during seasonal outbreaks. Four pts suffered from complications (1 secondary bacterial pneumonia, 1 marked muscle tenderness, 2 prolonged acute diarrheal illness); in the opposite cohort, only 16 pts showed fever, chills, headache, myalgias and sore throat associated or not with rhinitis whose serology proved 5 viral episodes (chi-square = 13.2; $p < .0003$), without serious sequelae; the remainder episodes were judged to be ascribed very likely to FLS, at times tardily emerging. The different hosts were characterized by a major frequency of sore throat and rhinitis, typical of true VRDs (34/48 cases compared with 2/5 ones; 71% versus 40%). Clinical manifestations were strictly treated by the means of analgesic-antipyretics and anti-inflammatory (overall paracetamol). In the following year the same pts were monitored to detect the need of administering flu vaccines and surprisingly the IFN-treated cohort had a significantly minor incidence of VRD episodes also after having stopped antiviral treatment (2 versus 39). Which conclusions could be drawn from these epidemiological observations? The main feature of IFN treatment-period seems to be the well-known FLS. QOL in pts with CCH is sometimes impaired but, globally considering the entire phase of IFN therapy, the decreased frequency of seasonal viral respiratory illnesses improves such feature, cuts-back the therapeutic costs and, what's more, lessens hospitalisation periods.

Finally, in our opinion, the IFN immune-modulating and antiviral actions play a pivotal role in inducing a marked reduction of C virus activity and probably other intercurrent viral affections.

Board 81. The Method of Extrapolation of Influenza Virus ID50 from One Mammals Species to Another. Perspectives of Its Application when Controlling and Preventing Infectious Diseases

V. Zhukov[1], L. Shishkina[1], A. Sergeev[1], A. Safatov[1], O. Piankova[1], V. Petrishenko[1], O. Piankov[1], E. Ryabchikova[2], E. Malkova[2], S. Morse[3]

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The scheme of extrapolation is based on a mathematical model of the formation of the infectious process in an organism. The model connects a parameter of an organism susceptibility to a virus, the virus ID50, to parameters of interaction of the virus with

susceptible cells of the host, the probability of virus productive adsorption on a susceptible cell and the average virus yield in a cell. The method was tested when extrapolating the value of influenza virus A/Aichi/2/68 ID50 from outbred mice to outbred rats. The primary cells of lungs of both animals were used to measure parameters of virus-cell interaction. The ratio of the numbers of the main types of epithelial lung cells susceptible to influenza such as ciliated cells and pneumo-cytes of the 1st and 2nd types was similar to the ratio of the cells in lungs. The extrapolated and experimentally measured values of the virus ID50 were statistically equal. It indicates the validity of the method of extrapolation. Some approaches how to use the method in the system of diseases control will be discussed. In particular, the method can be applied to the solution of the following problems:

- assessment of an infectivity for human of emerging viruses of non human origin;
- epidemiological investigation of human sub-population with respect to their susceptibility to viruses.

[Supported by ISTC/DARPA Agreement #450p.]

60 International Cooperation

Tuesday, March 26, 8:30 a.m.
Grand Hall East

Board 82. Prevalence of Sexually Transmitted Diseases Among Injection Drug Users in St Petersburg, Russian Federation

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Background: Epidemics of HIV and syphilis have appeared within the last half dozen years. Injecting drug users (IDUs) are the nexus for these emerging epidemics. Infectious disease prevalence among IDUs can be estimated by testing the small amounts of blood left inside syringes in a simple, non-invasive way. We have collected used syringes to conduct a point prevalence study and have investigated the associated risk behaviors among the IDUs visiting a needle exchange program in St. Petersburg, Russia. **Method:** IDUs returning syringes to the St. Petersburg "Vozvrastcheniye"" syringe exchange program (SEP) from June to July 2000 were invited to anonymously complete a 64 item questionnaire requesting demographic, knowledge, and behavioral information, and to provide their used syringes to be tested for antibodies indicating previous infection to HIV, Hepatitis C (HCV), Hepatitis B (HBV) and syphilis. **Results:** A sample of 101 subjects was interviewed, and 136 syringes were collected for testing. The median age of IDUs was 23 years (IQR: 19-26) and median number of drug injections in the previous month was 40 (IQR: 18-70). Syringe prevalences were 10.9% for HIV, 78.2% for HCV, 15.8% for HBV, and 6.9% for syphilis. All respondents recognized that the sharing of syringes or the use of unsterile syringes is a significant risk factor for getting AIDS and all were aware that cleaning used syringes with water alone is insufficient to kill residual HIV. Only 65.3% of subjects recognized condoms as an effective means of STD prevention. 49% thought oil based products were good lubricants for condoms or were not sure. Although several items on the questionnaire were significant predictors for returning contaminated syringes to the SEP, none was an item which identified an important behavioral risk or a gap in risk knowledge. **Conclusion:** The IDU population studied was young and although it possessed a high level of knowledge about injection drug use risk behavior it requires additional interventions to encourage safer sexual behaviors. HCV prevalence is approaching saturation and syphilis infections appear to be much higher among IDUs than in the general population. The SEP might serve as a useful vehicle to institute a STD prevention intervention. Such an intervention might have the synergistic effect of reducing syphilis infections while keeping the sexual transmission of HIV and HBV low.

Board 83. Surveillance of Viral Gastroenteritis Outbreaks in Europe: 1995 to 2000

B. A. Lopman[1], M. Reacher[1], D. Brown[1], G. Hernández[2], M. Koopmans[3]

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Viral agents are the most common cause of acute gastroenteritis, but estimates of the importance of foodborne transmission vary widely among different countries. To gain understanding of surveillance and epidemiology of viral gastroenteritis outbreaks, data were compiled from ten surveillance systems associated with the "Foodborne Viruses in Europe" network. Most surveillance systems found Norwalk-like viruses to be responsible for at least 85% of all viral outbreaks. However, the absolute number and population-based rates of viral gastroenteritis outbreaks differed markedly among European surveillance systems. A wide range of estimates of the importance of foodborne transmission was also found: from nearly 100% in Denmark and France to 7% in England and Wales. These differences must be seen within the context of the sources of information, clinical definitions and structures of the outbreak surveillance systems.

Board 84. International Trade and Emerging Infections: What Can Trade Data Tell Us?

A. Kimball, T. A. Harrison, N. Pautler

University of Washington, Seattle, WA

Background: Emergent infections (Nipah virus, Avian Influenza, Bovine Spongiform Encephalopathy, etc.) have cost billions of dollars in lost trade and travel worldwide over the past decade. Control of emerging infections is a new priority within the Asia Pacific Economic Cooperation (APEC), according to the Leaders Declaration (Shanghai, 2001). Beyond humanitarian concern, the cost to global trade of emergent diseases is unacceptable because: 1) it is not predictable or manageable, 2) it can profoundly affect corporate and national trade revenues through the disruption of trade, and 3) it can lead to long-term unpredictable changes in global market position for trading nations. The action of APEC follows similar actions by the European Union and ASEAN trading communities. The World Trade Organization (WTO) collects and disseminates data on trade. However, WTO information has not previously been analyzed for the impact of infections on global trade. Objectives: 1) To create an analyzable data set of independent variables from the collected urgent measures notifications of the World Trade Organization, 2) Use this dataset to describe the experience with emergent infections and trade restriction as reported to the WTO. **Methods:** 394 urgent measures reports were received by WTO, Geneva between April 1996 and August 2001. A database to accommodate these forms was designed consisting of 16 independent variables. Data was entered using STATA, and simple frequency analysis has been carried out. Data linkage and comparison using other trade data sources is underway and should be completed by early spring 2002. **Results:** Of the 394 forms analyzed to date, the distribution of reporting economies

among regions was uneven, with reporting frequency higher for countries in Europe and Australasia. The two most common causes of urgent import restriction were concern for animal health (54%) and food safety (24%). Two infections, bovine spongiform encephalopathy and foot and mouth disease, were the major causes of trade disruption reported in this system. Discussion: If volume of trade quantifies exposure to risk for urgent disruption of trade, we would have expected that high volume countries preferentially reported through the system. Our data do not support this. Concern for animal health is the leading cause of trade disruption, however, categories used for reporting are not mutually exclusive. For this reason, data may suffer from misclassification. There is tremendous potential value in using this information system to describe the impact of emerging infections on trade. This value will require additional data gathering and refinement to be realized, given current information collection.

Board 85. International Circumpolar Surveillance: Invasive Bacterial Disease Surveillance in the Arctic.

A. J. Parkinson[1], A. Bell[1], J. Spika[2], F. Steinz[3]

[1]CDC, Arctic Investigations Program, Anchorage, AK, [2]LCDC, Bureau of Infectious Diseases, Ottawa, ON, CANADA, [3]Institute of the Chief Medical Officer, Nuuk, GREENLAND

Background: The International Circumpolar Surveillance (ICS) project was established in 1999 and aims to create an infectious disease surveillance network of hospital and public health laboratories and authorities throughout the Arctic States: USA (Alaska) northern Canada, Greenland, Iceland, Norway, Finland, Sweden and northern regions and Oblasts of the Russian Federation. ICS will allow for the collection, comparison and sharing of uniform laboratory and epidemiological data on infectious diseases of concern, and assists in the formulation of prevention and control strategies. **Methods:** In 2000 isolates of *Streptococcus pneumoniae* (Sp), *Haemophilus influenzae* (Hi), *Neisseia meningitidis* (Nm), Groups A (GAS) and B (GBS) streptococcus recovered from normally sterile sites at 23 and 14 clinical laboratories in Alaska (AK), and northern Canada (NC), respectively, were forwarded to one of three reference laboratories for characterization. Greenland (GL) submitted only Sp isolates from 17 clinical laboratories to a reference laboratory in Denmark. Identified cases were reported to local public health personnel who review and provide clinical, demographic, and immunization history. Case and culture information was forwarded to the ICS coordinator at the Arctic Investigations Program, for analysis, report generation and dissemination. **Results:** A total of 159 Sp isolates were submitted from AK (111), NC (45) and GL (3) in 2000. Estimated annual rates of invasive Sp disease per 100,000 population were 18, 34, and 5 for AK, NC, and GL respectively. Rates among children < 2 were similar in NC and AK (189 vs 193/100,000), with 82% of Sp isolates from NC and 74% from AK being serotypes contained in the 7-valent vaccine. Among isolates from those > 2 years of age 100%, 89% and 100% from NC, AK and GL respectively were serotypes contained in the 23 valent polysaccharide vaccine. The predominant Sp serotype in NC was serotype 1 (31%), and in AK was serotype 14 (17%). In AK 23% of Sp were non susceptible to penicillin. In NC 14% were fully resistant and all were serotype 9V. The estimated rates for Hi and GAS were 2 times higher in NC than AK. While no cases of Hi serotype b were detected in Canada in 2000, 9 occurred in AK. Rates of Nm and GBS were similar in NC and AK. **Conclusions:** Collaborative standardized international surveillance for invasive bacterial diseases is feasible and allows for direct comparisons of disease rates, pathogen characteristics, and intervention effectiveness between participating countries.

Board 86. Shortage of Vaccines During a Yellow Fever Outbreak in Guinea

N. Nathan

EPICENTRE, Paris, FRANCE

Yellow fever (YF) is a viral hemorrhagic fever transmitted by mosquito bites that can be prevented by the 17D YF vaccine which protects for at least 10 years. YF is endemic in rural areas in the vicinity of tropical forests. Large epidemics usually occur when a specific vector (Aedes aegypti) transmits the virus in urban settings. The largest outbreaks were reported in the sixties in Ethiopia and in Nigeria (100,000 cases each). Re-emergence of the disease is observed in West Africa. A YF epidemic erupted in Guinea in September 2000. From September 4th 2000 to January 7th 2001, 688 clinical cases (of which 88% from rural districts) and 225 deaths were reported. The peak of the epidemic occurred between November 20th and November 26th. The outbreak spread to 16 of the 33 districts of the country. Entomological investigations identified Aedes aegypti in the investigated towns (Labé, Coya, Conakry), but at low density. A mass vaccination campaign was organised by the Guinean Ministry of Health with the support of international NGOs. Initial target population was all individuals aged more than 9 months living in the affected areas (352,278 inhabitants). An appeal for vaccines was made on November 1st. First vaccines (630,000 doses) were available 10 days later.

Because of the rapid extension of the outbreak, the target population was re-estimated at 1,679,648 persons and a second appeal for vaccines was made on November 13th. However, 300,000 doses only were brought 5 weeks after. Vaccination strategies had to be revised and target populations were restricted to affected urban areas and to the most affected rural areas. The initiation of the mass vaccination campaign was delayed until 4 weeks after the peak of the epidemic in the region of Labé. At the end of the intervention, 856,031 persons had been vaccinated in 2 regions where the vaccine coverage was estimated at 56%. The Guinean episode demonstrated that the international stocks of YF vaccines were not sufficient to provide an adequate and quick response to large outbreaks, in spite of a WHO recommendation made in 1998 that an emergency stockpile of 1 million doses be held in Africa and America for outbreak response. Since the outbreak in Guinea, the International Coordinating Group on Vaccine Provision for Epidemic Meningitis Control decided that 2 million doses being stored as part of a UNICEF stockpile to be used for response to outbreaks only. This stock shall limit shortages of vaccines during future epidemics. However, the problem of the prevention of the occurrence of YF epidemics will remain. This can only be addressed by the organisation of pre-emptive mass vaccination campaigns or by the successful introduction of YF vaccination in the EPI of countries at risk.

Board 87. External Quality Assurance System (EQAS) Demonstrates Continued Need for Improvement in *Salmonella* Serotyping and Susceptibility Testing: WHO Global Salm-Surv, 2000 and 2001

A. Petersen[1], F. M. Aarestrup[1], A. B. Jensen[1], D. Lo Fo Wong[1], M. C. Evans[1], F. J. Angulo[2], B. C. Imhoff[2], H. C. Wegener[1], WHO Global Salm-Surv[3]

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Background: WHO Global Salm-Surv is an international network of individuals and institutions involved in *Salmonella* surveillance. WHO Global Salm-Surv strives to enhance *Salmonella* serotyping and antimicrobial susceptibility capacity among member institutions, and thereby improve surveillance data, through training courses and an External Quality Assurance System (EQAS). **Materials and Methods:** Laboratories participating in EQAS (44 laboratories in 2000 and 103 in 2001) received eight

blinded *Salmonella* strains and one *E. coli* reference strain. Laboratories serotyped and susceptibility tested the isolates following their routine laboratory protocols and reported the number of specimens and *Salmonella* isolates tested yearly. Further analysis is underway to compare performance before and after training courses. **Results:** Between 2000 and 2001, the proportion of correct serotyping results increased from 73% to 78% and correct antimicrobial susceptibility results of the reference strain increased from 78% to 83%. Correct serotyping results from national reference laboratories were 14% higher than other laboratories, and antimicrobial susceptibility test results of the *Salmonella* strains and the *E. coli* reference strain were 5% and 11% higher, respectively. Thirty-nine of the participants in EQAS 2001 had attended a WHO Global Salm-Surv training course. Trained laboratories had a higher percentage of correct results (84% versus 79%) than untrained laboratories for susceptibility testing of the reference strain, but a lower percentage of correct results in serotyping (70% versus 81%). **Conclusion:** Although progress has been made in improving the quality of serotyping and susceptibility results, further improvement is needed. Such performances can be enhanced by WHO Global Salm-Surv activities such as training courses and EQAS. It is anticipated that these activities will improve surveillance data worldwide.

Board 88. WHO Global Salm-Surv: Strengthening Laboratory-Based Surveillance to Reduce the Global Burden of Foodborne Diseases

P. Braam[1], B. C. Imhoff[2], H. C. Wegener[3], M. C. Evans[3], A. Petersen[3], M. Jouan[4], F. J. Angulo[2], WHO Global Salm-Surv[5]

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Background: World Health Organization (WHO) Global Salm-Surv is a global network of national and regional public health, veterinary, and food reference laboratories and individuals involved in *Salmonella* surveillance. WHO Global Salm-Surv strives to enhance the capacity and quality of *Salmonella* isolation, identification, serotyping, and antimicrobial resistance testing throughout the world and support local interventions that reduce the human health burden of *Salmonella* and other foodborne diseases. Initiated in January 2000, WHO Global Salm-Surv is coordinated by a Steering Committee including WHO Headquarters (Geneva, Switzerland), the Centers for Disease Control and Prevention (Atlanta, Georgia, U.S.), Institut Pasteur (Paris, France), and the Danish Veterinary Institute (Copenhagen, Denmark). **Methods:** WHO Global Salm-Surv program elements include: regional training courses, a moderated electronic discussion group, an external quality assurance system (EQAS), a country databank of annual *Salmonella* surveillance summaries, a web site, and reference testing services. **Results:** WHO Global Salm-Surv currently has 404 members and 110 participating member institutions from 106 countries. Of the member institutions, 66% test non-human specimens and 58% test human specimens (some laboratories test both human and non-human specimens). The WHO Global Salm-Surv members live in the following regions: Africa (5%), the Eastern Mediterranean (9%), Europe (32%), the Americas (31%), South-East Asia (10%), the Western Pacific (13%). WHO Global Salm-Surv Regional Centers have been established in Asia (Thailand) and South America (Argentina). In 1999-2001, we conducted 8 regional training courses (one in China, Greece, and Mexico, two in Argentina, and three in Thailand), resulting in training more than 160 microbiologists on *Salmonella* isolation, identification, serotyping and antimicrobial susceptibility testing methods. WHO Global Salm-Surv sent 80 electronic discussion group messages in 2000 and 2001. Thus far, we have conducted 2 cycles of EQAS (2000 and 2001) with 113 laboratories from 67 countries. A web-based country databank for *Salmonella* surveillance summaries has been created; this and other information, including the WHO Global Salm-Surv Strategic Plan, is available on the WHO Global Salm-Surv website at www.who.int/salm-surv. **Conclusion:** Future WHO Global Salm-Surv activities include regional training courses in Poland, Russia, the Caribbean, and Africa, and continuing training courses in Thailand, Argentina, Mexico, and the Eastern Mediterranean. Through these and other activities, WHO Global Salm-Surv continues to strengthen the capacity of local, national and regional laboratories, with the ultimate goal of reducing the global burden of *Salmonella* and other foodborne diseases.

Board 89. WHO Global Salm-Surv: Asian Regional Center

T. Chalermchaikit[1], A. Chongthaleoung[1], S. Kanarat[1], WHO Global Salm-Surv[2]

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Background: Foodborne diseases and antimicrobial resistance of foodborne pathogens are major global public health concerns. In addition to contributing to a public health burden, foodborne diseases may also result in economic loss. The impact of these problems may be more serious in developing countries and food exporting countries; however, laboratory-based surveillance of foodborne diseases, including antimicrobial resistance of foodborne pathogens, is limited in many of these countries. To address these needs, the World Health Organization (WHO) established The Center for Antimicrobial Resistance Monitoring in Foodborne Pathogens in Thailand in 1999. The Center's goals were to establish a laboratory for antimicrobial resistance monitoring of foodborne pathogens, support standardization of antimicrobial susceptibility testing in important foodborne pathogens isolated from food-animals and food of animal origin in Asian countries, and assist in the development of sustainable national policy for prudent use of antimicrobials in food-animals. **Methods:** In 2000, WHO Global Salm-Surv, a project created to improve laboratory capacity and decrease the burden of foodborne illness worldwide, established the WHO Global Salm-Surv Asian Regional Center in Bangkok, Thailand. **Results:** Regional Center activities thus far include hosting 3 regional training courses with participants from Cambodia, China, India, Indonesia, Korea, Laos, Myanmar, Malaysia, Nepal, Papua New Guinea, Philippines, Sri Lanka, Vietnam, and Thailand and developing a plan to provide antisera to WHO Global Salm-Surv member institutions. Additionally, during the regional training course in 2001, participants noted that *Salmonella* serotype Weltevreden was the second most common serotype in Asia; this serotype is apparently rare elsewhere in the world. In partnership with the Danish Veterinary Institute, the WHO Global Salm-Surv Asian Regional Center launched a special study to understand the epidemiology of *Salmonella* Weltevreden in Southeast Asia. The Regional Center is also conducting a National Program for Antimicrobial Resistance Monitoring in Foodborne Pathogens and a National Program for Promoting Prudent use of Antimicrobial Drugs in Food-Animals, which are supported by governmental agencies' research funds. **Conclusion:** Future goals for the WHO Global Salm-Surv Regional Center include hosting a regional training course for microbiologists and epidemiologists in 2002, providing antisera to regional WHO Global Salm-Surv members, and providing leadership in the Southeast Asian Region.

61 Molecular Epidemiology II

Tuesday, March 26, 8:30 a.m.
Grand Hall East

Board 90. An Outbreak of Swine *Streptococcus suis* Illnesses Occurred in China

F. C. Zhu, H. Wang, X. S. Hu, H. F. Yang

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Streptococcus suis (*S. suis*) is responsible for a wide variety of infections in pigs. Illness will happen if human is involved, characteristic of meningitis, arthritis, septicaemia, endocarditis, polyserositis, bronchopneumonia and abortions. Outbreak of illnesses caused by *S. suis* through contacting infected swines or its carcasses occurred in Jiangsu , eastern China in 1998. The objectives of this study were to elucidate the epidemiological characterization and scales of the disease through case-control study, and genotype the isolates of *S. suis* isolated from cases and infected swines by RAPD with 10 primers. The underlying hypothesis is that if the epidemiological characterization of the diseases caused by *S. suis* is clear, there will be preventive methods made to control it. All 12 isolates isolated from the cases and infected swine were confirmed using a battery of methods including API biochemical test, serum coagulate test and thalli fatty acid profile analysis. In 1998, 25 cases were found in 4 counties of Jiangsu province in the consecutive month of July and August, among whom 16 cases progressed into Streptococcal toxic syndrome, and 9 meningitis. Fourteen of 25 cases died of Streptococcal toxic shock syndrome or meningitis. All the cases had histories of contacting infected swine or its carcasses 4 days before they got illnesses. The isolates were *S. suis* serotype 2. The results of the homologous regions (products of OPB3, OPB8, OPB10, OPB10, OPB12, OPB13, OPB14, REP1, REP2, ERIC1 and ERIC2 as primers) found in the 12 isolates isolated from the cases and the swine indicated that the outbreak was caused by contacting swine infected by *S. suis*. The predominate clinic symptoms of the outbreak are Streptococcal toxic shock syndrome and meningitis. This is the first report that an emerging infectious of *S. suis* occurred in China. The results suggest that human can get illness through intimately contacting with livestocks infected by *S. suis*. Health promotion that help people know the epidemiological knowledges on the disease , and surveillance for *S. suis* in livestock need be carried out.

Board 91. A Study of the Emerging Sequence Types of Multiple Drug Resistant Streptococcus Pneumoniae in Queensland

S. Byrne, D. Davis, D. Murphy, J. Bates, **J. Savill**

Queensland Health Scientific Services, Brisbane, AUSTRALIA

A molecular-based surveillance study was carried out in Queensland for the presence of the sixteen recently described international multi-drug resistant *Streptococcus pneumoniae* clones. A representative set of twenty-three invasive cases of multiple drug-resistant pneumococcal infection in Queensland children and adults were selected from all 1600 isolates referred in 1998 and 1999.A study of global genetic relatedness was undertaken. The isolates were examined by BOX -PCR fingerprinting and DNA multi-locus sequencing to determine clonality and sequence type (ST). The sequence type was determined by sequence comparison with an international database. BOX-PCR fingerprinting discriminated between serotypes and identified clones within several serotypes. Multi locus sequence typing identified an isolate of serotype 6A to be a new clone. Isolates representing serotype 6B were found to be the multi-drug resistant Spanish serotype 6B ST 90. Several 19F isolates were found to be a new single locus variant of the Danish ST 77 clone and another 19F to be a new single locus variant of the Taiwanese ST 236 clone. Four isolates were found to be that of the Spanish serotype 23F clone sequence type 81. New variants and four recently described multi drug resistant *Streptococcus pneumoniae* clones were identified for the first time in Queensland isolates. BOX-PCR fingerprinting was demonstrated to be an excellent screening tool for determining clonality. Multi locus sequence typing was found useful to systematically provide an internationally derived nomenclature to these clones. This sequence type data on clones will serve a useful baseline for monitoring emerging multi-drug resistance *Streptococcus pneumoniae* infections in the future.

Board 92. Meningococcal Disease in a Christian Pilgrim – Use of Molecular Approaches to Differentiate Sporadic from Outbreak-Associated W135 *Neisseria meningitidis* Strains

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Background: Over 400 laboratory confirmed cases of meningococcal disease caused by N. meningitidis serogroup W135 (NMSW135) have been reported in Saudi Arabia and subsequently worldwide among Hajj 2000 and 2001 pilgrims to Saudi Arabia and their close contacts. Recently, extensive molecular characterization of these isolates demonstrated that they were of porA type P1.5,2, had identical 16S rRNA gene sequences, indistinguishable PFGE (NheI) profiles, and by multilocus-enzyme electrophoresis (MEE) and multilocus sequence typing (MLST) belonged to the ET-37 complex. Here we present the utility of molecular subtyping of NMSW135 strains in an epidemiological investigation of a case of meningococcal disease in a Croatian Christian pilgrim following a religious event in a neighboring, predominantly Muslim country. **Results:** On April 26, 2000, a previously healthy forty-one year old housewife presented to the emergency room with signs of septicemia and meningitis. Two days earlier she returned from a Catholic pilgrimage in Bosnia and Herzegovina where hundreds of people from throughout the world were in attendance. No other cases were reported associated with this event. From the patient's blood, cerebrospinal fluid and a throat swab NMSW135 was isolated. Molecular characterization of the isolate was carried out by PFGE (NheI) and sequencing of the 16S ribosomal RNA gene. Both PFGE pattern and 16S sequence type were clearly different from those identified in all NMSW135 strains associated with the Hajj pilgrimage to S. Arabia in 2000 and 2001. **Conclusion:** The utility of molecular subtyping for rapid and precise identification of N. meningitidis isolates associated with epidemic situations was clearly demonstrated by the ability of molecular subtyping to rapidly differentiate NMSW135 isolate from a Christian pilgrim in Croatia from those NMSW135 strains associated with the 2000 and 2001 outbreaks of meningococcal disease following the Hajj in S. Arabia. Recognition of this case as a sporadic one, rather than being the first sign of potential transmission of the outbreak-associated NMSW135 strains to a not yet affected country, was helpful to the public health officials.

Board 93. Prevalence and Virulence Profiles of *Escherichia coli* O157:H7 in Livestocks in Jiangsu, China in 1999 and 2000

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Verotoxigenic *Escherichia coli* O157:H7 has emerged as an important foodborne pathogen, causing bloody diarrhea and hemolytic-uremic syndrome (HUS) in most of countries of all the world. Cattle, sheep and deer are considered as reservoirs of *E.coli*

O157. In China, there are some reports about sporadic isolates in cattles and pigs, and cases caused by *E.coli* O157. Jiangsu province is an important region in agriculture products in eastern China. The objective of this study is to elucidate the prevalence of *Escherichia coli* O157:H7 in livestocks in Jiangsu province through epidemiological investigation. The underlying hypothesis is that if the prevalence of *E.coli* O157 in livestocks in Jiangsu province, preventive strategies can be made to control probably its outbreak. In the summer of 1999 and 2000, 1733 (in 1999) and 1427 fecal samples (in 2000) were detected for *E.coli* O157:H7 using a battery of methods including Immunomagnetic separation (IMS), CT-SMAC agar, Chromagar®O157, and biochemical test, anti-serum agglutination test. One hundred and sixty seven (167) of total 252 isolates were detected for virulence genes (SLTs, eaeA, hlyA) by multiplex PCR. In 1999, the prevalence of *E.coli* O157 was 19.05% in cattles, 12.01% in sheep, 7.75% in chicken and 7.54% in pigs, compared to 9.34% in cattles, 7.47% in sheep, 3.65% in chicken and 4.04% in pigs in 2000. Almost half of detected isolates (82/167) carried at least one virulence gene. The results of virulence gene pattern suggest that SLT2+eaeA+hylA pattern (52/82) is predominate, next is SLT1+SLT2+eaeA+hlyA pattern (15/82). These results indicate that the prevalence of *E.coli* O157:H7 is significantly higher in livestock in Jiangsu province than that in other reports , and livestock are potential infectious source for *E.coli* O157:H7 outbreak in population. Effective strategies and management practices for control *E.coli* O157:H7 transmission need be carried out in Jiangsu province to prevent outbreaks.

Board 94. Use of an AFLP-PCR Technique To Fingerprint and Differentiate Isolates of *Salmonella enterica* Serotype Typhimurium DT104

S. C. Rankin, J. P. Holt, S. R. Young, J. Cassidy, D. S. Munro, C. E. Benson

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Background: A wide range of methods exist for typing foodborne pathogens, though none appear to be universally applicable or acceptable for *Salmonella*. This is largely due to the highly clonal nature of this pathogen. Sporadic isolates of *Salmonella enterica* serotype Typhimurium phage type 104 (DT104) have been shown to be virtually indistinguishable and patterns or profiles derived by a variety of molecular techniques indicate the spread of an epidemic clone, rather than a diverse group of organisms. The potential value of highly discriminating and reproducible typing data cannot be underestimated when supplying information on outbreak sources and routes of infection. **Methods:** All Typhimurium isolates obtained at the University of Pennsylvania *Salmonella* Reference Center from 1997 to 1999 were phage typed. We used a single enzyme AFLP assay and evaluated two restriction endonucleases (*Hin*dIII and *Eco*RI) and two selective primers for each enzyme to determine the usefulness of this technique for discrimination of Typhimurium DT104. SRC also has an extensive collection of isolates of DT104 from outwith the United States and 36 of these were included for comparison with DT104 strains that originated in the United States. Antibiotic susceptibility testing was performed on all isolates. **Results:** AFLP-PCR with the *Eco*RI-A, *Eco*RI-C, *Hin*dIII-A and *Hin*dIII-C primers suggested that discrimination within *Salmonella* Typhimurium DT104 is possible with this technique. When results from all four primers were combined nineteen different profiles could be discerned. Eighty-seven isolates (62%) were classified as the predominant type and a further 26% of the isolates comprised only four different combined types. This combined typing is highly discriminating given that DT104 has been shown to be highly clonal. However, the application of four primers would be a costly and time-consuming process. Therefore, we examined the level of discrimination achieved using a combination of two primers. The most successful of all the available combinations in this case, *Eco*RI-C and *Hin*dIII-A showed a total of 16 combined profiles rather than the nineteen observed with all four primers. The two-primer combination had little effect on the distribution of the strains. Eighty-nine isolates (63%) were now classified in the predominant type. As before a further 26% of the isolates comprise only four additional combined types. **Conclusions:** This level of discrimination among such a highly clonal group of organisms clearly indicates the advantage of using a sequenced-based method. Minor mutations to the genome sequence are more readily observed and this leads to greater discrimination between unrelated strains. The ability to discriminate different "types" within Typhimurium DT104 represents a major asset to the surveillance and subsequent control of this pathogen in livestock.

Board 95. Molecular Characterisation of an Outbreak Strain of Multiresistant *Salmonella enterica* Serotype Typhimurium DT104 in the United Kingdom

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In summer 2000 a significant increase in confirmed cases of multiresistant *Salmonella* enterica serotype Typhimurium, definitive phage type 104 (MR DT104) was observed in England and Wales — from 150 cases in August 1999 to 372 cases in August 2000. The majority of these isolates were from cases in the West Midlands of England and included one fatality. Outbreak associated isolates were Pulsed-Field Gel Electrophoresis (PFGE) profile xtm 1 and were resistant to ampicillin, chloramphenicol, streptomycin, sulphonamides and tetracyclines (R-type ACSSuT). These common profiles occur in 90% and 70% (respectively) of MR DT104. However, Plasmid Profiling (PP) demonstrated that in addition to the 60 MDa serotype-specific plasmid (found alone in 79% of MR DT104), a 2 MDa plasmid was present in isolates from the outbreak cases. This profile (PP 60, 2) usually occurs in only 5% of MR DT104. In 2000 the frequency of PP 60, 2 among human isolates of MR DT104 rose from 6% in June/July, to 64% in August/September, and fell to 9% in October/November. Statistical analysis of case-control studies from the outbreak implicated lettuce and other salad items used as garnish in fast-food establishments as the most likely vehicle for infection. MR DT104 is a zoonotic pathogen principally associated with infection in cattle. Further investigation of animal isolates collected in 1999/2000 detected the 'R-type ACSSuT, PFGE xtm 1, PP 60, 2' profile among 13% of MR DT 104 isolates from pigs, 12% from poultry and 3% from cattle. Strains from animals and humans were further characterised by Fluorescent Amplified Fragment Length Polymorphism (FAFLP). Using the restriction enzymes HindI and HhaI FAFLP analysis demonstrated that the MR DT104 isolates from the summer 2000 outbreak were identical to the predominant FAFLP genotype found in the UK (shared by the first UK human isolates of MR DT104 from 1984). Non-outbreak human and animal isolates were a mixture of FAFLP genotypes - despite all being of the same, PP, R-type and PFGE profile. This investigation demonstrates the importance of a hierarchical molecular approach for the investigation of outbreaks of S. enterica.

Board 96. Pulsed-Field Gel Electrophoresis (PFGE) Comparison of Pharyngeal and Sterile Site Group A Streptococcal Isolates

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Minnesota Department of Health, Minneapolis, MN

Background: The Minnesota Department of Health (MDH) does PFGE subtyping of all group A streptococcal (GAS) isolates from invasive sites in MN. PFGE subtypes from invasive GAS isolates were compared with throat culture isolates collected during a 5-month period. An earlier MN study found that during a

community-wide outbreak of invasive GAS disease, the PFGE subtype of the outbreak strain matched the predominant strain found in pharyngeal isolates. **Methods:** Cases of invasive GAS disease are reported to MDH through active surveillance and isolates are submitted to the MDH laboratory. Five clinics representing different regions of the state sent up to 30 consecutive pharyngeal isolates collected each month for the first 5 months of 1999. PFGE on all invasive isolates obtained during the study period were compared to a representative sample of throat isolates. **Results:** Isolates were available for 96 of 108 (89%) of invasive GAS cases during the study period. The most common PFGE subtypes were: GA3 (12, 13%); GA131, GA34 and GA86 (7, 7% each); GA1 and GA5 (6, 6% each); and GA2 (5, 5%). Thirty-five other PFGE subtypes were identified, including 8 that were unique. Two hundred forty-three (45%) pharyngeal isolates were subtyped. The most common were: GA131 (71, 29%); GA3 (25, 10%); GA5 (6, 2%); GA1 (5, 2%); and GA2 and GA9 (4, 1% each). Sixty-two other subtypes were identified, including 11 that were unique. Geographic variation was noted for the distribution of the pharyngeal GA131 subtype, which accounted for 0-52% of isolates at each clinic. The GA3 subtype was the most evenly distributed with a range of 7-18%. Of 19 invasive cases from facilities in the same regions, 13 (68%) had a PFGE subtype that was found in throat cultures in that region. **Conclusions:** The most common PFGE subtypes for invasive GAS disease were also the most common for GAS pharyngitis. Although regional variability of certain PFGE subtypes was noted for both pharyngeal and invasive isolates, a similar distribution of PFGE subtypes was found among pharyngeal and invasive isolates from the same region. This concordance between invasive and pharyngeal GAS PFGE subtypes at a statewide level in a non-outbreak setting is consistent with findings from a previous regional study during an outbreak of invasive GAS disease. Monitoring pharyngeal isolates may be useful for detecting the presence of strains that have potential to cause an increased incidence or severity of invasive disease, and may be useful in guiding development of a GAS vaccine.

Board 97. Evaluation of Potential Behavioral and Household Risk Factors for *Pneumocystis carinii* Pneumonia

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Pneumocystis carinii pneumonia (PCP) is the leading life-threatening opportunistic infection in patients with AIDS in the United States, where it is responsible for an estimated 3,000 deaths per year. Despite recognition of the disease as an important cause of pneumonia in immunocompromised individuals, its exact mode of transmission remains unclear. This study investigates the potential behavioral and household risk factors for *P. carinii* exposure in immunocompromised and healthy individuals. Non-hospitalized patients with HIV/AIDS in the greater Atlanta area were recruited through local AIDS relief organizations. Non-immunocompromised individuals were recruited at the Centers for Disease Control and Prevention — Chamblee campus. Volunteers were interviewed using standardized questionnaires that collect data about demographics, medical history, potential exposures, and household information. Oral washes and environmental dust and dirt samples were collected and analyzed for the presence of *P. carinii*. DNA extracted from the samples was amplified by PCR to examine regions of the mitochondrial large subunit ribosomal RNA (*mtlsurRNA*) gene and the dihydropteroate synthase (DHPS) gene. Genotypes from environmental samples were compared with those from oral washes. To date, 65% of the 23 oral washes analyzed from AIDS patients were positive by PCR at one or both gene loci, while there were no positive samples found in 20 oral washes from the non-immunocompromised group ($p<0.001$). Of the environmental samples taken from the homes of AIDS patients and non-immunocompromised participants, 36% and 4% were positive, respectively N=36, N=27 (OR=14.70, p=0.0024). The genotypes observed were qualitatively and quantitatively similar to those observed in clinical studies. No statistically significant association ($p > 0.05$) was observed between a positive *P. carinii* oral wash and a variety of clinical and environmental or behavioral factors, including CD4 lymphocyte count, PCP prophylaxis, the use of central air, presence of house plants, outdoor activity, and exposure to cigarette smoke. The significant difference in the number of *P. carinii* positives in the HIV/AIDS versus non-immunocompromised groups suggests the possibility of human colonization and carriage of *P. carinii*.

Board 98. Heterogeneity in the Genetic Structure of *Toxoplasma gondii*

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Previous studies on the genetic structure of *Toxoplasma gondii* found little difference in strain composition between animal hosts or geographic locations. We genotyped 120 *T. gondii* isolates from various hosts including humans, bears, cats, chickens and pigs at 6 microsatellite loci. Homogeneity of allele distribution between isolates from different hosts was rejected ($P<0.05$, Fisher Exact Test) in 5 of the loci, indicating different strain composition between hosts. The most extreme differences in allele composition were associated with isolates from chickens. However, nearly all our chicken isolates originated from Brazil whereas most of the other isolates were from North America and Europe. Thus, either host or geographic effects may explain these results. Differences were also found in genetic diversity between host groups. Interestingly, diversity measured by the number of alleles (adjusted to sample size) was highest in human isolates ($P<0.05$). The same trend was observed based on expected heterozygosity, but the difference was not significant. Our results suggest a substantially greater genetic structure for *T. gondii* than previous studies have shown. A comprehensive analysis of these data is under way and will be presented.

Board 99. Genotyping and Characterization of Mycobacterium avium paratuberculosis Using Amplified Fragment Length Polymorphism

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AFLP (amplified fragment polymorphism) has been employed to compare Mycobacterium avium subsp. avium (M. avium) and Mycobacterium avium subsp paratuberculosis (MparaTb) for genetic differences that may be used as diagnostic probes that vary between or within subspecies. The AFLP technology is not simply a fingerprinting technology, but an enabling technology for genome research. It detects not only the primer sequence, but allows the detection of restriction fragment polymorphism (RFLP) and can be used to bridge genetic and physical maps. AFLP markers can be used to construct high-density genetic maps and is an effective method to construct DNA marker maps. We have employed this technology to map deletions in M. avium

relative to MparaTb and exploit these in the identification of knockout mutants and the study of host response. Ninety-six primer sets have been employed to characterize 23 MparaTb naturally occurring isolates and two M. avium isolates. Specifically, 16 MseI primers bearing selective dinucleotides at the 3'end were used in combination with PstI primers also bearing 3' selective nucleotides. Using specific primer sets, diagnostic patterns have been established for the identification of M. paratuberculosis isolates when compared with the ATCC strain of M. avium or with a field isolate of M. avium. One AFLP fragment unique to the MparaTb genome has been cloned, sequenced and identified. Primers generated within this region produce an appropriate PCR product in 12 of 19 clinical MparaTb isolates as well as the ATCC MparaTb isolate. The M. avium isolates and 7 of 20 MparaTb isolates fail to act as template for this primer set. This work reveals the presence of at least one polymorphism in the genome of MparaTb. The nature and extent of this polymorphism is under investigation. Additional MparaTb-specific bands, have been cloned and are being tested for their diagnostic and epidemiological value.

Board 100. Changing Patterns of Infection with Vero Cytotoxin-Producing *Escherichia coli* in Britain and Continental Europe

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During the 1980s Vero cytotoxin-producing *Escherichia coli* (VTEC), and particularly those belonging to serogroup O157, emerged as a cause of severe human disease including haemolytic uraemic syndrome. Increased incidence of infection is due partly to improved detection and reporting and also the ability to identify VTEC of all serogroups. Surveillance of VTEC infections has been increased both nationally and internationally through Enternet. Enternet is the surveillance network for VTEC and *salmonella* infections, funded by the European Commission and the participants include all 15 European Union members plus Australia, Canada, Japan Norway, South Africa and Switzerland. Laboratory based methods for strain characterisation are applied in combination with epidemiology and use serotyping, phage typing, VT gene typing as well as DNA-based methods such as pulsed field gel electrophoresis (PFGE). The rates of infection from 1995 to 2001 with VTEC O157 varied considerably from less than 0.2/100,000 in several continental European countries to 1 to 2/100,000 in England and Wales. Rates in Scotland are consistently the highest in Britain and peaked at 9.25 / 100,000 in 1996, the year of the very large central Scotland outbreak. Phage typing of VTEC O157 isolates from up to 12 countries has allowed the types to be followed over time. These data show a significant change in Britain with the emergence of PT21/28 as the currently predominant type and the decline of certain other types such as PT49. PFGE has been the key method for examination of heterogeneity within the common PTs. Surveillance of non O157 VTEC is limited but outbreaks caused by VTEC O26 have occurred in Europe recently. Detailed strain typing combined with increased surveillance and case-control studies have provided the evidence for demonstrating the importance of transmission of infection directly or indirectly from animals and their faeces in addition to foodborne and person to person routes. Rapid information exchange has been applied to both national and international outbreaks of VTEC O157 infection in Europe.

62 New or Rapid Diagnostics II

Tuesday, March 26, 8:30 a.m.
Grand Hall East

Board 101. The First one-block Revese Transcriptase Polymerase Chain Reaction (one-block-RT-PCR) for Diagnostic of Lassa-, Marburg-, Ebola- (Zaire, Sudan & Reston), Rift-Valley- and crimean-congo hemorrhagic Fever Virus in Clinical Specimen

A. Vahhabzadeh

Virology, Marburg, GERMANY

The term viral hemorrhagic fever (VHF) refers to a group of illnesses, which belong to four viral families (Arenaviridae, Bunyaviridae, Filoviridae and Flaviviridae). Most of these are endemic, but the deadly viral hemorrhagic fever could be spread to areas which are previously free from outbreaks. The diseases are characterized by an acute onset and, in some cases, a high mortality rate. Typical for these severe diseases is bleeding as a complication. We present some aspects of VHF: epidemiology, anomaly of blood values, pathogenic mechanism and membrane proteins, risks and prevention of nosocomial transmission, treatment, and future studies. The molecular biology of these agents has provided nucleotide sequence data that are the basis for the development of VHF-specific reverse transcriptase-polymerase chain reaction (RT-PCR) assay. Therefore, we developed the first one-block-RT-PCR, that allows simultaneous amplification for the rapid detection, diagnosis, surveillance and identification of viral RNA in specimen.

Board 102. Expression of Hepatitis E Virus Capsid Protein

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Hepatitis E virus (HEV) is a single-stranded positive-sense RNA virus and the etiological agent of acute hepatitis transmitted by the fecal-oral route. The capsid protein of HEV is encoded by open reading frame 2 (ORF2), containing 1,980 nucleotides, located at the 3' end of the HEV genome. By using recombinant DNA technologies, we expressed the full-length ORF2 in two insect cell-based expression systems: recombinant baculovirus (Bac-to-Bac, Gibco-BRL) and InsectSelect (Invitrogen). We took advantage of the ability of insect cells to posttranslationally process recombinant proteins in a way that closely resembles posttranslational modification of proteins in mammalian cells. The HEV capsid protein was expressed in Hi-5 cells and purified by sucrose density gradient centrifugation. Fractions were tested by immunoblotting with pooled sera obtained from HEV-convalescent patients. We observed three protein bands, which reacted with antibodies from patients' serum: a 75 kDa protein, which corresponded to the predicted molecular weight of the ORF2 gene product, a 150 kDa protein, which could represent a multimer of the ORF2 protein, and a 30 kDa product that may have been generated by proteolytic processing of the full-length ORF2 polypeptide. Analysis of the protein preparations by electron microscopy revealed the presence of self assembled virus-like particles (VLPs). The diameter of the VLPs was approximately 27-30 nm, which corresponds to the diameter of the native HEV virions. Both expression systems allowed the expression of full-length capsid protein, which assembled into VLPs. The time required to produce the recombinant protein in both systems was similar. The InsectSelect cloning procedure offered the convenience of being able to modify the length of the cloned fragment without the need for construction and amplification of recombinant baculovirus. In addition, InsectSelect

provided the continuous production of the recombinant protein by continuous culture.

Board 103. Improvement of Methods of Getting Erythrocytes Preparations for Plague Diagnostic

O. Y. Aimanova, T. I. Tugambaev, T. N. Kunitsa, G. I. Denisov, E. A. Ryabushko, A. G. Zhansarina

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Serological reactions using for plague diagnostic are bases on reveal of capsular antigen or antibodies to them. Conventional method of F1 getting (Baker at al., 1947) has defects, the very importance is decay of capsular antigens molecular on fragments, during acetone action. That is why we used for cells inactivation the warmed microbe mass 30 minutes on 70 C degrees with following bacteriological control. Immunology activity of getting plague erythrocytes antigen diagnostics, with using our capsular antigen was 2-4 higher in compare with commercial preparations, investigated different series of plague agglutinating serums. We have got experimental series of erythrocytes preparations, based on plague F2 and LPS. Diagnosticums prepared by using polyethilenglycol (PEG). Principle of this polymers action is displacement of sensitine to sorbent from solution, in water medium containing protein or LPS molecular, that promoting to raped sensibilization of formalized erythrocytes and getting possibility of preparations prepare in one stage. Sensitivity of antitoxic plague antigen diagnosticum in different series plague agglutinating serums were 1:32950, in serums of immunized laboratory animals - 1:2500. Diagnosticum didn't give positive result in RDGA with tularensis, brusselosis, salmonellesis ABCDE and enteroyerseniosis agglutinating serums, but revealed antibodies with pseudotuberculosis agglutinating serum in titer 1:1280. Specific activity of plague erythrocytes diagnosticum based on LPS with different series of plague agglutinating serums were 1:2560, with serums of immunized animals - 1:8240. Diagnosticum didn't reveal antibodies in RDGA with different agglutinating serums, and pseudotuberculosis too. Our results permission us to recommend these preparations for serological plague diagnostic.

Board 104. Evaluation of Two Biphasic Media for the Primary Culturing and Transport of Pathogenic Agents Associated with Meningitis and Acute Febrile Illness

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Background: Bacterial meningitis and undifferentiated fever (or acute febrile illness) are serious priority diseases in Egypt. As part of a collaborative surveillance activity between the Egyptian Ministry of Health and Population and NAMRU-3, clinical samples (CSF and blood, respectively) from both syndromes were collected from suspected patients presenting to 12 fever hospitals in diverse regions of the country. In this setting, blood is inoculated into Biphasic Blood Culture Bottles (BBC, PML Microbiologicals, Wilsonville, Oregon) and CSF is centrifuged and the sediment is Gram-stained, plated on suitable agars (if available) and Biphasic Trans-isolate medium (TI, Ajello et al., 1984), which has been designed as a growth and transport medium. Blood cultures are incubated for up to 2-3 weeks, while CSF cultures are incubated on TI for 1-2 days. Cultures are then kept at room temperature and transported every 3-4 weeks to NAMRU-3 for pathogen identification and QC of hospital results. Objectives: To evaluate the use of BBC and TI, as growth and transport media for a number of specific blood and CSF pathogens. **Methods:** Pure triplicate cultures of *S. typhi*, *Brucella melitensis*, *S. aureus*, *Neisseria meningitidis*, *H. influenzae*, and *S. pneumoniae* (clinical and ATCC strains) were suspended in sterile saline to 0.5 MacFarland, serially diluted ten-fold and inoculated into BBC and TI bottles (1ml inoculum /70 ml BBC and 0.5 ml/15 ml TI). Seven ml of fresh human blood were inoculated into each BBC. 100 ul of each bacterial dilution was also spread on blood and chocolate plates for CFU determination. All biphasic bottles were incubated at 37°C without venting. Identity and viability of growth was checked on a weekly basis. When no growth was observed within 2 weeks, the experiment was repeated. **Results:** Both types of culture media supported the viability of *H. influenzae* for 3-4 weeks and 9 weeks for *S. aureus* and *S. typhi* when 10-8 - 10-10 bacteria/ml (>5 CFU/ml) were inoculated. TI was superior for *B. melitensis* (>47 vs. 29 days in BBC). BBC seemed better than TI for *N. meningitides* and *S. pneumoniae* (32 and 30 days vs. 24 and 25 days, respectively), presumably because of the presence of blood. **Conclusion:** TI and BBC can support growth and transport of blood and CSF pathogens for 3-9 weeks depending on the species and inoculum concentration. Venting was not performed in this study to minimize the possible contamination of cultures, a modification which can be of value under field conditions.

Board 105. Use of PCR to Evaluate Patients with Meningitis in Egypt

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Objective: Bacterial meningitis is an important public health problem in Egypt and its epidemiology is complex due to the wide range of pathogens. The objective of this study was to evaluate polymerase chain reaction (PCR) as a method to enhance the diagnosis of the most important causes of bacterial meningitis in Egypt and evaluate its role as part of a meningitis surveillance project. **Methods:** Bacterial cultures and latex agglutination (at some institutions) were used to evaluate patients with a clinical diagnosis of meningitis admitted to infectious disease hospitals in diverse areas of Egypt. Excess cerebrospinal fluid (CSF) samples were stored in liquid nitrogen and sent to NAMRU-3 for further evaluation. When possible, bacterial isolates were collected and cultures were confirmed at NAMRU-3. PCR assays were carried out on specimens classified by laboratory personnel as "purulent" using primers specific for the ply gene (pneumolysin) of *S. pneumoniae* (SP), the bexA gene (capsule synthesis) of H. influenzae (HI) and the ctrA gene (capsular transport) of *N. meningitides* (NM). **Results:** Of the 105 CSF samples from patients with culture confirmed disease, 101 (96%) were PCR positive for the appropriate bacterial target sequence. The sensitivity of the assay for CSF from patients with culture confirmed SP was 97%(56/58), HI was 96%(25/26), and from patients with NM 95%(20/21). Of the 73 samples that were not culture confirmed at NAMRU-3, 40 (55%) were PCR positive for one of the three major agents. Most discordant results occurred in institutions with limited experience in microbiology or institutions that used latex to diagnose patients. Among the 1,135 culture-negative samples tested by PCR, *S. pneumoniae* was detected in 74 samples (6.5%), *H. influenzae* in 31 samples (2.8%) and N. meningitidis in 34 samples (3.2%). **Conclusions:** PCR is highly sensitive in the evaluation of patients with the most common causes of bacterial meningitis and can be used to confirm a bacterial etiology in culture-negative patients. PCR can also be used as a quality control measure to evaluate the performance of clinical laboratories developing microbiologic capability. The finding that < 15% of patients with unexplained purulent meningitis have evidence of infection with SP, HI, and NM by PCR warrants further investigation.

Board 106. Function of Enterohaemolysin Reaction in Marks Shiga-like Toxin (Verotoxin) Production *Escherichia coli*

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Function of enterohaemolysin reaction in marks Shiga-like toxin (Verotoxin) production *Escherichia coli* Vero (Shiga-like) toxin-producing *E.coli*(VTEC) infection is an emerging infection in China. In the last two years, the morbidity of the infection has been increasing. Antibiotics are widely used to treat diarrheic patients at all levels and that leads to acute renal failure and HUS in some patients. In order to control VETC infection, we carried out an investigation in 2000. We studied the patients, the surrounding environment and the cattle in the near farms. During the normal pathogens culturing and identification, we employed washed sheep blood agar plates which could easily screen out positive-enterohaemolysin-reaction strains. 65 strains 0157:H7 *E.coli* were isolated from the environment and the health sheep. 89.29% strains showed positive enterohaemolysin reaction and harbored one or more SLT genes by multiplex PCR assay. In some serious bloody diarrhea fecal samples, we didn't find 0157:H7 *E.coli*. It may imply that sporadic cases infection are mainly caused by no-0157:H7 in the region. For the 98 strains *E.coli* isolated from diarrheic children, 5 strains showed clear enterohemilysin reaction. Only one strain occured agglutination with 0157:H7 serotype. In addition, lysis zones are seen in 11 strains which showed week positive enterohemilysin reaction, but not as clear as standard 0157 lysis zone(not determined Stx gene at present). There are 9 strains 0157:H7 *E.coli* from diarrhea patients that did not carry SLT genes also exhibited haemolysis reaction. Although we found that 69 no-*E.coli* showed enterohemilysin phenomenon in washed sheep blood agar plates, this enterohemilysin reaction still has important significance. At present, many clinical laboratories report the isolation of *E.coli* from 40-60% samples that are not further characterized. Washed sheep blood agar plate is a simple tool for rapid isolation and identification of major VETC. It is especially fit for developing countries, for they lack funding, techniques and equipment. As the method induces some question, further studies are still needed.

Board 107. A Statistical Method to Improve Limit-Of-Detection for Microbead-Based Immunoassays

F. Y. Chuang, D. O. Nelson

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The use of microbead-based immunoassays to perform flow cytometric, multi-analyte determinations from single biological samples has grown increasingly popular for a number of clinical applications. We propose that this method may be well-suited for rapid screening of respiratory pathogens (such as influenza or inhalational anthrax) in nasopharyngeal swab samples. In order to be a useful screening tool for early or presymptomatic stages of infection, the proposed assay method may be required to detect microbial levels that are comparable to (or possibly less than) the concentration of microbeads used to capture the pathogens. Conventional flow cytometric measures of mean or median reporter fluorescence inherently require larger numbers of captured particles to meet the criteria for a "positive" test. We performed a series of titrations using fluorescent microbeads to capture either influenza Type A virus, or *Bacillus globigii* (a laboratory surrogate for *B. anthracis*) to characterize the progression of discrete changes that occur in the distribution of individual microbead reporter fluorescence intensities as the microbial concentration rises from normal baseline (i.e., zero antigen) to levels that approach the conventional limit-of-detection by FACS analysis. These observed concentration-dependent changes in intensity distribution were converted into a mathematical model describing the distribution of fluorescence intensity as a function of microbial concentration. We then evaluated a statistical detection approach based on the likelihood ratio test. In this approach, the observed distribution of fluorescence intensities in a new sample is used to estimate the underlying microbial concentration and test whether or not sufficient evidence exists to conclude that the pathogen is present. The test is considered positive when a quantity called the likelihood ratio exceeds a threshold parameter, K (which can be correlated to a false-positive rate that is deemed acceptable for the given screening application). Receiver-Operating Characteristic (ROC) curves were then used to estimate test sensitivity and specificity as a function of K. After comparing the limits-of-detection using this method versus conventional FACS analysis, we will discuss strategies to better utilize microbead-based immunoassays for direct microbial analysis of clinical samples.

Board 108. Rapid One Step RT-PCR for Diagnosis of Oropouche Virus Infection in Human Serum Samples

M. R. Nunes[1], A. T. Rosa[2], S. G. Rodrigues[1], G. B. Araújo[1], R. B. Tesh[2], R. E. Shope[2], **P. F. Vasconcelos**[1]

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Objective: The present study reports the development of a rapid one step RT-PCR protocol for diagnosis of *Oropouche virus* (OROV) infection in human samples. **Materials and Methods:** RNA extraction of 34 human serum samples (stored at -20°C) with confirmed OROV isolations was performed using the TRIZOL LS technique. Subsequently, a rapid RT-PCR protocol using specific primers for the OROV SRNA segment was used for viral RNA detection and amplification. The RT-PCR products were then viewed in a 1.2% agarose gel. Later, the results obtained were compared with previous results of serology, standard RT-PCR and virus isolation for determination of the sensitivity and specificity of the one step RT-PCR. **Results:** From a total of 34 samples tested, 11 (32,35%) were positive for OROV genome detection by this modified technique. Electrophoretic analysis in agarose gel revealed products with approximately 600 bp according with the molecular weight marker position. This procedure showed more sensitivity and less time consuming in comparison with standard RT-PCR. **Conclusion:** The development of this technique will allow early detection of OROV in future outbreaks, facilitating a rapid diagnosis and the improvement of control measures during outbreaks.

Board 109. Kinetic Analysis of a Peptide Nucleic Acid Synthesized to Bind the Crystal Protein Gene of Bacillus thuringiensis: Applications as a Simulant for Bacillus anthracis in Diagnostic Assays

C. Kolanko[1], S. C. Francesconi[2], A. Churilla[1]

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PNA is a synthetic molecule in which the standard nucleobases are attached to a polyamide backbone as opposed to the phosphodiester backbone of DNA. It is capable of forming highly stable duplexes with complimentary sequences, therefore making them more conducive as a probe used in diagnostic assays for environmental sampling. A custom peptide nucleic acid (PNA) comprised of the sequence AAG-TAA-CCC-TGA-AGT-Lys was synthesized matching a highly conserved region of the crystal protein gene (CryIA(c) gene) from the organism Bacillus thuringiensis subsp Kurstaki. This organism is being used as a simulant for *Bacillus anthracis* to develop a capture/detection diagnostic assay system. *B. thuringiensis's* genome is nearly identical to that of *B. anthracis* except for the presence of extrachromosomal cry sequences in *B. thuringiensis* and in the case of *B. anthracis*, sequences encoding lethal/edema factors. Employing surface plasmon resonance (SPR), using a BIAcore 3000 biosensor, the PNA probe was immobilized on a carboxyl-methyl dextran (CM5) surface via amine-coupling through the lysine residue located on the C-terminus of the probe. Direct detection of a 24-bp sequence tar-

get DNA was achieved over a detection range of 10-100 nM. After each detection of the target DNA, regeneration of the immobilized probe was carried out by exposing the surface to a wash of 50 mM NaOH. Additional binding studies were conducted determining binding kinetics, varying target DNA size and binding under different sampling conditions (salt, pH).

Board 110. Detection of Bacillus anthracis in Veterinary Clinical Samples Using Field Deployable Real-Time TaqMan PCR Technology

L. A. Cooper[1], T. L. Hadfield[2], W. Barnes[1], K. L. Lohman[1]

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Anthrax is a disease of both animals and humans. Its causative agent, the spore forming bacterium *Bacillus anthracis*, is endemic to the state of Texas in which periodic animal outbreaks occur. In early July of 2001, the Texas Animal Health Commission reported that suspected anthrax cases from the counties of Edwards, Uvalde, and Val Verde had been confirmed by the Texas Veterinary Medical Diagnostic Laboratory in College Station, Texas. Subsequently, numerous reports of downed animals with antemortem and/or postmortem pathology consistent with anthrax infection were reported from ranches throughout this region. Field observations also indicated that an unusually large anthrax outbreak was underway. In late July 2001, we initiated studies in which fluorescent real-time PCR was used to detect anthrax DNA in veterinary clinical samples. Specifically, we used five sets of *B. anthracis*-specific PCR primers and TaqMan probes to detect anthrax in cultured material, blood, tissue, nasal swabs, and environmental samples collected from suspect cases. The PCR targets were the genes encoding for *B. anthracis* capsular antigen (CAP), lethal factor (LF), edema factor (EF), and protective antigen (PA). The genetic regions encoding LF, EF, and PA are located on the PX01 plasmid and the CAP gene resides on the PX02 plasmid. The fifth primer set amplified a *B. anthracis* genomic region encoding small acid soluble proteins (SASP). Each reagent set was user-ready and supplied as pre-packaged ampules containing a dried down formulation of the primers, probe, and all required PCR reagents. Control organisms included Bacillus cereus, as well as the Pasteur and Sterne strains of *B. anthracis*. Thermocycling was performed with a mobile, capillary-based real-time PCR instrument known as the Ruggedized Advanced Pathogen Identification Device (RAPID; Idaho Technologies). Our main objective was to test our *B. anthracis* molecular reagents and protocols using real-world clinical material. Secondarily, the work establishes a proof of principle for the veterinary applications of rapid, field ready molecular tests and demonstrates the future applications of this technology during anthrax outbreaks.

Board 111. A Real-Time PCR Assay for the Universal Detection of Influenza A Viruses

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Molecular Epidemiology Branch, AFIERA/SDE, Brooks Air Force Base, San Antonio, TX

Influenza A viruses infect numerous avian and mammalian species and can undergo genetic reassortment in a process known as antigenic shift. Aquatic birds are the reservoir for fifteen hemagglutinin subtypes (H1-H15), several of which have crossed the species barrier to infect humans and other animals. PCR methods for the rapid identification and subtyping of influenza A viruses in humans have been described but are limited to the detection of currently circulating H1N1 and H3N2 viruses. These assays specifically target the hemagglutinin (HA) and neuraminidase genes (NA) of human influenza viruses but would not be able to distinguish novel influenza A reassortants. To universally detect influenza A viruses from humans and other animals, a 5'-nuclease TaqMan PCR assay targeting the highly conserved matrix (M) gene was developed. This assay was shown to be extremely sensitive, capable of detecting all 15 influenza subtypes (H1-H15) within three hours, and showed no cross reactivity to a reference panel of respiratory viruses and bacteria. From a public health perspective, this assay could be valuable for detecting antigenic shift variants that would otherwise go undetected using conventional PCR methods which are based on amplification of currently circulating HA and NA genes. Furthermore, state and federal laboratories could employ this rapid PCR assay to differentially diagnose influenza A from other upper respiratory infections and bioterrorism agents that exhibit flu-like symptoms.

Board 112. Development of a High Throughput Flow Analysis for the Detection of *Bacillus globigii* Spores

P. Estacio, N. Cahanding, S. Hadley, F. Milanovich, K. Venkateswaran

Lawrence Livermore National Laboratory, Livermore, CA

Unlike a single, short-lived high-explosion event, the use of biological warfare agents has the potential to produce a devastating number of casualty days and possibly months beyond the initial exposure incident. While there is no evidence of infection transmission between individuals by direct contact, *Bacillus anthracis* is capable of maintaining infection capability in a dormant spore form, allowing a sustained presence that provides the potential for delayed exposures. Recent acts of bioterrorism involving *Bacillus anthracis*-containing mail sent through the US Postal Service have left many trace elements of pathogenic spores on letters and packages, sorting machinery, and workspaces, endangering postal employees and the general public. Inherent in the timely response to an imminent threat to public health and safety comes the need to quickly identify anthrax infection-producing spores contained in a large number of individual samples with sensitivity and specificity comparable to current standard protocols. We demonstrate the development and usefulness of a multiplex immuno assay suited for the detection of bacterial spores with *Bacillus globigii* as a model system. This system is rapid and amenable for high-throughput analysis for differentiating the presence or absence of the bacterial antigen in the sample. Fluorescent-encoded microspheres are used in a liquid suspension array format in this multiplex assay. Measurement of intensity of the fluorescent-reporter antibody bound to each set of distinct microsphere population enables the detection of the bacterial antigen in the sample. In our initial investigations, up to one hundred samples were rapidly analyzed simultaneously for the presence of antigen. Twenty-five random samples contained the anthrax surrogate *Bacillus globigii* at 1x107cfu/ml. The twenty-five samples containing *Bacillus globigii* were correctly identified. The results display promise in a laboratory method that detects the presence of bacterial agents without sacrificing the integrity of an individual sample when analyzed in a multiplex format. This rapid and cost effective detection method will be used to evaluate environmental samples for the *Bacillus anthracis* presence in parallel with standard culture methods for comparison analysis.

Board 113. Signature Screening for Assay Development

E. A. Vitalis, J. R. Avila, L. E. Danganan, N. K. Montgomery, L. Radnedge, C. L. Strout, L. L. Ott, T. A. Kuczmarski, T. R. Slezak, P. M. McCready

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Early detection and accurate identification of biological agents are critical for successful handling of bioterrorist attacks or outbreaks of infectious diseases. The speed and reliability provided by DNA-based diagnostics allow for rapid, unambiguous detection of pathogens. We are developing signature-based real-time PCR assays to be provided to a community of users including domestic emergency response, (eg CDC and CBNP Domestic

Demonstration and Application Programs), USDA, public health agencies, and others. Accurate, reliable DNA-based pathogen detection requires the identification of genetic signatures that are regions of DNA both unique to that pathogen and conserved amongst its strains. We have developed a computational process that uses available DNA sequence information to generate a large number of potential DNA signatures. To ensure extremely high selectivity and sensitivity, we have established a screening protocol that rigorously screens DNA signatures. First, the candidate signatures are *in silico*screened against an immense DNA sequence database. This database contains sequence from over 600 microbes and viruses and has been compiled from multiple research centers around the world. Surviving candidate signature primer pairs then proceed to wet chemistry screening utilizing standard PCR with agarose gel electrophoresis. This step ensures that the primers will react across strains representative of the diversity of the pathogen (avoid false negative), but will not react with the DNAs of other organisms that could be present in a sample (avoid false positives). The collection of over 100 purified DNA templates used in this screening process include: 1) Strain panels—representative of the diversity of the target organism in nature; 2) Near neighbors—organisms that are closely related at the genetic level and therefore have the greatest likelihood of cross-reaction; 3) Soil samples from around the country—complex mixtures of organisms from diverse environmental collections; 4) Organisms causing similar clinical symptoms—organisms causing nonspecific clinical symptoms common to many infections agents; 5) Microbial diversity based on 16S analysis—organisms representative of microbial diversity; and 6) Eukaryotic DNA—DNA that may carry over from sample collection procedures. As a result of this screening process, more than 300 DNA signatures have been found to be highly specific for six top-priority threat bacteria and several high-impact viruses. Signatures are further tested for suitability for real-time TaqMan® fluorogenic PCR detection protocols. Assay performance is validated for a broad range of users in accordance with the FDA approval process. This work was performed under the auspices of the U. S. Department of Energy by the University of California, Lawrence Livermore National Laboratory under Contract No. W-7405-Eng-48.

Board 114. A Study of Virus-Cell Interaction by the Method of Dielectrophoresis

V. M. Generalov, T. S. Bakirov, A. G. Durymanov, A. A. Medvedev, V. D. Poryvaev, V. S. Toporkov, G. I. Tunnikov, A. N. Sergeev, V. A. Petrischenko, L. N. Shishkina, O. V. Fefelov

Research Institute of Aerobiology at State Research Center of Virology & Biotechnology "Vector", Koltsovo, RUSSIAN FEDERATION

An attempt to study theoretically and experimentally the changes in the cell membrane characteristics initiated by a virus even at the adsorption stage was undertaken in this work. The cell dielectrophoresis in the inhomogeneous alternate electric field (IAEF) was used as a basic method for determination of electrophysical characteristics of cells. The experimental data obtained by us show that adsorption of the viruses of enteritis and grippe in the cell membrane of erythrocytes of monkey and mouse leads to considerable decrease of the membrane capacity and increase of the cell equilibrium frequency as early as at the first minutes of interaction. The cell equilibrium frequency measurements can be used as a basis of the method for identification of cells infected by a virus and the method for measurement of the virus concentration in cell suspension.

Board 115. A Study of Cell Membrane Properties During Virus-Cell Interaction by the Method of Dielectrophoresis

A. G. Durymanov, V. M. Generalov, L. F. Bakulina, L. N. Shishkina, B. N. Zaitsev, T. S. Bakirov, O. V. Fefelov, E. P. Goncharova, L. E. Bulychev, V. S. Toporkov, A. A. Chepurnov

State Research Center of Virology & Biotechnology "Vector", Koltsovo, RUSSIAN FEDERATION

With the help of the of dielectrophoresis method it was shown that at the first stage of adsorption of virus by cell, for example: monkey erythrocyte — parvovirus, chicken erythrocyte — grippe virus, goose erythrocyte — rubella virus, occurs important changing of the cell membrane electrical capacity. Electron microscopy also confirmed that one minute after mixing of cell and virus suspensions on the membrane take place considerable morphological alternations, probably connected with large redistribution of the electrical charge on the cell surface. All study of virus-cell interactions were made in the special isotonic solution with low ionic force. Experimentally chosen components of the solution provide the possibility of dielectrophoresis (due to small conductance) and simultaneously very effective virus-cell interaction. It was offered a new approach for study the degree of external physical influences and chemical factors acting on biological activity of the cell.

63 Prions and Public Health

Tuesday, March 26, 8:30 a.m.
Grand Hall East

Board 117. Modeling the Age Distribution of vCJD and Predictive Epidemiology of the Disease

A. J. Valleron[1], P. Y. Boelle[2], R. Will[3], J. Y. Cesbron[4]

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The age distribution of the vCJD cases presently notified in the UK (as of May 2001) is strikingly young, with a mean age of 28 yrs, and only 7% of the subjects are more than 50 yrs. This young age distribution is not yet explained, as there are no published epidemiological, nor experimental work which explain this fact.

We have therefore devised a new epidemiological model of the vCJD, which focuses on this age characteristic of the vCJD: we have hypothesized that the risk of infection during the 1980 - 1989 period —where roughly 500,000 BSE infected cows are supposed to have entered the chain food- — was strongly dependent on the age: this risk was asumed to follow a plateau function of age before age 15, then to decrease exponentially after (Valleron et al., Science, 2001; 294: 1726-8). From this asumption, analysing the available information, we have derived an estimation of the incubation time (mean: 16.7 yrs) and of the future number of cases (less than 403 cases).

We shall present the results obtained with alternative models of the age-risk function. We shall present the sensitivity analysis of the results when possible contaminations that may have occured after 1989 are considered (1989 is the date of the UK bovine specified risk materials ban).

The results will be updated using the latest surveillance data available at the time of the conference.

64 Plenary Session III
Tuesday, March 26, 10:00 a.m.
Centennial Ballroom I/II

65 Plenary Session IV
Tuesday, March 26, 10:00 a.m.
Centennial Ballroom III/IV

68 First Encounters with New Diseases: The Clinician's Perspective
Tuesday, March 26, 11:30 a.m.
Regency Ballroom VI/VII

69 Pathogen Discovery
Tuesday, March 26, 1:00 p.m.
Centennial Ballroom I

70 Emerging Issues in Healthcare Settings
Tuesday, March 26, 1:00 p.m.
Centennial Ballroom II

71 Anthrax 2001: Lessons That Stunned Us
Tuesday, March 26, 1:00 p.m.
Centennial Ballroom III

72 Preventing Infectious Disease Through Behavior Change
Tuesday, March 26, 1:00 p.m.
Centennial Ballroom IV

73 The World and Its Moving Parts: Implications for Emerging Infectious Diseases
Tuesday, March 26, 1:00 p.m.
Regency Ballroom V

74 Emerging Zoonoses II
Tuesday, March 26, 2:45 p.m.
Centennial Ballroom I

Emerging Rickettsioses of the Thai-Myanmar Border

P. Parola[1,2,3], R. S. Miller[2], P. McDaniel[4], P. E. Fournier[3], D. Raoult[3], **S. R. Telford, III**[1], C. Wongsrichanalai[2]

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Background: Human rickettsioses known to occur in Thailand include mainly murine typhus (caused by *Rickettsia typhi*) and scrub typhus (caused by *Orientia tsutsugamushi*). Spotted fever group (SFG) rickettsioses have been occasionally noted but to date cases there have only been confirmed by general SFG serology. The etiologic agent(s) of SFG rickettiosis patients in Thailand have never been specifically identified by isolation or molecular characterisation, or by the use of specific serological assays using panels of SFG antigens. **Methods:** Fourteen patients clinically suspected (fever and/or rash and/or eschar and/or arthropod bites) or with sera positive for rickettsioses using a dot-ELISA test (PanBio-InDx multi-test Dip-S-Ticks) or microimmunofluorescence were selected from volunteers enrolled in a fever surveillance study conducted at the AFRIMS/Kwai River Christian Hospital Clinical Center in 2000-2001. This study site is located on the central part of the Thai-Myanmar border (Sangkhlaburi District, Kanchanaburi Province, Thailand), where rickettsioses have never been described. There, local Karen, Mon, Burmese and Thai populations are commonly exposed to flea- and tick- bites. Diagnostic tools for rickettsioses included serology by immunofluorescence using a panel of 13 rickettsial antigens of acute and convalescent (Day 21) samples. **Results:** Rickettsioses were serologically documented in all of the 14 patients by evidence of seroconversion and/or IgM. Three were murine typhus cases, three cases were scrub typhus and eight were SFG rickettsioses. All of these eight SFG rickettsioses cases demonstrated the highest titres to (i) *R. conorii* strain Indian, known as an agent of SFG rickettsiosis in India, and (ii) *R. helvetica*, an emerging pathogen known to be prevalent in Europe and in Japan. However, an unknown *Rickettsia* sp. cross-reactive with *R. conorii* and *R. helvetica* could also be implicated in our cases. These results provide for the first time a more precise documentation of SFG rickettsioses as well as murine typhus and scrub typhus in Kanchanaburi Province. Attempts at molecular detection or isolation are being undertaken to specifically identify the SFG agent(s) infecting residents of this area, with the ultimate objective of estimating its public health burden.

Clinical Management and Outcomes of Lyme Disease in Wisconsin

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Background: Lyme disease (LD) is a rapidly emerging public health problem, but little is known regarding diagnostic and treatment practices. We reviewed medical records of patients diagnosed with LD between 1992 and 1998 at two integrated health care networks in Wisconsin to assess clinical management and outcomes. **Methods:** We searched a health care database for encounters with ICD-9 codes consistent with LD (088.81, 695.9, 066.9) and reviewed the corresponding medical charts. We classified patients as having erythema migrans (EM), late (disseminated) LD, or not LD. We classified LD as 'probable' if the manifestations met the national surveillance case definition for LD, and 'possible' if there was 1) a clinically diagnosed EM with diameter < 5cm or unspecified, or 2) a positive serologic test with recurrent arthralgias or neurologic manifestations in a patient who did not otherwise meet the national case definition criteria. We classified illness episodes not meeting the criteria for probable or possible LD as 'not LD'. We assessed patient outcomes by reviewing all clinic visits up to three years after the initial visit. We classified patients as having 'complete resolution' if there was no mention of LD manifestations at the last clinic visit, as 'persistent LD' if manifestations persisted at the last visit, and 'insufficient information' if there was no follow-up visit documented in their medical record. **Results:** We identified 1,287 patients who were suspected to have LD by their healthcare providers. Six hundred forty-five (50%) of these patients had probable or possible LD: 304 (47%) had probable EM; 107 (17%) had possible EM; 72 (11%) had probable late LD; and 162 (25%) had possible late LD. The median age of all LD patients was 37 years, and 56% were male. Serologic LD testing was performed for 240 (79%) of probable EM patients, 71 (99%) of probable late LD patients, and 559 (87%) of 642 patients determined not to have LD. Of the 559 patients without LD who had serologic testing performed, 192 (34%) had three or more tests. Antimicrobials were given to 97% of patients with probable late LD and 92% of those without LD. Two or more courses of antimicrobials were given to 16% of patients with probable EM, 57% of patients with probable late LD, and 29% of patients without LD. Sixty-nine percent of patients with probable late LD had complete resolution of symptoms based on the medical record; 20% had persistent LD, and 11% had insufficient information. **Conclusions:** In this LD-endemic area, many symptomatic patients without LD have repeated serologic tests or multiple courses of antimicrobials. The majority of patients with disseminated LD appear to have complete resolution of symptoms.

A Neighborhood Outbreak of Q Fever Linked to a Goat Ranch in California

M. T. Jay[1], J. Douglas[2], K. Carter[1], J. D. Miller[3], J. McQuiston[3], G. Rishwain[4], E. Schneider[4], H. Thompson[3], D. Kelaita[2]

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Q fever, a rickettsial zoonoses caused by *Coxiella burnetii*, may manifest in humans as an acute nonspecific febrile illness or an insidious chronic disease often characterized by endocarditis. In the past decade, 1-8 sporadic cases of Q fever have been reported annually in California; two notable outbreaks in urban areas occurred during that time period and were associated with goats at a humane society and sheep at a petting farm, respectively. We describe the investigation of a recent goat-associated outbreak of Q fever among neighbors in a rural area of the Sierra Nevada foothills in California. The index case was a 56-year-old woman who was hospitalized in May 2001 with a febrile illness, adenopathy, interstitial lung infiltrates, and progressive weakness. A presumptive diagnosis of gall bladder disease led to surgery, but her signs and symptoms did not resolve. The patient developed hepatitis and was diagnosed with Q fever by serology approximately 6 weeks after illness onset. Interviews with the patient revealed that her husband had concurrently experienced a nonspecific febrile illness and subsequent serologic evaluation indicated a recent Q fever infection. The local public health nurse canvassed their neighborhood and discovered a 76-year-old man who had complained of intermittent fever and headache since April. Serologic testing of this patient was also consistent with a recent Q fever infection. All three patients were treated with doxycycline and recovered; however, we continue to monitor them for chronic manifestations. The patients lived at the end of a dusty dirt road approximately one-quarter mile past a goat herd pastured adjacent to the road. The goats were moved to this neighborhood during the previous year and had kidded in March-April. The ranch owner reported no history of reproductive problems in the herd, but a serosurvey revealed that 38/40 females (95%) and 4/6 (67%) males demonstrated antibodies to *C. burnetii*. The patients denied direct contact with the goats, therefore inhalation of aerosolized contaminated dust particles spread downwind or while driving past the goats was the suspected source of transmission. Recommendations were given to the ranch owner to minimize environmental contamination during the birthing season. In California, Q fever is emerging in rural and urban settings where susceptible individuals may have direct or indirect contact with infected small ruminants. This outbreak illustrates the potential for patients infected with Q fever to present without a history of direct contact with animal reservoirs and it underscores the importance of a thorough public health investigation to identify additional cases and implement control measures.

Q fever in the United States: Experience of Infectious Diseaes Consultants and Comparison to National Reporting During 2000

J. H. McQuiston[1], L. J. Strausbaugh[2], D. B. Jernigan[1], L. A. Liedtke[2], J. E. Childs[1], H. A. Thompson[1]

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Q fever, caused by *Coxiella burnetii*, is a zoonotic disease that is considered a potential agent of bioterrorism. Adequate surveillance and reporting of Q fever is important to understand disease patterns, and to help distinguish natural outbreaks from intentional release. Although Q fever was made nationally notifiable in 1999, little is known about the current prevalence or geographic endemnicity of this disease in the United States. In order to assess current diagnostic and reporting practices for Q fever, we sent a questionnaire to 784 infectious disease consultants that were members of the IDSA Emerging Infections Network (EIN). We queried EIN members regarding diagnoses of Q fever made during 2000, and whether they sought a diagnosis of Q fever for cases with compatible clinical presentations, including pneumonia or hepatitis of unknown etiology, and cases of culture-negative endocarditis. We also assessed members' knowledge about the types of laboratory tests that were available to them at different diagnostic laboratories. Responses were received from 419 (53%) EIN members. Twenty-four cases of Q fever were reported by 16 members from 12 states during 2000, including 16 cases of acute Q fever and 8 cases of chronic Q fever. Members also reported encountering over 3000 cases of pneumonia and over 1000 cases of hepatitis of unknown etiology; most members (75%) tested less than 5% of these cases for Q fever. EIN members also encountered 437 cases of culture-negative endocarditis, of which 64% were tested for Q fever. Serology was the most common laboratory test available to members, and most (>50%) used commercial laboratories rather

than state health department or hospital laboratories. Only 21 cases of Q fever were reported to CDC through the National Electronic Telecommunications System for Surveillance (NETSS) in 2000. At least 18 of the cases identified through the EIN survey were not reported to NETSS based on differences in reporting states. This survey indicates that Q fever is under-reported in the United States. Most EIN members surveyed did not routinely test cases of pneumonia or hepatitis of unknown etiology for Q fever, even though *C. burnetii* is sometimes associated with these syndromes. Although *C. burnetii* is a proven cause of culture-negative endocarditis, one third of cases encountered during were not tested for this agent. Furthermore, this survey indicates that at least 75% of diagnosed cases go unreported to national authorities. Improved recognition and reporting of Q fever by physicians will be important to assist with national bioterrorism preparedness goals.

Emerging Zoonoses: A Novel Epizootic of Skunks Infected with a Bat Variant of Rabies

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In January 2001, a striped skunk (Mephitis mephitis), submitted from a residential area in Flagstaff, Arizona was confirmed to be rabid. Historically, Flagstaff and the surrounding areas were considered to have enzootic rabies virus activity in bats, but not terrestrial mammals. Due to the unusual location of this rabid animal, tissues were sent to a regional reference laboratory at the Texas Department of Health for antigenic variant identification. Monoclonal antibody typing and genetic sequence analysis demonstrated that the skunk was infected with a variant of rabies virus associated with insectivorous bats. In the following six months, 18 additional skunks from Flagstaff were confirmed as infected with the same rabies virus variant. Further analysis at the Centers for Disease Control showed that rabies virus associated with bats was present in the salivary glands of some of these skunks. A multiphased campaign was initiated in response to this novel outbreak including active case surveillance, public awareness and education, low cost pet vaccination clinics, and a trap, vaccinate and release (TVR) program to attempt to control the epizootic. As of December 1, 2001, more than 210 skunks trapped in Flagstaff were parenterally vaccinated, eartagged and released. Surveillance efforts continue to assess the extent of the epizootic as well as the effectiveness of the TVR program. This epizootic represents the first documented sustained transmission of a rabies virus variant associated with insectivorous bats among terrestrial mammals. The importance of exploring unusual disease events and the need to develop new techniques to control rabies in wildlife are highlighted along with the critical roles of public health laboratories, community rabies prevention programs, and collaboration among local, state, federal and private entities.

Epidemiology of Raccoon and Skunk Rabies in the Eastern United States

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Since 1981, an epizootic of raccoon rabies that began near the Virginia/West Virginia border has spread through the eastern US. Because of the close association of this species with the human population, there is the possibility of an increased risk of rabies. In several eastern states cases of rabies among skunks now outnumber rabies cases in raccoons, which has raised concerns about the emergence of an independent maintenance cycle of rabies virus in skunks which would affect intervention strategies and control programs. The objectives of this study were to determine the temporal and spatial characteristics of rabies epizootics in raccoons and skunks. These data were then used to investigate the evidence for independent rabies virus cycling in skunk populations versus the sporadic spillover of rabies infection from raccoons. Surveillance data from 1981 through 2000 was obtained from the database compiled yearly by CDC from health departments of Connecticut, Delaware, Massachusetts, Maryland, North Carolina, New Jersey, New York, Pennsylvania, Rhode Island, Virginia, and West Virginia. The number of rabid raccoons and skunks submitted to county health departments per month was used to construct county-specific epizootic curves for time series analysis and to define intervals of epizootic versus enzootic rabies in both species. The first raccoon epizootic was significantly larger (median=40; range 4-785, $p<0.05$) than subsequent epizootics in raccoons, and also significantly greater than the first skunk epizootic (median=10; range 4-85, $p<0.05$). The size of subsequent epizootics among raccoons showed damped oscillations consistent with theoretical models, while skunk epizootics appeared uniform. There was a high degree of spatial correlation between epizootics in raccoons and skunks in regions where the raccoon-associated variant of rabies virus was enzootic. In several counties in Massachusetts and Rhode Island, cases of skunk rabies outnumbered cases in raccoons following the initial raccoon epizootic. However, in these counties there was a significant cross-correlation between the numbers of rabid raccoons and skunks. From our analysis we conclude that skunk rabies is temporally and spatially correlated with raccoon rabies in the eastern United States. The temporal patterning of skunk rabies is different from raccoons, and also from the patterns expected from theoretical models of rabies dynamics in raccoon and fox populations. There is currently insufficient epidemiologic and virologic data to conclude independent maintenance of rabies virus among skunks in areas where the raccoon-associated variant of rabies virus is enzootic. Future investigations need to assess environmental factors, such as differences in habitat suitability and population densities, and evidence of genetic changes in regional rabies virus variants associated with adaptation to a new host.

75 Foodborne and Waterborne Illness II

Tuesday, March 26, 2:45 p.m.
Centennial Ballroom II

Three Outbreaks of *E. coli* O157 Infections Due to Retail Ground Beef in Minnesota, 2000: Detection, Investigation, and Characteristics

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Background: *E. coli* O157 (O157) is the primary cause of hemolytic uremic syndrome (HUS) in the United States. Ground beef is a major source of O157. This report summarizes three O157 outbreaks due to retail ground beef that occurred in Minnesota during 2000. **Methods:** In Minnesota, clinical O157 isolates must be submitted to the Minnesota Department of Health (MDH). Isolates are subtyped by pulsed-field gel electrophoresis (PFGE) in real time, and cases are interviewed about potential exposures, including ground beef sources. If a temporal cluster of ≥5 cases with an indistinguishable PFGE subtype is observed, a community case-control study may be initiated if a common source is not apparent. Two controls obtained by sequential digit dialing using

the case's telephone number are matched to each case by age. **Results:** Outbreak 1 - Ten O157 isolates with the same PFGE subtype were submitted to MDH from 5 counties from December 1999 to February 2000. The median age of cases was 18 years (range, 4 to 62 years). A case-control study implicated consumption of ground beef from one chain of grocery stores (matched odds ratio [MOR], 11.8; 95% confidence interval [CI], 1.5-93). Outbreak 2 - In September 2000, MDH identified 3 O157 isolates with the same PFGE subtype; all 3 cases had consumed the same brand of ground beef patties; cultures of leftover patties from one case household yielded the outbreak PFGE subtype of O157. Outbreak 3 - During November 27-29, 2000 MDH identified 10 isolates of O157 with the same PFGE subtype. A case-control study implicated consumption of ground beef from one chain of grocery stores (MOR, 10.0; 95% CI, 1.0-434). Forty-two laboratory-confirmed outbreak cases were ultimately identified from 14 counties. The median age of cases was 20 years (range, 1 to 87 years); 24 cases were hospitalized, 3 had HUS, and 2 had colectomies. Twenty grocery stores were identified as sources of ground beef for cases. Ground beef exposures for most cases were comprised of non-hamburger items (e.g., casseroles, spaghetti sauce). O157 was isolated from ground beef from 3 case households, and from 18 of 43 intact packages from 3 grocery stores. Positive ground beef packages varied widely in weight and fat content. Store grinding records implicated a single supplier, resulting in a nationwide recall of 1.1 million pounds of ground beef. **Conclusions:** Retail ground beef outbreaks are difficult to identify because cases may not be tightly clustered in time and space. Strategies to enhance outbreak detection include real-time PFGE subtyping of all O157 isolates, rapid interviewing of cases with detailed questions about ground beef sources, community case-control studies, and aggressive culturing of ground beef from case households and retail sources. Contaminated ground beef from a common source may be sold in numerous grocery stores, in packages of variable weight and fat content.

Epidemiology of Shiga Toxin-Producing *Escherichia coli* (STEC) Infections in Connecticut, February 1, 2000 - January 31, 2001

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Background: Infections with Shiga toxin-producing *Escherichia coli* (STEC) are an important public health problem. *E. coli* O157 is the most common STEC in the United States (US). However, standard culture methods for *E. coli* O157 do not detect non-O157 STEC. Studies in other countries suggest that disease caused by non-O157 STEC is as prevalent as O157 STEC. Recognizing that standard cultures do not detect non-O157 STEC, some clinical laboratories in Connecticut have begun using tests to detect Shiga-toxin directly rather than culture for *E. coli* O157. We took advantage of the change in laboratory methods to characterize the prevalence and epidemiology of non-O157 STEC infection. **Methods:** To determine the relative frequency of non-O157 STEC, we conducted statewide laboratory-based surveillance for STEC at each of the 40 clinical microbiology laboratories in CT. As part of reporting requirements, clinical laboratories submit O157 isolates or shiga-toxin positive broths depending on which test they use to the State Laboratory for confirmation and further testing. Laboratory audits were performed to ensure that all cases of STEC were reported. To determine the spectrum of illness and risk factors for O157 and non-O157 STEC infections in Connecticut, we interviewed patients with STEC from February 1, 2000 through January 31, 2001. Differences between case-patients with non-O157 and patients with O157 STEC were assessed. **Results:** From February 1, 2000 through January 31, 2001, a total of 90 STEC infections were reported: 61 were detected by laboratories that culture for O157 and 29 were detected by laboratories that test directly for Shiga toxin. Among STEC infections identified by Shiga toxin testing only, 17 (59%) were found on subsequent testing by the state laboratory to be O157 and 12 (41%) were non-O157 STEC, comprising nine different serotypes. Overall, 78 O157 STEC and 12 non-O157 STEC were identified. Compared with patients who had O157 infection, patients with non-O157 were less likely to have diarrhea (p=0.017) or bloody stool (p=0.001), and were less likely to be hospitalized (p=0.005). No differences in demographics, food, or other exposures were identified between patients with non-O157 and O157 STEC infection. **Conclusions:** Based on results of Shiga toxin testing in Connecticut, non-O157 STEC was detected nearly as often as O157 STEC. Severity of illness caused by non-O157 STEC infection appears to be milder. Differences in risk factors between non-O157 STEC and O157 were not identified. Clinicians evaluating patients with diarrhea should consider infection with non-O157 STEC. Ongoing surveillance for both O157 and non-O157 STEC is needed to better define the incidence and epidemiology of STEC infections in Connecticut.

Microbiologic Testing to Identify Shiga Toxin-producing *E. coli* in HUS Patients: FoodNet 1997-2001

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Background: Hemolytic uremic syndrome (HUS) is a life threatening illness characterized by hemolytic anemia, thrombocytopenia, and acute renal failure. In developed countries, nearly all cases of HUS in children are caused by infection with Shiga toxin-producing *E. coli* (STEC), of which the most well known serotype is O157:H7. *E. coli* O157:H7 may be identified by the characteristic color of its colonies on Sorbitol-McConkey agar (SMAC). Other serotypes may be responsible for a portion of HUS cases, but their isolation from stool specimens is difficult since they do not share this distinguishing characteristic. With the advent EIA and PCR tests for Shiga toxin, and the potential for human serology to identify antibodies to STEC in HUS cases, the etiology of STEC in HUS may be better understood. **Methods:** Since 1997, HUS surveillance has been part of CDC's Foodborne Diseases Active Surveillance Network (FoodNet) at all sites (California, Colorado, Connecticut, Georgia, Maryland, Minnesota, New York, Tennessee, Oregon). Pediatric nephrologists in catchment areas for sites were contacted at least monthly for surveillance. Adult cases are reported in a passive system, as are cases outside of catchment areas. Case information is collected using standard medical and microbiologic record abstraction forms. **Results:** From 1997 through October, 2001, 322 cases of HUS were reported. The average incidence among sites was 0.2 per 100,000 population, with a range from 0.04 to 0.5. There were a total of 25 deaths (8%). Of 288 cases for which information was available, microbiologic testing identified STEC for 169 cases (59%). The proportion of cases with an STEC isolate identified increased from 38% in 1997 to 64% in 2000. All but 2 STEC identified were serotype O157:H7. Among all cases, 97% had stool cultured on SMAC and 38% had

stool tested for Shiga-toxin. Among cases without STEC identified, only 24% had Shiga toxin testing done. This proportion increased from 5% in 1997 to 47% in 2000. A total of 21 cases had STEC serology done to identify anti- O157, O111 or O126 antibody; 10 cases (48%) had detectable antibody to O157. No antibody against non-O157 STEC serotypes was detected among these cases. **Conclusion:** *E. coli* O157 causes the majority of pediatric HUS cases: the proportion caused by other STEC is uncertain. To determine the etiology of HUS in the United States, a complete microbiologic assessment should be conducted. Although SMAC culture is done for high proportion of cases, serotype indiscriminate tests for Shiga-toxin was conducted for only a minority of cases. Increased efforts by clinicians and clinical laboratories to conduct complete STEC testing will aid the specific diagnosis. Serologic testing for antibodies against the major STEC serotypes may be helpful if microbiologic tests are not done or negative.

Risk Factors for Sporadic *Escherichia coli* O157 Infections in the United States: a Case-control Study in FoodNet Sites, 1999-2000

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Background: *Escherichia coli* O157 (*E. coli* O157) infections can cause severe gastrointestinal illness, characterized by abdominal cramps and profuse, often bloody, diarrhea. In the United States, *E. coli* O157 infections cause an estimated 62,000 foodborne illnesses, 1,800 hospitalizations and 50 deaths each year. To identify new risk factors for illness and collect more information on previously identified risk factors, we conducted a matched case-control study of sporadic *E. coli* O157 infections in 1999-2000.

Methods: Culture-confirmed *E. coli* O157 cases were identified through active laboratory surveillance in 7 sites (California, Connecticut, Georgia, Minnesota, Maryland, New York, Oregon) as part of the CDC's Foodborne Diseases Active Surveillance Network (FoodNet). Age-matched controls were interviewed for each case within 7 days of the matched-case interview. Interviews were conducted by telephone using sequential digit dialing and a standardized questionnaire. Information was collected on demographics, clinical illness, and exposures (e.g., food, water, animal contact) in the 7 days before the case's onset. **Results:** Between February 1999 and April 2000, 326 cases and 591 matched controls were enrolled. In preliminary univariate analysis, infection was associated with eating pink hamburgers in the home (mOR=2.2, 95% CI= 1.2-4.3), thawing ground beef in microwave (mOR=1.5, 95% CI= 1.0-2.2), swimming in a pond, lake, river, or stream with cattle nearby (mOR=15.8, 95% CI=1.9-127.7), drinking pond, lake, river or stream water (mOR=3.5, 95% CI= 1.6-7.6), drinking from water fountains or pool water (mOR=3.5, 95% CI= 1.5-8.2), living on a farm (mOR=1.9, 95% CI= 1.1-3.4), and visiting a farm <12 times a year (mOR=3.0, 95% CI= 1.1-8.5). Consumption of ground turkey, pork chops or roast pork, organic produce, bottled water, or any of 12 produce items (romaine lettuce, red leaf lettuce, raw cabbage, onions, broccoli, carrots, cantaloupe, honeydew, strawberries, watermelon, apples, parsley, cilantro) had odds ratios of less than one. **Conclusions:** Preliminary analysis indicates undercooked ground beef, surface waters, and farms continue to be sources of sporadic *E. coli* O157 infections in the United States. However, unlike previous case-control studies, infections were not associated with restaurant consumption of undercooked ground beef, possibly reflecting improvements in restaurant handling of ground beef or changes in eating habits. Consumption of several produce items was negatively associated with *E. coli* O157 infections. Final interpretation awaits multivariate analysis.

Re-Estimating the Global Burden of Typhoid Fever

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Background: Reliable disease burden information is necessary to guide health policy decisions. Typhoid fever is common in the developing world, where surveillance data are extremely limited because the nonspecific clinical presentation of typhoid fever limits the value of syndrome-based surveillance and modern laboratory methods including blood culture are frequently not available to confirm infection. In 1986, a global estimate was 16 million illnesses and 600,000 deaths annually. We developed a method for refining this estimate. **Methods:** We reviewed the literature for population-based studies of typhoid fever incidence, complications, and mortality. Because studies of typhoid fever incidence frequently used age cohorts, we developed and used age-specific incidence curves for typhoid fever at various levels of endemicity to extrapolate incidence rates from age cohorts to other age groups within populations. Where countries lacked reliable typhoid fever incidence data, we extrapolated from neighboring countries within the regions that experience similar socioeconomic conditions. The regional, age-stratified, year 2000 population estimates of the United Nations Sex and Age Distribution of the World Populations were used to derive total annual cases from incidence data. Morbidity and mortality estimates were made from published series. **Results:** We found 22 population-based typhoid incidence studies from which extrapolations within regions could be made to develop a new estimate of the global typhoid fever burden. These were predominantly vaccine studies, or population-based studies designed specifically to measure typhoid incidence. We found that high typhoid fever incidence (>100/100,000/year) regions include south-central Asia and southeast Asia. Medium incidence (10-100/100,000/year) regions include the rest of Asia, Africa, Latin America and the Caribbean, and Oceania except for Australia and New Zealand. Europe, North America, and the rest of the developed world enjoy low typhoid fever incidence (<10/100,000/year). Overall, our model yields an estimate of the global typhoid fever disease burden of 11 million illnesses and 110,000 deaths. **Conclusions:** New data and improved understanding of typhoid fever epidemiology allowed us to further refine the global typhoid burden estimate. Using these, we find that typhoid fever remains a major global health burden. More detailed incidence studies in selected countries and regions are needed to further improve the estimate.

Yersinia enterocolitica Surveillance in Minnesota

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Background: *Yersinia enterocolitica* is an important cause of acute febrile enteritis, accounting for an estimated 96,000 cases annually in the U.S. *Y. enterocolitica* is ubiquitous; human pathogenic strains have been associated with defined bioserogroups. **Methods:** To improve our understanding of yersiniosis in Minnesota, we reviewed the clinical histories of *Y. enterocolitica* cases reported to the Minnesota Department of Health (MDH) from 1995 to 2000. We characterized *Y. enterocolitica* isolates by biotype and pulsed-field gel electrophoresis (PFGE). From the FoodNet Survey of Clinical Laboratory Practices 2000, we evaluated laboratory practices for enteric culture that might affect surveillance for *Yersinia* in Minnesota. **Results:** There were 151 cases of *Y. enterocolitica* reported to MDH from 1995 to 2000. The median age of cases was 35 years (range, 2 months to 93 years), and

59% of cases resided outside the Minneapolis-St. Paul (Twin Cities) metropolitan area. Thirty (22%) of 136 patients with known status were hospitalized for a mean of 8.2 days (range, 1-33 days). Of 126 *Y. enterocolitica* isolates submitted to MDH, 52 (41%) were classified as pathogenic biotypes, and 74 (59%) were classified as non-pathogenic biotypes based on pre-existing literature. Reported symptoms and length of hospitalization were similar for cases whether isolates were characterized as pathogenic or non-pathogenic. Thirty-eight (75%) of 51 pathogenic isolates subtyped were represented by one of five closely related PFGE patterns. All 74 of the non-pathogenic isolates were biotype 1A, and all 74 had different PFGE patterns. Of 61 Minnesota laboratories responding to the *Yersinia* section of the laboratory survey, 33 (54%) routinely test for *Yersinia* as part of their enteric screen. Only two of 28 Twin Cities metropolitan area laboratories that handle enteric samples test for *Yersinia*; 31 of 33 laboratories that test for *Yersinia* are located outside the Twin Cities metropolitan area in small city or county hospitals. Overall, the number of stool samples tested for *Yersinia*, both as part of enteric screens and specific physician requests, was 15,229 (21%) of 71,735 stool samples submitted for culture. **Conclusion:** Case-patients with yersiniosis in Minnesota had similar clinical illness regardless of whether their *Y. enterocolitica* isolates were classified as pathogenic or non-pathogenic based on biotype; isolates classified as non-pathogenic accounted for 59% of all isolates submitted during 1995-2000. Therefore, the clinical significance of putative non-pathogenic strains of *Y. enterocolitica* warrants further investigation. Survey of laboratory testing practices in Minnesota indicated that a minority of stool samples submitted for enteric culture were tested for *Yersinia*; thus, yersiniosis may be substantially under-diagnosed in Minnesota.

76 Antimicrobial Resistance II

Tuesday, March 26, 2:45 p.m.
Centennial Ballroom III

Randomized Trial of Day Care Staff Education to Improve Parent Knowledge and Attitudes Regarding Appropriate Antibiotic Use.

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Background: Antimicrobial resistance is an emerging public health problem and has focused attention on the importance of appropriate antibiotic use. Approximately 45% of children with a common cold who present to healthcare providers receive antibiotics inappropriately. Children in day care have frequent viral respiratory illnesses and parent education might reduce demand for antibiotics. We conducted a group-randomized trial to determine if presentations and materials for day care staff promote improved knowledge and attitudes among parents. **Methods:** Day care centers with capacity of 50 to 70 children were randomly selected from a database of all licensed facilities in Wisconsin. They were assigned to the intervention or control group and recruited sequentially until 300 households were represented per group based on information from the day care centers. Workers in intervention centers received a presentation about appropriate antibiotic use along with parent education materials. All centers subsequently distributed a self-administered survey to parents of children <5 years old. The survey asked questions about knowledge and attitudes of antibiotic use, resistance, and demand. One parent or guardian per household was requested to complete the survey. The data were analyzed using univariate, stratified, and multivariate analyses to control for confounding. **Results:** Six intervention centers and nine control centers participated and distributed the survey. Surveys were returned by 150 (50%) of 298 of parents at intervention centers and 150 (42%) of 361 parents at control centers. The mean age was 32 years in each group; intervention center parents were significantly more likely to be non-Hispanic white, college graduates, and insured. Analysis stratified by education level revealed that the college-educated intervention group parents correctly answered the nine knowledge questions more often than college-educated control group parents (> median) was significantly associated with white race (p=0.02) and being a college graduate (p=0.02) after adjusting for the design effect of day care clusters. There was a borderline association between a high knowledge score and the intervention group after adjusting for the design effect (p=0.06). There were no significant differences in attitudes of appropriate antibiotic use between the intervention and control groups. **Conclusions:** Presentations and distribution of educational materials to day care staff promote improved knowledge among parents of children <5 years old, particularly among more highly educated parents. Changing attitudes and beliefs might require more sustained or multifaceted interventions.

Quinupristin/Dalfopristin-Resistant *Enterococcus faecium* Isolated from Human Stools, Retail Chicken, and Retail Pork: EIP Enterococci Project

K. Gay, K. Joyce, J. E. Stevenson, F. J. Angulo, T. Barrett, and the NARMS Working Group

Centers for Disease Control and Prevention, Atlanta, GA

Background: With the emergence of vancomycin-resistant *Enterococcus faecium*, quinupristin/dalfopristin (Q/D) has become an important therapeutic for life-threatening enterococcal infections. Q/D was approved for human use in 1999. However, virginiamycin, a Q/D analogue, has been used in food animals since 1974. **Methods:** Between July 1998 and June 1999, laboratories in Georgia, Maryland, Minnesota, and Oregon used gram-positive selective media (CNA agar) to culture human stools from outpatients submitted to public health laboratories for other diagnostic reasons (n=334) and from chickens purchased from grocery stores (n=407). From July 1999 until June 2000 Michigan was added to the study and culture of pork samples (n=585) replaced chicken. *Enterococcus* isolates were forwarded to CDC for antimicrobial susceptibility testing by broth microdilution and Q/D-resistant isolates (MIC ≥ 4 µg/ml) were speciated by biochemical testing. **Results:** We examined enterococci isolates isolated from outpatients (n=286), retail chicken (n=984) and retail pork (n=897). Of 119 Q/D-resistant enterococci isolates isolated from humans, 3 (2%) were determined to be *E. faecium*. All 3 of the Q/D-resistant human *E. faecium* isolates had MICs for gentamicin < 250 µg/ml. Of 740 Q/D-resistant enterococci isolates isolated from retail chicken, 299 (40%) were *E. faecium*. Among the 299 Q/D-resistant *E. faecium* isolates from chicken, 80 (27%) had MICs for gentamicin ≥ 1000 µg/ml. Q/D resistance was found in 348 of the enterococci isolates isolated from pork. Of the 348 Q/D-resistant pork isolates, 7 (2%) were *E. faecium*. One of the Q/D-resistant pork *E. faecium* isolates had a MIC for gentamicin ≥ 1000 µg/ml; the other 6 had MICs < 64 µg/ml. **Conclusion:** Q/D-resistant *E. faecium* are more common in retail chicken than pork and human populations. Isolates from retail chickens are more likely than Q/D-resistant *E. faecium* from pork or human stools to also express high-level gentamicin resistance. Q/D-resistant *E. faecium* from retail chicken could potentially colonize humans, posing a serious threat to public health. The possibility that genetic determinants for Q/D resistance could be transferred from retail chicken and pork to human enterococcal isolates will be explored further.

Antimicrobial Resistance in *Salmonella* Serotype Typhimurium, R-Type ACSSuT, is Associated with Bacteremia: NARMS 1996-2000

K. Molbak[1], J. K. Varma[2], S. Rossiter[2], J. C. Lay[2], K. Joyce[2], K. Stamey[2], F. J. Angulo[2], and the NARMS Working Group[2]

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Background: Antimicrobial resistance in *Salmonella* increased during the 1990s, particularly amongst the most common serotype, *S.* Typhimurium. Multidrug-resistant *S.* Typhimurium phage type DT104, which usually is resistant to five drugs: ampicillin, chloramphenicol, streptomycin, sulfonamides, and tetracycline (R-type ACSSuT) is the most prevalent strain among *S.* Typhimurium. **Methods:** After serotyping, public health laboratories at 17 sites forward every 10th non-typhoidal *Salmonella* isolate to the National Antimicrobial Resistance Monitoring System (NARMS) for Enteric Bacteria. NARMS performs susceptibility testing for 14 antimicrobials, using broth microdilution according to NCCLS standards. **Results:** In 1996-2000, 1,513 (23%) of 6,670 isolates were serotype Typhimurium; of which 95% were from stool and 5% from blood. The median age of patients with *S.* Typhimurium from stool was 9 years (interquartile range 3-33 years) and from blood 42 years (interquartile range 32-63 years). Of the 1,513 isolates, 818 (54%) were resistant to ≥ 1 agent; 6% (53) of resistant isolates were from blood compared with 3% (21) of pan-susceptible isolates (OR 2.2; 95% CI 1.3 to 3.7). 462 (31%) isolates were R-type ACSSuT; 7% (33) were from blood compared with 3% of pan-susceptible (OR 2.5; 95% CI 1.5 to 4.5). Adjusting for age in a multivariable logistic regression model, R-type ACSSuT was 2.5 times (95% CI 1.3 to 4.6) more likely to be from blood, and resistant isolates other than R-type ACSSuT isolates were 1.7 times (95% CI 0.9 to 3.5) more likely to be from blood than pan-susceptible strains. **Conclusions:** Antimicrobial resistance in *S.* Typhimurium, particularly R-type ACSSuT, is associated with an increased risk of bacteremia. Further studies are needed to confirm this increased invasiveness and determine the potential biological mechanisms.

Antimicrobial Resistance in *Salmonella* is Associated with Increased Hospitalization:NARMS 1996-2000

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Background: Non-Typhoidal *Salmonella* is a leading cause of foodborne illness, and the prevalence of antimicrobial resistance has increased. Few studies have explored the human health consequences, other than treatment failures, associated with increasing resistance among *Salmonella*. **Methods:** The Foodborne Diseases Active Surveillance Network (FoodNet) has conducted laboratory-based surveillance for *Salmonella* since 1996. In 2000, nine sites, representing 11% of the U.S. population, completed case reports on all *Salmonella* infections confirmed at one of the >400 laboratories in surveillance. Case reports included hospitalization status at the time of culture collection or up to seven days later. Clinical laboratories send isolates for serotyping to public health laboratories, which forward every 10th non-Typhoidal *Salmonella* to the National Antimicrobial Resistance Monitoring System (NARMS). NARMS performs susceptibility testing via broth microdilution using NCCLS standards for 14 antimicrobials. We linked susceptibility results from NARMS to FoodNet case reports. **Results:** From 1996-2000, 15,653 cases of non-Typhoidal *Salmonella* were reported in FoodNet sites, and 1020 (7%) of these reports had both data on hospitalization and NARMS susceptibility results. Of these, 557 (55%) patients were female, and 163 (16%) were non-white. The median age was 25 years (inter-quartile range 5 to 42). The most common serotypes were Typhimurium (29%) and Enteritidis (19%). Isolates came from blood in 68 (7%), and hospitalization occurred in 238 (23%). Resistance to antimicrobials commonly used to treat *Salmonella* (cephalosporins, quinolones, or aminoglycosides) was found in 63 patients, 22 (35%) of whom were hospitalized. Patients with isolates resistant to one of these agents had a higher risk of hospitalization compared to patients with isolates susceptible to these agents (OR 1.8, 95% CI 1.1-3.2). Other risk factors for hospitalization included age, race, surveillance site, serotype, and bloodstream infection. After controlling for these factors in multivariate analysis, the association between resistance to one of these agents and hospitalization persisted (OR 2.0, 95% CI 1.1-3.7). Hospitalization also occurred more frequently in patients with isolates resistant to any antimicrobial, compared to those with pan-susceptible isolates (OR 1.5, 95% CI 1.0-2.2). **Conclusions:** Antimicrobial-resistant *Salmonella* infections were associated with an increased risk of hospitalization, particularly when isolates were resistant to commonly used agents. Given the limited number of patients studied, further research should explore factors that may have contributed to increased hospitalization, including failure of empiric antimicrobial therapy, increased co-morbidity among patients infected with resistant bacteria, and increased virulence of resistant *Salmonella*.

Emerging Fluoroquinolone Resistance among Non-Typhoidal *Salmonella* in the United States: NARMS 1996-2000

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Background: Fluoroquinolones (e.g., ciprofloxacin) commonly are used for treating *Salmonella* infections in adults; fluoroquinolones (e.g. enrofloxacin) also are used in cattle, chickens, and turkeys in the United States. Among *Salmonella*, cross-resistance occurs for all fluoroquinolones and usually arises from accumulation of two mutations in the *gyrA* gene. A single mutation of the *gyrA* gene confers decreased susceptibility to fluoroquinolones and has been associated with treatment failures. **Methods:** The National Antimicrobial Resistance Monitoring System (NARMS) for Enteric Bacteria was established in 1996 to monitor antimicrobial resistance in *Salmonella* and other enteric bacteria. After serotyping, public health laboratories in the 17 NARMS participating sites forwarded every tenth non-typhoidal *Salmonella* isolate to CDC for susceptibility testing to ciprofloxacin and 16 other antimicrobial agents using broth microdilution (Sensititre®) according to NCCLS standards. Patients with isolates exhibiting decreased susceptibility (MIC ≥ 0.25 µ?g/ml) to ciprofloxacin, including ciprofloxacin resistance (MIC ≥ 4 µg/ml), were interviewed. **Results:** From 1996-2000, 57 (0.8%) of 6970 non-typhoidal *Salmonella* isolates tested demonstrated decreased susceptibility to ciprofloxacin. The percent of isolates that demonstrate decreased susceptibility to fluoroquinolones was 0.4% (5/1326) in 1996 and 1.4% (20/1378) in 2000. Seven (0.1%) of these isolates were ciprofloxacin-resistant (MIC ≥ 4 µg/ml) and included serotype Senftenberg (n = 3), Schwarzengrund (n = 3), and Indiana (n = 1). All 7 infections were associated with international travel. Of the 50 isolates with ciprofloxacin MICs ≥ 0.25 µg/ml and < 4 µg/ml, the most common serotypes were Enteritidis (n = 14), Berta (n = 7), Typhimurium (n = 6), and Virchow (n = 5). Twenty-eight (56%) of these 50 patients were interviewed; 20 (71%) of the 28 patients interviewed did not travel internationally in the week before illness

onset. **Conclusion:** Emerging fluoroquinolone resistance in non-typhoidal *Salmonella* is evident. Resistant isolates were associated with international travel, whereas other isolates with decreased susceptibility were from infections acquired domestically. The sources of infection were not investigated, but many presumably were acquired through eating contaminated food. Mitigation efforts in partnership with the agricultural and veterinary communities are needed to limit use of fluoroquinolones and to preserve the efficacy of this commonly used antimicrobial agent.

Prevalence of Salmonella spp. and Campylobacter spp. Following the Discontinued Use of Antimicrobial Growth Promoters in Broilers and Swine in Denmark

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Introduction: Previous studies have suggested that the use of antibiotics in food-producing animals may affect pathogen shedding, causing either an increase or decrease in pathogen load. In 1998, the food animal industries in Denmark decided to stop the use of antibiotics for growth promotion in food animals by the end of 1999. We examined the effect of discontinued use on pathogen load by comparing the mean prevalence of Salmonella and Campylobacter in broiler flocks and swine herds before and after the withdrawal of antimicrobial growth promoters in Danish food animal production.

Methods: Broiler flocks were examined for Salmonella 3 weeks prior to slaughter by sock samples and after slaughter by neck-skin samples. Campylobacter in broilers was measured by cloacal swab samples of ten birds per flock at slaughter. Salmonella in swineherds was monitored by serological testing of meat juice samples. Herds were then classified into levels 1, 2 or 3 with level 1 herds having no or few sero-reactors and level 3 herds having a high level of sero-reactors. Salmonella in pork was measured by monthly slaughterhouse samples. A t-test for comparisons of means was performed using SAS Version 8.0. Equal time periods were used for comparisons, however periods varied between pathogen and animal species.

Results: Salmonella in broilers: The mean percent of flocks testing positive during period 1 (before withdrawal) was 14.4 (range: 3.7-33.6) for ante-mortem examination and 17 (range: 8.1-38.8) for post-mortem. Period 2 samples averaged 2.4 (range: 0.2-5.8) and 4.9 (range: 0.7-24.9) respectively. A comparisons of means showed that period 2 (after withdrawal) was significantly lower for both ante-mortem ($p<0.0001$) and post-mortem samples ($p<0.0001$). Campylobacter in broilers: The percentage of positive flocks during period 1 was 35.3 (11.4-64.8) and period 2 was 40.8 (18-77). There was no difference in the means ($p=0.2470$). Salmonella in pigs: The percentage of herds classified as level 2 or 3 during period 1 was 5 (4.2-6.2) and 3.3 (2.5-4.4) for period 2. A comparisons of means showed that period 2 was significantly lower ($p<0.0001$). Salmonella in pork: The percentage of positive samples at slaughter was 1.1 (0.5-1.8) for period 1 compared with 0.8 (0.4-1.5) for period 2. A comparisons of means showed that period 2 was significantly lower ($p=0.0290$).

Conclusion: Contrary to producer concerns that the discontinued use of antibiotics would lead to an increase in pathogen shedding, our study showed that there was a significant decrease in the levels of Salmonella in broilers and swine, and no change in the prevalence of Campylobacter in broilers or Salmonella in fresh pork. Although it is likely that the decreases are mainly due to successful control programs and better sampling methods, we cannot discount the effect that the removal of growth promoters may play. Additional research and more in-depth analysis are needed to fully explain the observed effects.

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Tuesday, March 26, 2:45 p.m.
Centennial Ballroom IV

A Greenhouse Study to Model Potential Field Use of Genetically Modified Bacterial Symbionts for Chagas Disease Control

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Chagas disease, a parasitic disease caused by the protozoan *Trypanosoma cruzi* and transmitted by triatomine bugs, affects 16-18 million people annually in Central and South America. While Chagas disease control strategies have primarily focused on the elimination of vector populations through insecticide spraying, drawbacks to this control method include the development of insecticide resistance, environmental hazards, as well as general issues concerning the sustainability and practicality of continual spraying. In exploring alternate possibilities for control measures, we have looked to genetic modification of the bacterial symbionts found in the gut of the triatomine bugs. These symbionts, which are transferred between bugs by coprophagy, are essential for growth and reproduction of the insects. In the vector-symbiont intervention (VSI) project, we genetically modified *Rhodococcus rhodnii*, a bacterial symbiont of the Chagas disease vector *Rhodnius prolixus*, to express genes whose products render the triatomine bug incapable of transmitting the disease. We also have developed a formulation of these genetically modified (GM) bacteria (CRUZIGUARD) that would enable introduction and spread of the GM bacteria into natural insect populations, thereby serving as a novel and potentially effective way to prevent disease transmission. In previous laboratory studies, we have shown that the bugs can easily acquire the GM symbionts and that these symbionts are stable within the bug, allow for normal development of the bug, and can reduce or eliminate the *T. cruzi* from the gut of the bug. In the current study, we have designed and executed a simulated field study inside a reed hut (dimensions 6 feet x 6 feet x 6 feet), enclosed within a double-containment tent system inside a greenhouse. Thirty-six *R. prolixus* females containing native bacteria were released in the hut and allowed to lay eggs. After the eggs hatched, CRUZIGUARD prepared with *Rhodococcus rhodnii* genetically modified to contain only the marker gene *LacZ*, was applied to the hut. Bugs were removed from the hut on four different occasions, at approximately one-month intervals, and the midguts were assayed at various instars for bacteria. Of the 67 bugs assayed to date, 38 (56.7%) contained transformed *R. rhodnii*, and 24 (35.8%) contained the native form of these symbiont bacteria. Three bugs harbored *Gordona*, another native bacterial symbiont of *R. prolixus*, and no bacterial isolates were obtained from two early instars. In addition to the midgut assays, we concurrently assayed the CRUZIGUARD each week in order to determine its viability as a function of time. Over a 5-month period, approximately one log reduction of the bacteria was noted. Observations were made on various ways of improving efficiency of preferential uptake of the GM symbionts. These initial results, however, are considered to be very positive.

Ecological Niche Modeling and Differentiation of Populations of *Triatoma brasiliensis* Neiva, 1911, the Most Important Chagas Disease Vector in Northeastern Brazil (Hemiptera, Reduviidae, Triatominae)

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Ecological niche modeling has allowed numerous advances in understanding the geographic ecology of species, including distributional predictions, distributional change and invasion, and assessment of ecological differences. We used this tool to characterize ecological differentiation of *Triatoma brasiliensis* populations, the most important Chagas disease vector in northeastern Brazil. The species' ecological niche was modeled based on data from the Fundação Nacional de Saúde of Brazil (1997-1999) with the Genetic Algorithm for Rule Set Prediction (GARP). This method involves a machine-learning approach to detecting associations between occurrence points and ecological characteristics of regions. Four independent 'ecological niche models' were developed and used to test for ecological differences among *T. brasiliensis* populations (brasiliensis, macromelasoma, juazeiro and melanica). These four populations can be distinguished on the basis of patterns of coloration. These differences are also reflected in morphological, ecological, and genetic variation. These models confirmed four ecologically distinct and differentiated populations, and allowed characterization of dimensions of niche differentiation. Patterns of ecological similarity matched patterns of molecular genetic distances, suggesting that "*T. brasiliensis*" is a complex of distinct populations at various points in the process of speciation. The brasiliensis population was best able to predict the distributions of the other populations. Interestingly, ecological similarity was not symmetric — brasiliensis predicts macromelasoma and juazeiro very well (0.87), yet the converse was not true (0.44 and 0.51). The distribution of melanica was poorly predicted by other populations (0.38, 0,10 and 0.21), and melanica was little able to predict other populations. Because of the remarkably widest niche model observed for brasiliensis population it is possible that this population also presents the highest potential to invade new areas. Application of GARP modeling technology in understanding species' distributions in geographic and ecological space is relatively new, and yet increasingly supported by rigorous empirical tests. This paper represents a first application in the field of epidemiology and disease transmission. Future analyses will approach the challenges of predicting dispersal potential for this species, changes to be expected as a part of climate change, and transitions between sylvatic and domestic distributional situations for Chagas disease vectors.

In vivo Sensitivity of *Plasmodium falciparum* to Chloroquine and Sulfadoxine/Pyrimethamine During an Outbreak of Malaria in Burundi, 2001

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Introduction: A major outbreak of *Plasmodium falciparum (Pf)* malaria erupted in Burundi in September 2000. Immediately, suspicions were raised about the clinical efficacy of the antimalarial drugs of reference used in the country, namely chloroquine (CQ, first-line drug) and sulfadoxine/pyrimethamine (SP, second-line drug). This malaria epidemic led to thousands of deaths between September 2000 and May 2001. In this context, the objective of the *in vivo* sensitivity studies was to estimate the efficacy of CQ and SP and of the combination CQ+SP in the treatment of uncomplicated Pf malaria in the provinces of Kayanza and Karuzi.

Methods: The protocol was adapted from the World Health Organization protocol for areas of intense transmission. Children 6 to 59 months old were recruited in health centres, and classified as therapeutic failures or adequate responders according to both clinical and parasitological criteria. Follow-up was of 14 days in Kayanza and of 28 days in Karuzi.

Results: The studies were conducted between January and April 2001. Overall, 465 children were included. Age, mean parasitaemia and temperature on inclusion were similar among the groups. The CQ parasitological failure rates (PFR) at day 14 were 100% and 97·8% [86·8 - 99·9] in Kayanza and Karuzi respectively. With SP, PFR at day 14 were 73·7% [64·7 - 81·2] and 89·7% [80·8 - 94·9] in Kayanza and Karuzi respectively. The PFR of patients treated with SP rose to 96·1% [90·4 - 98·9] when followed until day 28. Finally, among 119 patients treated with CQ+SP, PFR at day 14 was 54·8 % [44·8 - 64·5].

Discussion: The high levels of resistance to CQ and SP observed in Burundi raise questions about the use of these drugs during the malaria epidemic in this country. Efforts were made during and after the outbreak to resort to more effective compounds, like combinations of antimalarials including an artemisinin derivatives. Future policies for treatment of malaria in Africa will necessarily rely on more expensive therapies. Their deployment should be foreseen along with improvements in the diagnostic capacities throughout health systems.

Risk Factors for Lyme Borreliosis: A German Case-Control Study

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Introduction: Although Lyme borreliosis is a public health problem throughout much of the world, most risk factor studies have been carried out in the USA, where only one of the 3 defined human pathogenic *Borrelia burgdorferi* s.l. species is found and whose tick vector species differ from those in Europe. We studied the risk factors for erythema migrans (EM), a characteristic early sign, in a German district, Landkreis Oder-Spree (LOS), where the reported disease incidence (48 cases/100,000 inhabitants) is high compared to other districts.

Methods: A case-control study was conducted. Cases were patients with EM ³5 cm, living in the district, reported between 1. May and 31. December 1999. Controls were selected using random digit dialling, and included if they lived in LOS and had no EM-like lesion during 1999. Standard telephone interviews were conducted. A 3:1 case-control ratio was attempted. Questions on exposures related to the 4-week interval before the lesion (cases) occurred, or before the interview (controls). In four areas, which were selected after mapping the residence and exposure location of cases and controls, ticks (Ixodes ricinus) were collected and tested for *B. burgdorferi* s.l. by immunofluorescence assay (IFA) and polymerase chain reaction (PCR).

Results: Analysis included 48 cases and 118 controls. Cases were on average 12 years older than controls (p=0.02). Cases spent twice as much time in gardens (p=0.04) and were 2.2 times more likely to have been in a garden within 200 metres of woods (CI 95% 1.1 - 4.6). Cases were more likely to have had skin contact with garden bushes (p=0.02) and countryside bushes (p=0.04). Cases were no more likely than controls to work or pursue recreational activities in the countryside. There was no difference in frequency of pet ownership, but pets of cases were more likely to have ticks (OR: 2.6; CI 95% 1.1 - 5.7). In a logistic regression model, age, having pets with ticks, visiting a garden within 200m of woods, and skin contact with bushes in the countryside were independent risk factors for EM. Sixty-five percent of cases and controls never used preventive measures, such as tick removal

after potential exposures. Twenty-two percent (100/455) of ticks from 3 areas were positive for *B. burgdorferi* s.l by IFA, with no difference in prevalence among areas. In contrast 12% (62/514) of ticks were positive by PCR, with a prevalence varying from 2-23% among the four areas.

Conclusion: Peridomestic exposures, particularly in gardens, were important risk factors for EM. Having pets with ticks may signal higher risk. Similar to US findings, these results indicate that tick exposure prevention in the peridomestic setting will likely have the greatest impact on disease incidence. The varying results of Borrelia testing of ticks using IFA and PCR indicate a need to further standardize test methods.

Dengue Fever Outbreak in Hawaii – 2001

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Background: Autochthonous dengue infections have not been reported in Hawaii since 1945. On September 12, 2001 a physician in Hana, Maui called the Hawaii Department of Health (HDOH) to report an unusual febrile illness in a local resident with no travel history. Dengue was confirmed at the Centers for Disease Control and Prevention and an investigation ensued to determine the extent of the outbreak and assess factors that contributed to the emergence of dengue in Hawaii.

Methods: Active surveillance for febrile illness was initiated at 50 clinics and hospitals statewide. HDOH staff interviewed suspected case-patients, queried location-proximal contacts, and obtained blood samples for dengue diagnostic testing at CDC and HDOH. Ad-hoc mosquito surveys were performed on 4 islands.

Results: As of December 1, 2001, 1380 persons have been evaluated for dengue and 89 locally-acquired infections have been confirmed; dengue virus, serotype 1, was isolated from 13 of those patients. Laboratory positive autochthonous dengue cases were identified with onset in June (4 cases), July (7 cases), August (9 cases), September (49 cases), October (17 cases) and November (3 cases), 2001. The island of residence was Maui, Oahu, and Kauai for 65, 20, and 4 of the cases, respectively. Fifty-five (85%) of the Maui cases had exposure in the Hana area; only 2 of 24 Oahu and Kauai cases had exposure in Maui. Patient ages ranged from 1 to 77 years (mean - 39 years); 62% were male. The most frequently reported symptoms for 86 patients with complete histories were fever (92%), body pain (88%), headache (84%), chills (80%), joint pain (69%), rash (62%), and eye pain (52%). Hemorrhagic manifestations included petechiae (17%), bleeding gums (9%), epistaxis (7%), melena (5%) and menorrhagia (5%). Although 3 patients were hospitalized, most illnesses were mild; there was no dengue hemorrhagic fever. To date, there have been no confirmed dengue infections among visitors staying in guest accommodations. All mosquitoes captured in the Hana area in September 2001 were identified as Aedes albopictus; Ae. aegypti was not found on any island. Preceding this outbreak 24 cases of dengue infection were imported to the islands of Oahu (15 cases), Hawaii (4 cases), Maui (3 cases) and Kauai (2 cases) in 2001. This compares to a mean of 2 imported cases per year for the period 1992-2000 (range 0-8). In 3 instances (1 each on the affected islands) one or more autochthonous cases were linked to persons with illness after recent travel to other Pacific Islands with epidemic dengue.

Conclusions: This is the first known transmission of dengue fever in Hawaii in 56 years. Available data implicate Ae. albopictus as the mosquito vector. In response to the outbreak, extensive mosquito control measures were initiated on all islands, including spraying with residual adulticides, house-to-house source reduction campaigns, and public education to residents and visitors.

Re-Introduction of Dengue 3 in Aragua, Venezuela: Clinical, Epidemiological and Laboratory Features of a New Outbreak

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A new outbreak of dengue occurred in Aragua, Venezuela, caused by a Den-3 virus reintroduced after 36 years of its last detection. In this study we analyzed clinical, epidemiological and laboratory-based surveillance data from 2,604 suspected dengue patients reported by sentinel health centers between September 2000 and November 2001. Clinical diagnosis was made following WHO guidelines for dengue case definition. Laboratory diagnosis were made by virus isolation in C6/36 cells followed by typing with monoclonal antibodies (VI), reverse transcriptase-polymerase chain reaction (RT-PCR), IgM- and IgG-capture ELISAs. We also performed phylogenetic analysis of 10 dengue 3 isolates from dengue fever (DF) patients, as well as RT-PCR dengue virus detection and typing on *Aedes aegypti* captured in some houses with confirmed dengue patients. Of 1,227 confirmed dengue cases, 979 (79.8%) were infected by Den-3, 126 by Den 2 (10.3%), 104 by Den 4 (8,5%) and 18 by Den 1 (1.5%). Also, Den-3 and Den-1 infected *A. aegypti* were detected in neighboring dwellings housing DF patients. Phylogenetic analysis revealed that Den-3 isolates belonged to subtype III, which includes viruses from Sri Lanka, India, Samoa, and probably the one introduced in Nicaragua in 1994. Den-3 virus transmission occurred uninterrupted throughout the studied period (61weeks), and circulated together with at least another serotype almost continuously during the 53 weeks and alone the remaining weeks. Den-3 virus was detected in all 17 municipalities of Aragua State and hyperendemicity of two or more serotypes was the rule in 16 (94,1%) of them. As expected, 95.1% of the Den-3 infected cases were <40 years old people. Infections were prevalent in males of all age groups but 5 - 9 and ≥ 40 years old ones. Undifferentiated febrile and DF were the predominant clinical forms in Den-3 infected patients (99.5%), and the very few cases that met all four WHO clinical criteria for DHF were grades I (0.1%), II (0,2%) and IV (0,2%). GAC-ELISA analysis of 46 paired sera of Den-3 infected patients revealed that 73.9% were secondary infections. This new Den-3 outbreak in Aragua, Venezuela, is the worst ever recorded in terms of morbidity and geographic extension; yet, severe clinical forms (DHF) were almost absent in spite of the intense hyperendemicity and the high rates of secondary infections.

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Tuesday, March 26, 2:45 p.m.
Regency Ballroom V

An Evaluation of an Educational Videotape to Prevent Botulism Among Alaska Natives

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Background: Rates of foodborne botulism in Alaska are the highest in the U.S. Since 1980, the incidence of foodborne botulism has doubled in Alaska, and all cases have been associated with eating traditional Alaska Native foods. We conducted a survey among southwestern Alaska Natives regarding traditional food preparation and consumption practices and used the results to guide prevention messages that were incorporated into an educational video. In April 2000, the video was distributed to all rural schools and medical facilities in Alaska. We repeated the survey to evaluate the specific impact of the video on food preparation and consumption practices.

Methods: In-person interviews of a population-based, 16% random sample of persons > 18 years old in 9 villages of southwestern Alaska were conducted during August 2001. Data collected included information about video viewing; frequency of consumption of traditional Native foods; knowledge about the cause, symptoms, and treatment of botulism; and methods of fermented food preparation.

Results: We interviewed 254 adults (40% male, 92% Alaska Native) and 97 (38%) reported they saw the video. Of these, 78% learned about the video on public televison; and most saw it either at home or in a medical facility (78% and 18%, respectively). In total, 220 (93%) individuals knew that botulism was a foodborne illness, 169 (77%) of whom knew it was associated with eating fermented foods. Compared with the pre-video survey, overall consumption (pre-video survey: 77%, post-video survey: 81%) and preparation (pre: 27%, post: 20%) of traditional Native fermented foods did not change. Among those who prepare fermented foods, the proportion who use plastic or metal buckets rather than traditional methods as encouraged in the video, did not differ significantly between pre and post video surveys (34% versus 33%, respectively); or between those who saw the video and those who did not (28% versus 37%, respectively). Overall, willingness to decrease the risk of botulism from fermented foods did not change for behaviors such as boiling foods to destroy toxin (pre: 45%, versus post: 43%), or avoiding foods fermented in plastic containers (pre: 65%, versus post: 68%). The prevalence of misconceptions about botulism did not appear to change, including the belief that some people were protected from becoming ill from botulism (pre: 23%, versus post: 17%), or that antibiotics could cure botulism did not change (pre: 3%, versus post: 7%).

Conclusion: While the botulism prevention video has been well received in Alaska and in the health care community, a year after distributing it to rural Alaskan schools and clinics, few changes that might reduce the risk of botulism from fermented foods were noted. This finding might be reflective of the limited number of adults saw the video. Methods to market the use of the video, reinforce prevention messages, and support behavior change are being explored.

Active Laboratory Surveillance in Massachusetts

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Introduction: Timely identification and reporting of infectious diseases to health departments is necessary to effectively implement appropriate control measures and prevent illness. In September 2001, the Massachusetts Department of Public Health (MDPH) began a statewide, laboratory-based, active surveillance project to monitor selected organisms and antimicrobial susceptibility patterns (if applicable). Organisms of interest include *Bacillus anthracis*, Brucella species, Cryptosporidium species, *E. coli* O157:H7, *Francisella tularensis*, Giardia lamblia, Streptococcus pyogenes (groups A and B), Haemophilus influenzae, *Listeria monocytogenes*, methicillin-resistant *Staphylococcus aureus* (MRSA), Neisseria meningitidis, *Salmonella* species, Shigella species, Streptococcus pneumoniae, vancomycin-resistant enterococci and *Yersinia* pestis. The goals of this surveillance project are to enhance timely identification of foodborne and waterborne outbreaks and unusual events, such as a bioterrorism incident, and to monitor antimicrobial resistance across the state.

Methods: Laboratories have been asked to submit retrospective data from January 2000 forward. Prospective data are submitted either electronically or in paper format, weekly or monthly, depending on laboratory size and capability. Data are entered or imported into an ACCESS database using National Electronic Data Surveillance System (NEDSS) guidelines.

Results: As of 10 December 2001, MDPH epidemiologists visited 40 of 85 hospital laboratories and received electronic data from 8 laboratories and data in paper format from 7 laboratories. In comparison to active surveillance reports received from the first 4 reporting hospitals, the existing passive reporting system had received 100% of the Shigella and *Listeria* cases, 93% of shiga toxin-positive *E. coli* cases, 89% of Cryptosporidium cases and 67% of Giardia cases from the same laboratories. Two invasive cases each of Neisseria meningitidis and Haemophilus influenzae occurred, none of which were reported.

Discussion: Through this active surveillance initiative, MDPH expects to increase notification of reportable conditions to allow for appropriate public health control measures, as well as initiate reporting and awareness around emerging pathogens. Additionally, MDPH will obtain antimicrobial resistance data to monitor resistance trends and facilitate appropriate public health action if an unusual or significant resistance pattern is identified.

The Emergence of Serogroup Y Disease and the Epidemiology of Invasive Meningococcal Disease in Colorado, 1997 - 2001

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Background: National surveillance data suggest that the recent increase in serogroup Y disease (SYD) is associated with a different clinical and epidemiologic picture of invasive meningococcal disease (IMD). We sought to describe the change in serogroup distribution in Colorado over the past decade and to characterize the subsequent effect of SYD on the clinical epidemiology of IMD.

Methods: A case of IMD was defined as the isolation of *N. meningitidis* from a sterile source. Eligible cases were identified through both active (Jul 2000-Jun 2001, ABCs project in the Denver Metro area) and passive (Jan 1997-Jun 2001, statewide) surveillance from 1997 through June of 2001 (N=171, serogroup available 77%). Information on type of infection was only available from January 1999 through June of 2001 (N=94, serogroup available 86%). For the purpose of assessing changes in serogroup distribution over time, serogroup data for IMD cases from 1991 through 1996 were also used (N= 225, serogroup available 64%).

Results: The overall serogroup distribution in Colorado has notably shifted in the past ten years with Y replacing C as the most prevalent serogroup. Serogroup Y comprised 7% of IMD cases from 1991-1994 and increased to 40% of IMD cases from 1998 through mid 2001. Persons with SYD were more likely than persons with IMD due to other serogroups to be ≥ 35 years (RR=2.5; 95%CI 1.5, 4.2). When stratified by gender, this association was limited to females (RR=4.3; 95%CI 2.0, 9.4). Female cases of SYD were significantly older than male cases (median age, 51 vs. 16 years; Wilcoxon Rank Sum, P=0.03). All cases of IMD with pneumonia for which serogroup information was available occurred in persons ≥ 35 years. Persons with SYD were much more likely to have pneumonia than were persons with IMD due to all other serogroups among all ages (RR=18.9; 95%CI 2.6, 137.7) and among persons ≥ 35 years (RR=5.5; 95%CI 0.9, 35.1). In persons with available outcome data (98%), serogroup C had the highest overall case-fatality ratio (22.7%). SYD had a higher case-fatality in persons ≥ 35 years (16.7%) compared to persons < 35 years (4.3%); whereas serogroup C had similarly high case fatality among both younger (23.5%) and older (20%) ages. When compared to cases with other serogroups and non-groupable disease, persons with SYD had similar distributions of race and ethnicity, metro vs. non-metro residence, and gender.

Conclusions: The emergence of SYD in Colorado has resulted in a changed epidemiology of invasive meningococcal disease. Compared with persons with IMD due to other serogroups, persons with SYD are more likely to have pneumonia and be ≥ 35 years. Among those with SYD, females are significantly older than males and persons ≥ 35 years have a much higher case fatality ratio than those < 35. Ongoing enhanced surveillance will continue to monitor the shift in serogroup distribution and characterize the resulting epidemiology of IMD in Colorado.

Transmission of the Main Viral Pathogens Causing Gastroenteritis, NLV, SLV and Rotavirus

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Viral pathogens are the most common causes of gastroenteritis in the community. To identify modes of transmission and thereby opportunities for prevention, a case-control study was conducted in the Netherlands in 1999, nested in a cohort study. Risk factors for Nowalk-like virus gastroenteritis, Sapporo-like virus gastroenteritis and rotavirus-gastroenteritis were studied, by comparing cases with gastroenteritis that tested positive for the virus and their matched controls without gastroenteritis, by using conditional logistic regression analysis. A food handling hygiene score was calculated based on several variables addressing hygiene at different steps in foodhandling. For NLV-gastroenteritis, having a household member with gastroenteritis, contact with a person with gastroenteritis outside the household, and poor food handling hygiene were associated with illness, with population attributable risk fractions (PARs) of respectively 17%, 56% and 47%. In a sub-analysis, excluding all cases with contact with symptomatic persons (with the aim to exclude cases due to contamination of food in the home), we found a PAR for food-handling hygiene of 12-16%. For SLV-gastroenteritis, only contact with a person with gastroenteritis outside the household was associated with a higher risk and with a population attributable risk fraction of 60%. For rotavirus-gastroenteritis, contact with a person with gastroenteritis outside the household and food handling hygiene were associated with a higher risk, with PARs of 86% and 46%. Transmission of these viral pathogens occurs primarily from person-to-person. However, for NLV-gastroenteritis foodborne transmission seems to play an important role, with an estimated 12-16% of infections being attributable to contaminated food entering the household. Strict hygiene measures when being in contact with a person with gastroenteritis, and good food handling hygiene may prevent an estimated 80% of all NLV-gastroenteritis cases, 60% of SLV-gastroenteritis cases, and 92% of rotavirus-gastroenteritis cases.

Improving Influenza and Pneumococcal Vaccination Rates for People 65+ in Rhode Island through Coalition Building Efforts

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Background: Vaccines are among the greatest public health achievements of the 20th Century. In recognition of the public health benefits of vaccines, the Ocean State (Rhode Island) Adult Immunization Coalition (OSAIC) was formed in 1997 in order to reduce the mortality and morbidity associated with influenza and pneumococcal disease among Rhode Island's elderly population (people aged 65+). In its first two years, the Coalition witnessed dramatic increases in both influenza and pneumococcal disease vaccination rates.

Coalition Activities: The OSAIC is composed of thirty-five agencies that are committed to increaseing influenza and pneumococcal immunization rates for people 65+. The members include hospitals, long-term care facilities, vaccine manufacturers, medical societies, managed care, Visiting Nurse Associates, RI Department of Health, RI Quality Partners, and community-based organizations. Strategies to improve immunization rates include:

1. Providing resources, materials, and training to medical providers;
2. Developng and conducting public clinics and education campaigns; parrticularly for under-served populations;
3. Facilitating partnerships among communicty groups, health care providers, and private organizations to make vaccines readily accessible and free to all seniors;
4. Improving adult immunization tracking and reporting systems; and
5. Monitoring national trends in adult immunization activities and promoting national adult immunization recommendations.

Trends In Immunization Rates: The immunization rates for Rhode Island's seniors jumped significantly after the OSAIC was formed in 1997. According to the CDC Behavioral Risk Factor Surveillance System, from 1997 to 1999, Rhode Island's influenza rates increased from 67% to 76%, and for pneumococcal from 43% to 57%. On a national level, these increases propelled Rhode Island from a ranking of #20 to #1 for influenza, and from #36 to #14 for pneumococcal disease.

Conclusion: Through the collaboration of organizations, significant progress can be made in improving immunization rates in just two years. Importantly, despite the substantial progress made by the OSAIC, the Healthy Poeple 2010 Objective is to reach of level of 90% coverage for influenza and pneumococcal. Reaching this objective will require broadening and intensifying OSAIC's efforts in coming years.

Evidence of Effectiveness of Egg Quality Assurance Programs, Mandatory Refrigeration, and Traceback Investigations To Mitigate Egg-Associated *Salmonella enteritidis* Infections in the United States

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Background: In the past 30 years, the reported rate of Salmonella Enteritidis (SE) infections in the United States has increased from a low of 0.55/100,000 in 1976 to a high of 3.88/100,000 in 1995. Shell eggs have been identified to be a major cause of SE, and so there is a need for interventions that reduce exposure to SE-tainted eggs. We examined correlations between SE incidence and introduction of programs to reduce SE contamination of eggs. The programs examined included egg quality assurance programs (EQAPs), state refrigeration requirements for eggs, and egg traceback investigations by USDA and FDA.

Methods: Regression models were used to determine programs associated with changes in national and state SE incidence. SE isolations from humans were reported to CDC by state public health department laboratories. Information concerning implementation of EQAPs and refrigeration requirements was obtained through interviews with state agricultural and public health officials, U.S. Census Bureau, USDA, and FDA records.

Results: The average 0 to 7-year post-EQAP SE incidence increased by 122% for the 5 states that had industry-sponsored programs but decreased by 22% for the 10 states with state-sponsored EQAPs. The average 7-year post-refrigeration requirement SE incidence for the 17 states requiring egg refrigeration from farm to table decreased by 13% and that for the 13 states requiring refrigeration at retail only decreased by 16%. The average 3-year post-USDA traceback SE incidence for 7 states decreased by 14%, and 3-year post-FDA traceback SE incidence for 3 public health regions decreased by 30%. SE outbreaks and SE outbreaks traced to eggs decreased by 18 percent and 37 percent, respectively.

The state-level regression model of the impact of EQAP found the following: A 1% increase in the population at high risk for SE (defined here as children 65 years) was associated with a 10% increase in SE incidence ($p<0.01$); a 1% increase in eggs produced under EQAP was associated with a 0.47% decrease in SE incidence ($p<0.04$); and having a state-sponsored instead of industry-sponsored EQAP was associated with a 72% reduction in SE incidence ($p<0.002$). The model for national-level data found that a 1% increase in the population at high risk for SE was associated with a 51% increase in SE incidence ($p<0.000$), a 1% increase in eggs produced under an EQAP was associated with a 2.2% decrease in SE incidence [$p<0.05$], and an additional FDA traceback investigation was associated with a 1.2% decrease in the following year's SE incidence ($p<0.06$).

Conclusions: These data indicate that state-sponsored EQAPs, egg refrigeration from farm to table, and egg trace back investigations probably played a major role in reducing SE illness in the U.S. and should be continued and expanded. Incidence of egg-related SE may be reduced through risk-reduction programs focused on populations at high risk for SE infections.

79 Molecular Diagnostics and Epidemiology II

Tuesday, March 26, 4:30 p.m.
Centennial Ballroom I

Detection of La Crosse Virus in Cerebrospinal Fluid and Tissues by Reverse Transcription-Polymerase Chain Reaction

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La Crosse encephalitis is one of the most common causes of reported arboviral illness in the United States. The causative agent is La Crosse virus, which has been historically distributed in the upper Midwestern States — Illinois, Indiana, Iowa, Minnesota, Ohio, and Wisconsin. In recent years, human cases of La Crosse encephalitis have increased in Southeastern States — West Virginia, Tennessee, and North Carolina. Our interest continues to be the determination of the appropriate role of nucleic acid amplification methods, particularly RT-PCR, in the diagnosis of such infections. Toward this end, a reverse transcription-polymerase chain reaction (RT-PCR) method was used to retrospectively detect La Crosse virus genome in patients with central nervous system infections. The RT-PCR method was evaluated directly on cerebrospinal fluid (CSF) and autopsied tissues of patients with La Crosse encephalitis. Since La Crosse virus is a member of California (CAL) serogroup viruses, universal primers for CAL serogroup viruses and specific primers for La Crosse virus were evaluated to determine their effectiveness with clinical specimens. Ten CSF samples from 8 patients were examined with group-specific primers and PCR bands with the expected size were obtained in 3 samples. In all 9 samples with enough CSF available for additional testing, La Crosse was detected by RT-PCR with virus-specific primers. La Crosse virus RNA was also detected in both frontal lobe and spinal cord of autopsied tissues. The results indicate that PCR may be a useful technique for identification of La Crosse sequence, particularly when La Crosse-specific primers are used. PCR offers the advantage of providing a rapid diagnosis at the time of clinical presentation. Based on the results, we suggest that PCR be considered as a complementary test for laboratory diagnosis of suspected cases of La Crosse encephalitis.

Real-time Fluorescence PCR Assays for the Detection and Characterization of Heat-labile and Heat-stable Enterotoxin Genes from Enterotoxigenic *Escherichia coli*

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Enterotoxigenic *Escherichia coli* (ETEC) is a major cause of watery diarrhea among children in developing countries and travelers from the industrialized world to endemic areas. In addition to sporadic infections caused by these organisms, ETEC strains also cause waterborne and foodborne outbreaks. Convenient methods for the detection ETEC are needed for outbreak investigations and for diagnostic efforts to estimate the burden of diarrheal disease attributable to these organisms. ETEC strains cause disease through the elaboration of one or more enterotoxins, designated heat-labile toxin (LT) and heat-stable toxin (ST), and are most reliably detected by assays that target the toxins they produce or the genes encoding these toxins. Conventional block cycler PCR assays for ETEC have proved useful for detecting ETEC; however, recent advances in PCR technology have facilitated the development of real-time fluorescence PCR assays with greatly reduced amplification times and more reliable methods for the detection of amplified target sequences. To improve our ability to diagnose ETEC infections, we developed and evaluated real-time fluorescence PCR assays for the LightCycler? against the enterotoxin genes present in these organisms. Separate LC-PCR assays for LT and ST were designed using the hybridization probe format to have identical cycling conditions so they could be run together on the same thermal cycler. Findings from the testing of 160 *E. coli* isolates of human origin (138 ETEC and 22 non-ETEC) with the LightCycler? PCR (LC-PCR) assays were compared with those obtained by block cycler PCR analysis. The sensitivities and specificities of the LC-PCR assays were each 100 % for the LT and ST genes. Findings from the melting curve analyses of the amplified LT and ST genes revealed sequence variation within each gene that was confirmed by DNA sequence analysis of the amplicons. In the case of the ST gene, variation observed in the melting point temperatures correlated with the presence of toxin variants ST Ia (STp) and ST Ib (STh). The rapidity and specificity of the LC-PCR assays make them attractive alternatives to block cycler PCR assays or other genetic and phenotypic methods used for the detection and characterization of ETEC.

Development and Evaluation of PCR-based Diagnostics for Identification of Salmonella O antigens based on the rfb Locus

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The Kauffman-White serotyping scheme includes about 50 different Salmonella O antigen groups, which together with the detection of H antigens, forms the basis for serotype identification. We have been characterizing the genes required for O and H antigen biosynthesis with the goal of developing a DNA-based system for serotype determination in Salmonella. We report PCR-based diagnostics for the identification of 15 Salmonella O serogroups; eight developed from our de novo sequence data, three developed from sequence data reported from other laboratories, and four evaluated from a previously described assay. We recently completed sequencing the rfb gene clusters from S. Sundsvall (O:6,7), S. Gaminara (O:16), S. Jangwani (O:17), S. Cerro (O:18), S. Marina (O:48), S. Ealing (0:35), S. Roan (0:38), and S. Ipswich (0:41) and used this information to design serogroup-specific primers to target defined regions of the putative wzy and wzx genes for these O serogroups. Preliminary evaluation indicated that each primer pair is specific for the appropriate O serogroup. We also developed PCR assays for identification of serogroups C1, E, and O:54 based on wzy (polymerase), wzx (flippase) and wbbF (transferase) O-antigen synthesis genes, respectively, using previously described sequence data. All 59 strains belonging to serogroups C1, E and O:54 were accurately identified to yield amplicons of 628 bp, 920 bp, and 538 bp, respectively. The 289 strains from the 46 other serogroups were negative in the PCR assays. In addition, a PCR-based assay for identification of Salmonella serogroups A, B, C2 and D had been reported previously, and is based on the selective amplification of abequose and paratose synthase genes. We are currently evaluating the sensitivity and specificity of these assays with the aim of including them in our panel of serogroup-specific assays. These PCR-based assays will be a rapid and sensitive technique amenable to high throughput O serogroup identification of Salmonella in the routine public health laboratory environment.

PulseNet Experience: Software Changes and Improvements to Online *E. coli* National Database

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PulseNet is the national molecular subtyping network of public health laboratories that performs pulsed-field gel electrophoresis (PFGE) on foodborne pathogens. *E. coli* O157:H7 PFGE patterns are electronically shared via the Internet among laboratories and the national database maintained at the Centers for Disease Control and Prevention (CDC). Use of the current PulseNet online database allows for rapid communication of PFGE subtyping data needed for the identification of clusters and outbreaks. The online *E. coli* database was begun in 1998 using Molecular Analyst Fingerprint Plus with Data Sharing (Bio-Rad, Hercules, CA) Tools as the analysis software, and an SQL server software was used to store isolate-related information. The local interface program facilitated uploading of data from a local Molecular Analyst Fingerprinting Plus database and isolate data from a local Microsoft Access database. Molecular Analyst itself contained minimal isolate information fields, making it necessary to maintain these data in a separate Access database. Also, security concerns also made it difficult to add participants to this system and hard for participating public health laboratories to connect to this system. In April 2001, we began migrating to a new system using a PulseNet customized version of BioNumerics (Applied Maths, Sint-Martens-Latem, Belgium). A major advantage of the new on-line BioNumerics database is the customized entry screens, which allow for the input of isolate-associated information such as date of isolation, serotype, geographic information, toxin type, phage type, and food vehicle-associated information. Security is maintained using a SecurID (Security Dynamics Bedford, MA) to authenticate to the CDC firewall and passwords to gain access to the specific server and database. Currently 28 U.S. public health laboratories have direct access to the database. Laboratories are given access after successfully PFGE typing a set of certification strains, obtaining the expected PFGE patterns, and correctly analyzing the resulting tiff image files. Currently, over 8,600 entries have been uploaded to the online server. There are 7875 XbaI patterns and 1383 BlnI patterns associated with these entries. Improvements in the setup of the PulseNet National online database for *E. coli* have allowed for more rapidly adding additional online participants, increased security of data, improved viewing and searches of isolate related data, inclusion of antimicrobial susceptibility data, and increased possibilities for analyzing data online.

Molecular Characterisation of a Multiresistant Strain of *Salmonella enterica* Serotype Typhimurium DT204b Responsible for an International Outbreak of Salmonellosis

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From July - October 2000 patients in five European countries (England, Scotland, Germany, The Netherlands, Iceland) were infected with a strain of *Salmonella enterica* serotype Typhimurium definitive phage type (DT) 204b (= DT204b) resistant to ampicillin, chloramphenicol, gentamicin, kanamycin, streptomycin, sulphonamides, tetracyclines, trimethoprim and nalidixic acid, and with decreased susceptibility to ciprofloxacin (R-type ACGKSSuTTmNxCp$_L$). Over 350 laboratory-confirmed cases were recognised. As a result of epidemiological investigations shredded lettuce was implicated as the vehicle of infection. Isolates from patients in Iceland, The Netherlands and Scotland were characterised in the PHLS Laboratory of Enteric Pathogens and compared with those from patients infected in England and from patients returning to England and Wales after visiting other countries in Europe. Methods included phage typing, antibiogram analysis, plasmid profile typing, pulsed-field gel electrophoresis (PFGE), fluorescent amplified fragment length polymorphism fingerprinting (FAFLP) and integron typing; specific resistance genes were characterised by PCR; the mutation conferring decreased susceptibility to ciprofloxacin was identified by a LightCycler *gyrA* mutation assay (GAMA). Isolates from Germany and Scotland were typed independently using the same phenotypic methods and also by plasmid profile and PFGE. All isolates possessed five plasmids ranging from 120 MDa to 2.0 MDa. With the exception of resistance to nalidixic acid/decreased susceptibility to ciprofloxacin, the complete resistance spectrum was transferable to *E. coli* K12 as an intact linkage group. When PCR amplification was performed on DNA extracted from transconjugants, positive results for *aad*A2, *bla*$_{TEM}$, *sul1* and *tet*A (class A) were obtained whilst *bla*$_{carb-2}$, *tet*A (class G) and *tet*A (class B) were negative. When studied by integron PCR, one discrete band of 1.6 kilobases (kb) was generated and one faint amplicon of about 4 kb was also consistently produced. When studied by GAMA the gyrA mutation was that of aspartate to glycine (GAC-GGC) at codon 87. PFGE profiles of all isolates were indistinguishable. To facilitate epidemiological investigations PFGE TIFs of these isolates and those from Scotland and Germany were exchanged electronically. In all cases

the resultant PFGE profiles were indistinguishable. Finally, The FAFLP profiles of all isolates were identical. These results confirmed that the strains of DT204b of R-type ACGKSSuTTmNxCp$_L$ responsible for outbreaks in five European countries in the summer of 2000 represented a single clone. A key aspect of this investigation was the use of harmonised techniques of phage typing and antibiogram analysis coupled with the rapid exchange of molecular fingerprints between laboratories. It would be of major benefit for the global control of salmonellosis if compatible networks were now developed for the international exchange of real-time molecular data for *S. enterica*.

Determination of Allelic Diversity in the *mec* Operon of Methicillin-Resistant *Staphylococcus aureus* in Wisconsin

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Background: Methicillin resistance in staphylococci is dictated by the presence of the *mec*A encoded penicillin binding protein 2a (PBP2a) which has low affinity for beta-lactam antibiotics. PBP2a is made in the absence of transcriptional repression due to mutated *mecI*, the repressor gene. It has been proposed that *mecI* receives a transducing signal from the membrane bound sensory protein, MecR1 after interacting with beta-lactam drugs. The extent of allelic diversity present in these genes affecting methicillin resistance is not well studied. We investigated the diversity of sequence variations in the mec operon and its correlation with oxacillin minimum inhibitory concentration (MIC), antibiogram, and pulsed-field gel electrophoresis (PFGE) profiles from a select group of MRSA strains isolated in Wisconsin. **Methods:** The isolates in the study were collected from 1989-1999 at Marshfield Laboratories in Wisconsin. We typed 316 MRSA strains by PFGE after *Sma*I restriction digestion. Antibiograms for seven drugs (ciprofloxacin, clindamycin, erythromycin, tetracycline, trimethoprim-sulfamethaxazole, gentamicin, and rifampin) were obtained by using the Vitek system. In addition, oxacillin MICs for 216 were determined by the E-test. We sequenced *mecA*, *mecI* and *mecR* genes from 316 MRSA. Colony PCR was used to amplify the *mecA* complex followed by direct sequencing of the PCR products. The generated sequences were assembled using the DNASTAR program and compared with *S. aureus* N315, a pre-MRSA strain that has an intact mecA complex. **Results:** Of the 316 MRSA isolates studied, 77 PFGE profiles were identified, of which 55 isolates (17.4%) had unique fingerprints. Sixteen different susceptibility patterns were identified; the largest group with 124 isolates had resistance to three drugs in addition to beta-lactam antibiotics. Mutations were detected in all three genes of the *mec* operon. Thirty-one percent of the isolates had a nucleotide substitution, G->T at position 7 upstream of the start site of *mecA*; and 64% of these isolates (n=88) had an oxacillin MIC ≥ 96 µg/ml. Interestingly, 70% of these strains were also resistant to erythromycin. Ninety-six percent of the isolates had a Glu->Gly change at codon 246 of *mecA*. About thirty isolates (9.5%) had a Asn->Lys change at codon 121 of *mec*I. In addition, mutations resulting in truncation of *mecI* were also identified in four isolates. About 8% percent of the isolates had synonymous changes in *mecR* at codon 583 (GAA->GAG). Polymorphisms identified in mecR correlated well with PFGE profiles indicating clustering. **Conclusion:** Multiple mutations were identified in various combinations in the mec operon suggesting differential regulation of methicillin resistance. Based on the MICs and sequencing analysis, it seems very likely that additional genes may be involved in the *mecA* regulation.

80 Surveillance and Information Systems

Tuesday, March 26, 4:30 p.m.
Centennial Ballroom II

Analysis of a Health Indicator Surveillance System: Its Ability to Detect Annual Influenza Activity for the 1999-2000 and 2000-2001 Seasons Compared to Traditional Surveillance Systems

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Introduction: We analyzed the ability of an automated data collection system using outpatient visits in a military beneficiary population to detect annual influenza epidemics in the Washington D.C. metropolitan area. The system is called the Electronic Surveillance System for the Early Notification of Community-based Epidemics (ESSENCE) developed by the Department of Defense Global Emerging Infections System. We analyzed illnesses that are coded at clinic visits by ICD9 codes during annual winter respiratory outbreaks for the 1999-2000 and 2000-2001 seasons and compared these to codes used at other nonepidemic times. Currently, ESSENCE has complete surveillance data for the Washington, DC area within three days of patient visit. Although we realize the need for improved timeliness in this system, we propose that its ability to rapidly detect an outbreak exceeds that of most traditional surveillance systems. However, its sensitivity may not be equal to traditional, active surveillance systems. **Methods:** To test this hypothesis, we compared the percentage of visits for combinations of specific respiratory and febrile conditions at primary care clinics and emergency rooms during the influenza seasons in ESSENCE with what is reported by the Centers for Disease Control and Prevention's (CDC) sentinel physician surveillance system. We determined the best combination of ICD9 codes that most closely approximated the epidemic curve observed by the CDC system during these two influenza epidemic periods. Results and Discussion: ESSENCE influenza data are as accurate and valid as CDC sentinel physician data in detecting an influenza outbreak by showing similar outbreak curves and peaks. Specifically, ESSENCE's measurements of the start date and the end date of the influenza outbreak season did not exceed seven days from similar dates reported by CDC sentinel physicians. Among the types of illnesses that are coded during winter respiratory outbreaks, particular ICD9 codes such as fever, upper respiratory infection, viral syndrome and cough, are the best indicators of respiratory outbreaks.

Lessons Learned from Implementing Electronic Laboratory Reporting, New York State

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Background: One of the main goals of developing the National Electronic Disease Surveillance System (NEDSS) is to promote the transmission of public health data by establishing uniform national standards for information exchange. New York State (NYS) has developed the Electronic Clinical Laboratory Reporting System (ECLRS) as one application of this approach. Implementation of ECLRS required developing solutions to several unanticipated challenges. **Methods:** ECLRS is an automated, internet-based, secure system that permits laboratories to transmit test results electronically to NYS counties to meet public health reporting requirements. The goals of the system were to replace

the past paper-based system with electronic reports, to increase the speed of reporting, to simplify the work of laboratories and to provide an automated alert system for diseases of urgent importance. The system was designed and implemented via a collaborative effort among epidemiologists, information technologists, lab specialists and administrators. **Results:** The initial expectation of integrated, standardized reporting capabilities of laboratories was unrealistic. The system ultimately had to accommodate the wide range of laboratory reporting capabilities. Because most laboratories do not use either the Logical Observation Identifier Names and Codes (LOINC) or the Systemized Nomenclature for Medicine (SNOMED) coding, or the Health Level 7 (HL7) file format, ELCRS allows laboratories to transmit results via any one of three specified file formats, and does not require LOINC/SNOMED codes. There are 27 laboratories currently using and 22 preparing to use ECLRS. Of the 27 using ECLRS, 3 report by ASCII file format, 22 by web page data entry, and 2 by HL7. Four laboratories report with LOINC/SNOMED codes. Quality, completeness and timing of reporting were also challenges. Not all test reports have complete information for patient address, which is critical to the correct routing of reports to counties. ECLRS has a hierarchical method of assigning each report to a county; nevertheless, there are still many reports that require manual assignment to counties. Many laboratories find it challenging to simply provide electronically what has been sent by paper in the past, and providing automatic alerts was more complicated than expected because of the problem of false alerts and messages being sent off-hours. **Conclusions:** The successes of ECLRS have shown the critical importance of involving all actual and potential system users throughout the planning and execution process. The challenges encountered indicate the need for evolutionary changes in existing commercial laboratory information systems. The successful outcome of this process can be effected only through close partnerships among commercial laboratories, CDC and state and local health.

Outbreak Surveillance: An Important Tool for Controlling Communicable Diseases

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Background: The identification, control and prevention of communicable disease outbreaks are important and enduring objective of public health services. Despite the importance of these objectives, many outbreaks are not identified or investigated and much of the information that could be used for preventing future outbreaks is lost because findings are often not reported in a systematic manner. **Method:** New Zealand introduced a national outbreak surveillance system in July 1996. This system provides a standardised way of reporting outbreaks, including details of the causal agent, characteristics of cases, mode of transmission, contributing factors, and outbreak management. The system is fully electronic and integrated with other components of the national infectious disease surveillance system. **Results:** The number of recognised outbreaks has increased from 45 in 1996 (6 months) to 289 in 2000. In 2000, outbreaks involved a total of 2296 cases, of which 150 required hospitalisation and 5 died. There were 200 common source outbreaks reported, of which 164 arose from common events. The most common pathogens or toxins implicated were Norwalk like virus (34 outbreaks), *Campylobacter* (37) and *Salmonella* (30). The most common non-enteric pathogen or toxin was Bordetella pertussis (11 outbreaks). Commercial food operations (mainly restaurants or cafés) were implicated in 147 outbreaks. Foodborne transmission accounted for 190 outbreaks in 2000. Person to person and waterborne transmission accounted for 114 and 23 outbreaks respectively. Abuse of temperature was the most common factor contributing to foodborne outbreaks. The most commonly implicated food type was poultry (43 outbreaks) though the quality of evidence establishing the link was relatively weak in most instances. **Conclusions:** These surveillance data are beginning to define the burden of disease caused by outbreaks in New Zealand. More importantly, they provide information that should be useful for policy makers, particularly those concerned with improving food safety. The outbreak surveillance system was significantly upgraded in 2000 with an 'active' process of integrating epidemiological data with that from communicable disease and food laboratories to improve the sensitivity and timeliness of outbreak reporting.

Lyme Disease Incidence in Wisconsin: A Comparison of State Reported Rates with Rates from a Population-Based Cohort

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Background: In endemic areas, Lyme disease (LD) is now frequently regarded by physicians as a routine medical condition and is often managed in urgent care centers or other high-volume outpatient settings. As a result, many cases of Lyme disease may not be reported to state health departments. Few studies in the past decade have assessed the accuracy and completeness of state-based passive LD surveillance systems, nor have any recent studies examined LD incidence using alternative data sources. **Methods:** Potential LD cases (1992-1998) were identified from chart review and laboratory results at two large multispecialty clinic networks in Wisconsin. Cases were confirmed if they met the CDC case definition, and they were then compared with cases reported to the Wisconsin Division of Public Health (DPH) that also met the CDC case definition. Using clinic data, incidence rates were calculated for residents of the Marshfield Epidemiologic Study Area (MESA), a dynamic population-based cohort of nearly 90,000 residents in north-central Wisconsin. The Marshfield Clinic is the main provider of health care in the 24 zip codes that comprise MESA, and capture of health events for MESA residents is nearly complete. Incidence rates were also calculated using DPH data for an eight county region that surrounds and includes MESA, and for the entire state of Wisconsin. **Results:** Four hundred definite cases of Lyme disease were identified through review of clinic records. The average incidence of definite Lyme disease (1992-1998) was 17.6 per 100,000 in MESA. Based on DPH case reports, the LD incidence was 17.7 per 100,000 in the eight county region surrounding MESA, and 9.5 statewide. Temporal trends in statewide incidence generally were comparable to those observed in MESA. LD incidence rose sharply from 1996 to 1998 in both MESA and the surrounding eight county region. Sixty-eight percent of definite Lyme disease cases meeting the CDC case definition were not reported to the Wisconsin DPH. **Conclusion:** These findings suggest that the state passive surveillance system accurately monitors trends in LD incidence, but is less useful for estimating the true burden of Lyme disease due to substantial underreporting of definite cases.

Surveillance for Patients with Acute Febrile Illness in Egypt

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Introduction: Acute fever of undetermined etiology (AFI) is a common clinical syndrome that is not well characterized in Egypt. In 1999, training on a standard clinical and laboratory evaluation of patients with AFI was provided to a network of providers in 13 infectious disease hospitals throughout Egypt. The results for the first 29 months are reported, demonstrating typhoid and brucellosis as the primary etiologies. **Methods:** Standard case definitions were used to identify patients. Case investigations forms included clinical, demographic, and risk factor information. Patients were classified as having confirmed *S. typhi* infection or

brucellosis based on positive blood cultures. Patients with Brucella tube agglutination titers > 1:160 were classified as having confirmed brucellosis. Patients with Widal titers > = 1:160 were classified as having probable typhoid fever. Nested analysis was performed to calculate age-adjusted prevalence ratios (PR) to identify risk factors for patients with brucellosis. **Results:** Of the 4906 patients evaluated between March 1999 and August 2001, 278 patients (6%) had positive blood cultures for *S. typhi* and 516 (10.5%) patients were classified with probable disease. Patients with typhoid fever were identified in all participating institutions with a peak in the number of cases during the fall (Sept-Nov). The mean age of patients with *S. typhi* infection was 19 (range 3 - 79); 50% were male. Brucellosis was identified in 533 patients (10.9%), including 114 persons with culture confirmed disease. Patients with brucellosis were diagnosed in all participating hospitals, both rural and urban, and in all months of the year, with a peak during the months of September to October. The mean age of patients with brucellosis was 32 yrs +/- 14.8; 64.8% of patients were male. Exposures significantly associated with brucellosis, as compared to other patients with AFI, included increasing age ($p<0.001$), contact with an animal abortus (PR 3.1), handling raw meat (OR 2.3), slaughtering animals (PR 2.2), daily contact with domestic animals (PRs of sheep 2.4, cattle 2.0, camel 4.9, buffalo 2.1), consumption of non-pasteurized milk (PR 1.6) and soft cheese (PR 1.2). **Conclusion:** The surveillance network has identified typhoid fever and brucellosis as the most commonly recognized causes of community-acquired bloodstream infections in Egypt. Improving laboratory capacity can lead to greater success in diagnosing causes of AFI to help tailor therapy and define burden of disease.

Foodborne Viruses in Europe: Web-Based Technologies for Investigation of Transnational Outbreaks of Viral Gastroenteritis

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Viral agents have been estimated to cause more human disease than any other foodborne pathogen. Transnational outbreaks of Norwalk-like virus (NLV) due to international food distribution have been documented recently as advances in molecular characterization have allowed for an improved capability to trace virus through the population. A network of surveillance systems of nine European countries has been initiated in order to allow more rapid and internationally standardized assessment of foodborne viruses. We have harmonized the collection of clinical information from outbreaks and virological characterization data. A standard questionnaire and minimum dataset for use in outbreak investigations has been agreed as well as molecular techniques and sequencing protocols for the characterization of NLV. The web-based data communication instruments (Active Server Pages (ASP) for clinical data and Bionumerics software for characterization data) will be described. The two databases are relational, accessible to all participants and data can be viewed over the Internet immediately following an outbreak report. Thus, the system functions both as an early alert tool for investigators and a comprehensive database of previously investigated outbreaks. Results from the winter 2001/2002 will be presented.

81 Influenza

Tuesday, March 26, 4:30 p.m.
Regency Ballroom V

PER.C6: A Human Designer Cell Line Providing a Pandemic Proof Platform for the Manufacturing of Safe Influenza Vaccines

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Influenza virus is killing thousands of people per year and causes widespread morbidity with an enormous social and economic impact. Influenza virus continuously evolves by antigenic drift causing yearly epidemics. In addition, new strains against which no immunity exists in the population can suddenly appear, giving rise to pandemics with catastrophic results as demonstrated by the Spanish Flu pandemic killing between 20 to 40 million people. The recent emergence of new strains — H5N1 in 1997 in Hong Kong that killed 6 out of 18 infected humans and H9N2 in 1999 isolated from children in Hong Kong and China — indeed show that influenza is 'standing at the gate'. Are we prepared to combat a new pandemic?

Vaccination is the cornerstone of influenza management and its benefits are firmly established.Influenza vaccines are presently produced on embryonated hen's eggs.

This production system is not flexible and an undercapacity to produce vaccine for future inter-pandemic periods is anticipated. In case of a pandemic threat it is unlikely that such a manufacturing system will be able to meet the global demand for a pandemic vaccine.

The human designer suspension cell line PER.C6TM, derived from human primary retina cells by transformation with an E1 minigene of adenovirus type 5, provides a safe cell substrate for the manufacturing of influenza vaccines. All strains tested replicate with fast kinetics (3-4-days) to high titres (1E+07-1E+09 PFU/ml) resulting in excellent yields of hemagglutinin in crude bulk as measured in the SRID (up to>65ug/ml). Furthermore, PER.C6 TM can be grown in large capacity bioreactors (>1000L) in high cell densities (>6E+06 vc/ml) in an animal component free medium.

Altogether, these properties make PER.C6 TM a powerful pandemic proof vaccine manufacturing platform .

Acute Respiratory Virus Surveillance in Cairo and Alexandria, Egypt, July 2000 to June 2001

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In collaboration with the Egyptian Ministry of Health and Population, the U.S. Naval Medical Research Unit No.3 (NAMRU-3) conducts influenza and respiratory virus surveillance as part of a region-wide surveillance program to characterize influenza viruses circulating within the WHO Eastern Mediterranean Region (EMR). In this report, we describe the results of this surveillance activity from July 2000 to June 2001 in two major cities in Egypt, Alexandria and Cairo. A total of 1923 and 375 throat swab samples were collected from Alexandria Fever Hospital (AFH) and Shoubra General Hospital (SGH) Cairo, respectively. These samples were processed for virus isolation(s) in four different cell cultures i.e. H292, LLCMK2, MRC5 and MDCK. Viral isolates were identified using immunofluorescent techniques (IFA) with commercial respiratory and enteroviruses virus screening panels (Chemicon International, Temecula, CA).

Subtyping of influenza isolates was done by heamagglutination inhibition (HI) using WHO influenza subtyping kits provided by the CDC Influenza Branch, Atlanta, GA. A total of 251 influenza viruses were isolated during the surveillance period with a 12% (229/1923) isolation rate from AFH and 6% (22/375) from SGH. Influenza viruses isolated included 241(96%) type B and 10 (4%) type A. Only influenza A (H1N1) and influenza B (B/Sichuan/379/99-like) were isolated. In addition, 2 parainfluenza, 27 adeno and 27 entero viruses were isolated. Representative samples from the influenza A and B isolates were submitted to the WHO Collaborating Center on Influenza at CDC for strain analysis. The H1N1 isolates were identified as A/New Caledonia/20/99-like and B isolates as B/Sichuan/379/99-like. The previous year surveillance showed a predominance of influenza A (H3N2) similar to that observed worldwide.

Influenza Surveillance in New York State, 1998-2001

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Background: New York State Department of Health influenza surveillance consists of laboratory surveillance, nosocomial outbreak reporting, sentinel physician surveillance, and the State Epidemiologist's weekly assessment of influenza activity. This report examines the corroboration of data and possible redundancy of collected information over a three-year period.

Methods: Ten laboratories in New York State participate in World Health Organization and Centers for Disease Control collaborating laboratory surveillance systems. Throughout influenza season (October-May), these laboratories report the number of respiratory specimens tested and the number positive for influenza each week. The state's hospitals and long-term care facilities report outbreaks of nosocomial influenza, as required by state public health law. Sentinel physicians report on the number of patients seen weekly, and the number with Influenza-like Illness (ILI). Based on population, laboratory and outbreak reporting, the State Epidemiologist categorizes the level of influenza activity (as none, sporadic, regional or widespread) each week. **Results:** Surveillance data were reviewed for the period 1998-2001. Peak periods of influenza activity each season were characterized by ≥ 10% of respiratory specimens testing positive for influenza. Periods of increased virus isolation ranged from 11 to 14 weeks. Peak periods were also characterized by receipt of ≥ 5 outbreak reports/week the first two seasons and ≥ 2 reports/week in the third. Periods of elevated outbreak activity ranged from 8 to 10 weeks. When ≥ 15% of specimens tested positive for influenza, nosocomial outbreaks increased. During all three seasons, outbreaks at least doubled coincident with high circulating virus. Increases in ILI appeared earlier, and showed more fluctuation, than increases in viral isolates or outbreaks in all seasons. **Conclusion:** Nosocomial outbreaks increased sharply at the same time laboratories reported ≥ 15% of specimens testing positive for influenza. Peak periods of outbreak activity in healthcare facilities were of shorter duration than peak periods of virus isolation from the community, which may be attributed to aggressive infection control and public health oversight. Sentinel surveillance is a sensitive system for early season ILI detection; early fluctuations may be due to reporting artifact and other circulating viruses. Three of the surveillance systems were complementary in defining influenza activity. The State Epidemiologist's Report was a summary of these surveillance systems for national comparison.

Geographical Coherence of Influenza Epidemics in the US, France and Australia: 1978-98

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There is a substantial inter-annual variability in the circulating strains, impact, and time of onset of influenza epidemics occurring in temperate areas of the world. It is assumed that the disease results from human to human transmission of influenza viruses, and that the global circulation of these viruses stems from rapid transportation fluxes (1,2). To what extent influenza epidemics display similarities, or coherence, in geographically distant areas has not been determined. Here we examine the coherence of influenza epidemics in the US, France and Australia over 20 epidemic seasons.

Weekly number of deaths from pneumonia and influenza (P&I) and demographic data were provided by national agencies for vital statistics from Jan 1st, 1978, to Dec 31st, 1998, in the US, France and Australia. We used codes 480-487 from the International Classification of Diseases, 9th revision. Mortality time series dating back to 1968-77 are currently analysed.

From the national weekly P&I mortality time series, we defined epidemic weeks and baseline mortality by a linear seasonal regression model (3). For each winter season, we measured the overall and age-specific excess mortality (< or ≥ 65 years old), i.e. the difference of the reported mortality to the expected baseline mortality (4).

We estimated an average of 6,000 P&I excess deaths in the US over the study period (range 0-14,700), 2,100 in France (range 0-8,600) and 300 in Australia (range 0-1,000). Two of 20 influenza seasons did not result in substantial P&I excess mortality in the US, 3 in France and 1 in Australia. The duration of the epidemic periods was similar in the 3 countries : on average 12.3 weeks in the US (range [4-18]),12.3 in France (range [8-18]), and 10.2 in Australia (range [2-19]) (P=0.80). The maximum incidence of P&I excess mortality in elderly (persons over 65 years old) was 40/100,000 in the US, 60/100,000 in France and 42/100,000 in Australia. The proportion of P&I excess mortality in elderly ranged from 46% to 96% in the US, 87% to 100% in France and 40% to 100% in Australia. The correlation coefficient between the numbers of P&I excess deaths in the US and France in contemporaneous winter seasons was 0.70 (P=0.001). The number of P&I excess deaths in Australia was not correlated with that in France or the US in the preceding or following influenza season. In the influenza seasons resulting in substantial P&I excess mortality both in France and the US, the median time lag between the epidemic onsets was 1 week (range 0 - 11 weeks).

There is a fairly good coherence in the overall impact of influenza epidemics on P&I mortality in France and the US, contrary to Australia. Whether the lack of coherence is associated with differences in the circulating strains, vaccination coverage, or demographic factors, will be explored.

A DoD Global Influenza Surveillance Program

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Military global influenza surveillance began in 1976 as a United States Air Force public health program. In 1997 the Department of Defense (DoD) Global Emerging Infections Surveillance and Response System (GEIS) expanded the program to include all US military services, as well as local residents in areas where DoD overseas research activities operated. This worldwide DoD surveillance infrastructure provides valuable information designed to provide rapid responses to outbreaks that are potentially a significant threat to military readiness. Although this was first recognized during the 1918 influenza pandemic that took the lives of 43,000 US military personnel, it has been underscored by

more recent outbreaks that have impacted training and operational missions. The influenza surveillance initiative combines viral isolation, antigenic characterization, and molecular sequencing with clinical and public health information. This information, as well as selected isolates sent for further antigenic characterization, is shared with the Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO) and has contributed to important decisions in influenza vaccine composition. From October 1999-October 2001, nearly 12,000 specimens were submitted to the Brooks Air Force Base virology laboratory in San Antonio, TX. These samples came primarily from 24 sentinel sites around the world and were processed according to standard virology protocols for the presence of any respiratory virus. A retrospective look at this data demonstrates the unpredictability from season to season of the type of virus that will circulate or the impact the virus will exert and the importance of continuing and even expanding the surveillance network. Since there are several respiratory viruses that cause "flu-like symptoms," any isolate is tracked, but influenza is the focus of the program. During the 1999-2000 season, 89% of the influenza isolates (337/377) were influenza A. Of those that were antigentically subtyped by hemagglutination-inhibition, 80% were H3N2. In contrast, during the 2000-2001 season, 43% of the influenza isolates (222/521) were influenza A and only 42% of those subtyped were H3N2. While the prevailing perception is that change originates in the Far East, the H3N2 (A/Panama) and the H1N1 (New Caledonia) components of the 2000-2001 and 2001-2002 seasons have emerged from Central America and the Southern Hemisphere respectively. Before that, Influenza A/Sydney/05/97(H3N2), also from the Southern Hemisphere, had predominated for three years (1997-2000). The DoD sponsors a unified program that is global in scope and is actually a microcosm of the larger international programs that pull from many geographically distinct surveillance programs.

Using CUSUM Techniques To Identify Influenza Outbreaks

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The objective of this research is to develop statistical methods for determining the beginning of an influenza epidemic. Each year influenza infections are responsible for large numbers of excess deaths, hospitalizations and physician visits in the United States, all of which are intensified during epidemic years. Influenza is a largely preventable illness because effective vaccines can be prepared and administered in advance of the typical November to March season. However, the timing of annual outbreaks can vary within this broad range, therefore timely identification of changes in the epidemiology of influenza can improve implementation of control and prevention programs. Additionally, influenza outbreaks occurring outside the typical season may elude detection until large numbers of cases have accumulated.

In the United States the Centers for Disease Control and Prevention's Influenza Branch coordinates surveillance for influenza using weekly mortality reports, laboratory data, disease reports, and sentinel physician reports. Because influenza is not a reportable disease, however, most cases are not reported to health officials. Surveillance is further complicated because many illnesses have "flu-like" symptoms, therefore laboratory confirmation is necessary for an accurate diagnosis. Reliance on laboratory confirmation or diagnoses that include influenza or influenza-like illness may miss the earliest cases in an epidemic because they appear as non-specific respiratory illnesses.

Emergency room visits at the George Washington University Hospital from Jan. 1, 1998 through May 15, 2001 were categorized according to five ICD-9 code groups: Flu (influenza), ILI (influenza-like illness), URI (upper respiratory infection), Viral NOS (not otherwise specified), and pneumonia. Exponential smoothing produced the equivalent of a non-symmetric running average. CUSUM methods with constant background and with exponential smoothing background level were compared to standard outbreak detection models (Z-scores) to detect the start of epidemics in 1999 and 2000.

For ILI and Viral NOS, CUSUM methods are preferable to standard Z-score methods because they have fewer false positives and no delay in recognizing outbreaks. Neither exponential smoothing nor constant (Poisson) CUSUM methods are clearly preferable to the other for identification of influenza epidemics. Because most agents of bioterrorism first appear with flu-like symptoms, the same data and methods described here can be used for early detection of bioterrorism attacks.

82 Global Health and GIS

Tuesday, March 26, 4:30 p.m.
Centennial Ballroom IV

Tuberculosis Status Among Iranian and Afghan patients Admitted to the National Research Institute of Tuberculosis and Lung Disease (1998-2000)

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Objectives: Surveys carried out world wide revealed that over 50% of refugees develop TB. Tuberculosis is of high prevalence in Afghanistan. No systematic study has been conducted on the evaluation of TB and the related treatment status among Afghan refugees in Iran yet. On the other hand, National Research Institute of Tuberculosis and Lung Disease (NRITLD), as a referral center, receives a high number of Afghans suffering TB from different parts of the country. Accordingly, during the past two years, a study was performed on the TB status among Afghan refugees in order to access preventive measures and anti-TB programs. **Method:** A cohort study was conducted on all adult TB cases (>15 years) referring to NRITLD from the beginning of 1998 to the end of 2000. A questionnaire containing personal data (age, gender, nationality and occupation) and TB status was distributed among the cases. The result of sputum smear before the treatment initiation and at the end of attack phase of treatment was recorded in the questionnaire as well. Result:A total of 1028 TB cases, 68.3% Iranian and 31.7% Afghan (326 cases) were studied. The mean age was 32.76 and 48.98 among Afghans and Iranians respectively (P<0.0001). Out of 712 patients with positive smear, grade of sputum smear of 686 cases were recorded. The minimum and the maximum of smear grade were +1(43.5%) and +3(37.4%) among Iranians, whereas, they were 32.4% and 44.1% among Afghans respectively (Table 2) (P<0.0001). Sputum smear was negative among 77.4% of Iranians (260 cases) and 63.3% (93 cases) of Afghans at the end of the second month, ($X^{2=10.36 \text{ and } df=1 \text{ and } P<0.001}$). Sputum smear of 70.6% (89 cases) of Iranians with smear grade of 3+ turned to negative at the end of the second month, however, this was 55.6%(32 cases) amongst Afghan cases (P=0.04, df=1 and X2=4.23). Treatment after default was seen among 49.2% of Afghan with smear positive pulmonary TB and 32.4% of Iranians (X2=40.2, df=1 and P<0.001). **Discussion:** The recent study suggested that Afghan TB patients were younger than Iranians and Afghans developed more severe forms of the disease compared to Iranians.Afghan refugees play an important role in transmission of Tuberculosis in Iran; therefore, controlling Afghan refugees for the presence of TB and the need to follow up the patients, while

being treated, should be taken into special consideration. As a consequence we will be able to prevent the dissemination of the disease, and also take an essential step in control of TB throughout the country.

Modeling Tuberculosis Dissemination in Harris County, Texas, 1995-1998, with Spatial Analysis and Geographic Information Systems (GIS)

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Modeling Tuberculosis Dissemination in Harris County, Texas, 1995-1998, with Spatial Analysis and Geographic Information Systems (GIS) The main focus of this study was to examine the spatial distribution of tuberculosis (TB) cases by area in Harris County, Texas over a three-year period, October, 1995 to September, 1998, using geographical information systems (GIS) software and spatial analytical techniques. A major objective of this study was to show how epidemiologic data could be merged with GIS in order to formulate study questions, generate and test hypotheses and critically evaluate topographic density maps that were prepared by merging systematic spatial analytical techniques with the database management and imaging qualities of a GIS. In-depth spatial analysis was conducted on a subset of 1480 incident TB cases gathered by the Houston Tuberculosis Initiative (HTI) during a 36-month period. Analytical methods included describing spatial point pattern distributions through the use of exploratory and analytical techniques in order to observe whether overall TB cases or subsets of TB cases exhibited any systematic patterns as opposed to being randomly distributed (according to theoretical Complete Spatial Randomness) throughout Harris County during the three year period. These methods included spatial point pattern techniques such as kernelling estimation, nearest neighbor analysis, (h) function methods, spatial filtering methods and a spatial scan statistical method. Analysis, after adjusting for underlying U.S. Census 2000 population, found that much of the intensity of TB cases in Harris County centered on a 5 mile radius from downtown Houston, inside the Highway 610 Loop. There was evidence of clustering of overall TB cases with larger clusters over smaller geographical areas (6-10 miles) and the 3-year incidence estimates climbed toward more than 300 cases/100,000 population. Black TB cases were found to be more concentrated in larger clusters over a smaller geographic area than other ethnic groups. Results of the spatial filtering process calculated the mean incidence for Black TB cases equal to 182 cases/100,000 population over 3 years. A spatial scan statistical method found significant ($P < 0.05$) clusters of four different molecularly characterized, clonally related groups. Further analysis of one specific cluster (Print 4) showed the individual risk of having TB for this Print type was 9 times higher than expected ($P < 0.01$). In addition, out of 7 individuals who rode public transportation in this cluster, 6 had a shared bus route.

Mapping of West Nile Virus Risk in the Northeast United States Using Multi-Temporal Meteorological Satellite Data

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West Nile Virus (WNV) was first discovered in the United States in September of 1999, after a cluster of cases of human neurological illness in the borough of Queens in New York City. Eventually, that outbreak led to 62 human cases of WNV, including 7 deaths. Multiple researchers identified and isolated the virus in several bird and mosquito species in New York. In 2000, an elaborate surveillance system was developed to detect the presence of WNV before human cases occur. This system was largely successful, as the number of WNV detections in birds and mosquitoes increased tremendously, while the number of human cases dropped to 14. In 2001, this surveillance system, and those like it in other states, detected the spread of WNV to over 20 states, with over 40 human cases. Detecting WNV in both birds and mosquitoes, however, is a time and labor intensive task, requiring dedicated staff and resources. In New York it has required hundreds of staff, and millions of dollars. It often takes at least 10 days from the time of specimen collection to the time when results are available. To improve efficiency and cost-effectiveness, proxies are sought to estimate the risk of WNV infection in a given area, preferrably on a real time basis. The project discussed here utilizes remotely sensed meteorological data to accomplish that goal. Data from the Advanced Very High Resolution Radiometer (AVHRR) on the NOAA series of meterological satellites provided the Normalized Difference Vegetation Index (NDVI) and land surface temperature proxies, as well as elevation, and were temporal Fourier processed. Bird and mosquito data (both infected and uninfected) were added to these images to suggest conditions favoring disease transmission. AVHRR data were also used to analyze changes over time that might be associated with the arrival of WNV in the United States, and with its potential spread over time. Maximum likelihood methods applied to these satellite data allowed production of a series of risk maps that measured the similarity of satellite conditions in a given area to the bird and mosquito data collected on the ground. Both bird and mosquito risk maps showed high kappa indices of agreement. As surveillance teams collect more field data on the ground, these risk maps should become more accurate. These risk maps can then be used by state and local authorities to better direct public health staff and resources, and hopefully prevent large-scale outbreaks of West Nile Virus in the future.

Investigation of Q Fever in Bosnia-Herzegovina, 2000: An Example of International Cooperation

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In July 2000, CDC and USDA investigators traveled to Bosnia-Herzegovina (BiH) to assist authorities with the investigation of reported outbreaks of Q fever in humans and animals. Local investigations of the disease had been hampered by limited diagnostic testing capability for *Coxiella burnetii*, the causative agent of Q fever. The CDC-USDA investigators worked with local health officials to establish a laboratory team to test human and animal specimens by immunofluorescence antibody assays (IFA). The team tested specimens from 415 persons, and detected antibodies in 177 (42.7%) from all over the country. The team also tested over 2000 animal specimens, and detected antibodies in 10% of cattle and 4% of sheep. Case control studies were conducted in two towns (Kakanj and Mostar) to further define risk factors for infection. Cases were defined as a patient with a clinically compatible illness that was also seropositive. Twenty-five cases and 23 controls were examined from Kakanj; most cases had illness onset in early March and early June consistent with two point-source outbreaks. Seventeen of 25 (68%) cases were male; mean age = 37 years, median age = 36 years. Unexpectedly, cases were less likely to have handled sheep (p=0.07) or cattle (p=0.02) than controls. Consuming milk purchased from a neighbor appeared to be a risk factor (OR 4.1 p=0.04), while consuming milk collected at home appeared protective (OR 0.23 p=0.05). Although not significant, cases engaged in general outdoor activities more often than controls (OR 2.8, p=0.12). In Mostar, 13 cases were examined with ill-

ness onset throughout January-June, consistent with sporadic exposures. Seven (54%) were male; mean age = 46, median age = 43. Eight cases were compared to matched controls in Mostar; cases appeared similar to controls with respect to livestock contact, but numbers examined were too small to determine significance. The serologic findings suggest widespread exposure in both humans and animals in BiH, which contradicts the perception that Q fever was a recent introduction to the country through animal importation. Q fever is probably endemic to the region, and the emergence of clinical disease and outbreaks may be associated with undefined changes in farming practices. The outbreak in Kakanj occurred in mainly persons with limited animal contact, indicating possible exposure by wind or dairy products. During their visit, CDC and USDA personnel worked to foster cooperation between the veterinary and medical communities in the Federation of BiH, and facilitated a meeting between veterinary officials from the Federation of BiH and the Republic of Srpska for the first time since the civil war. The team worked closely with these national representatives to make recommendations regarding the diagnosis, control, and prevention of zoonotic diseases such as Q fever.

A WHO Global Salm-Surv Retrospective Study Examining *Salmonella* Serotypes in South America, 2000: Dominance of *Salmonella* Serotype Enteritidis

WHO Global Salm-Surv South America Working Group[1],WHO Global Salm-Surv[2]

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Background: *Salmonella* is a leading cause of foodborne illness around the world. Laboratory-based surveillance data are needed to understand the epidemiology of *Salmonella* and other foodborne pathogens, influence public health action, and ultimately facilitate a decrease in the global burden of foodborne disease. In response to a need to strengthen national and regional laboratory capacity and foster collaboration between microbiologists and epidemiologists involved in human and animal health and food-related disciplines, World Health Organization (WHO) Global Salm-Surv was created. This is a collaborative project of WHO, the Danish Veterinary Institute, the Centers for Disease Control and Prevention, and Institut Pasteur. Key components of the program include an external quality assurance system and regional training courses. The first South American (SA) regional training course was conducted in Argentina in July 2000. During the second regional training course in September 2001, the WHO Global Salm-Surv SA Working Group, which involves microbiologists from national public health, veterinary, and food reference laboratories from SA countries, was established to exchange information and communicate *Salmonella* surveillance data. **Methods:** As an initial step in the surveillance of *Salmonella* in the SA Region, we conducted a retrospective study examining the distribution and rank of *Salmonella* serotypes during 2000. The SA Working Group member laboratories received *Salmonella* isolates for confirmation and serotyping using the Kaufman-White scheme with the O and H antisera available in each country. The SA WHO Global Salm-Surv members reported *Salmonella* surveillance data using country report forms. **Results:** In 2000, the SA Working Group member laboratories received 9,468 specimens, of which 9402 (99.1%) were serotyped. The specimen sources were human (n=2476, 26.3%), animal (n=2297,24.4%), food (n=1577, 16.7%), feed (n=2007,21.3%), and environmental (n=1045, 11.1%). Looking at all sources, the most frequent serotype in SA in 2000 was S. Enteritidis (n=4197, 44.6%). In humans, 1148 (46.3%) of the serotyped strains were S. Enteritidis, followed by *S. typhi*murium (12.7%) and *S. typhi* (9.8%). In food, S. Enteritidis accounted for 60% of the serotyped strains, *S. typhi*murium was found in only 5.2% and Agona in 3.4%. *Salmonella* Enteritidis was identified in 49.5% of the animal isolates, S. Heidelberg in 12.3%, and *S. typhi*murium in 5.4%. **Conclusion:** *Salmonella* Enteritidis was the most frequently isolated serotype from human and non-human sources in the SA Region in 2000. These data provide baseline information for a surveillance program that will monitor, over time, the prevalence of *Salmonella* serotypes in SA. Regional differences in isolation rates have been observed and reasons for these differences will be explored by the SA Working Group.

Recurrent Histoplasmosis Outbreaks in Acapulco, Mexico

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Although Histoplasmosis has a worldwide distribution it is often overlooked in the differential diagnosis of acute respiratory illness. Recently, 2 outbreaks of acute pulmonary histoplasmosis occurred in tourists in Acapulco. In a cohort study by CDC of the outbreak in American students, the only significant risk factor was staying at a beach hotel. In September a new outbreak occurred in convention attendees in the same hotel. We describe clinical and epidemiological characteristics of this outbreak and identification of the source. **Methods:** 291 persons, all guests in a hotel in Acapulco in September 13-21, 2001 were studied. Diagnosis was made by clinical and X-ray findings and serology and urine antigen. Controls were matched by date of stay; cases and controls answered a questionnaire on risk factors. Environmental sources were searched for by direct culture, and by peritoneal inoculation of samples and direct exposure of sentinel BALB/C mice. **Results:** Of 291, 227(78%) were ill (cases). Of these, 152 (67%) were male; median age was 38 yr, range 20-64. The most frequent symptoms were headache (89%), fatigue (82%), fever (81.5%; median 39.2°C), night sweats (78%), chills (71%), cough (63%), chest pain (55%), anorexia (52%), weight loss (43%; mean 3.7 Kg) and diarrhea (14%). Histoplasma Ag was found in 7/27 (26%) urine samples taken after 10 days of illness. Specific Abs were found in 41% and 89% of acute and convalescent sera, respectively, from 104 ill pts. Of the environmental samples, H.capsulatum was isolated only from soil of plants from the beach restaurant. The hotel was closed for study and remodeled following our recommendations. There have been no further cases after the last outbreak. Results of the case-control study of risk factors will be presented. **Conclusions:** A third outbreak of acute pulmonary histoplasmosis occurred in Acapulco, affecting 227 convention attendees (attack rate of illness 78%). Recurrence of outbreaks stresses the importance of source detection and elimination. Contaminated plant soil prepared from compost was the source of the outbreaks. Interestingly, plants and soil were changed by the same nursery before each outbreak. Histoplasmosis should be considered in the differential diagnosis in travelers with respiratory symptoms who visit endemic areas. Detection of H. capsulatum antigen in urine is low in acute pulmonary histoplasmosis. Acute/convalescent serology is recommended, since over 50% of acute sera were negative.

83 Late Breakers II

Tuesday, March 26, 4:30 p.m.
Centennial Ballroom III

84 Meet-the-Experts II

Wednesday, March 27, 7:30 a.m.
Regency Ballroom VI/VII

85 Plenary Session V

Wednesday, March 27, 8:30 a.m.
Centennial Ballroom I/II

86 Plenary Session VI

Wednesday, March 27, 8:30 a.m.
Centennial Ballroom III/IV

89 Emerging Vaccines for Emerging Diseases

Wednesday, March 27, 10:30 a.m.
Centennial Ballroom I

An Effective Proteoliposome-Based Vaccine Against B&C Meningococcal Disease

G. Sierra

Finlay Institute, Habana, CUBA

A purifed vaccine VAMENGOC-BC consisting of purified OMP(s) from *N. meningitidis* B and purified C polysaccharide from *N. meningitidis* C presented as a protein-polysaccharide complex based on a Proteoliposome model has been developed and carefully tested.

In a well controlled, randomized, stratified, prospective, double blinded placebo-vaccine trial this vaccine has shown an efficacy of 83%;95% Cl (42%-95%). After ten years (1987-97) of massive application in Cuba and many other countries of more than 40 millions of VA-MENGOC-BC doses under epidemic and endemic situations an effectivity ranging from 75 to 98% have been proved under different trial conditions (cohort studies, case-control studies, etc.)

A satisfactory low reactogenic and safe profile has been demostrated for this vaccine in vaccinees ranging from 3 monthes to adult age.

This Finlay's vaccine is the first in the world with proven clinical efficacy against group B meningococcus coused disease. The protective capacity of this vaccine has been tested against many different patogenic Men B-Sero-Subtypes.

Laboratory as well as clinical data based on more than 18 years of experience will be discussed during the presentation.

90 Anatomy of Emerging Infectious Diseases

Wednesday, March 27, 10:30 a.m.
Centennial Ballroom II

91 Antimicrobial Resistance

Wednesday, March 27, 10:30 a.m.
Centennial Ballroom III

Promoting Appropriate Antimicrobial Drug Use in Developing Countries

S. Sirinavin

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Appropriate antimicrobial drug use is defined as use that maximizes therapeutic benefit while minimizing development of resistance, adverse reaction, and cost. Antimicrobial drug use is a major cause of antimicrobial-resistance problems. Although methodology to maintain the useful life of antimicrobial drugs is available, but all are still far from adequacy. "Drugs" and "users" are the two key components.

Antimicrobial drugs are not adequately available in the poorest countries, while overloading with too many items and preparations of drugs is the problem in the others. Competitive business promotion of many new drugs usually results in overuse and rapid resistance. Too many drugs also give confusion to users and appropriate use is more difficult. Locally manufactured drugs are sometime of substandard which can cause inadequate therapy and also contribute to antimicrobial-resistance problems.

Antimicrobial drugs in developing countries are usually available "over-the-counter". Effects of antimicrobials on creating resistant microbes are difficult to be perceived while the drugs seems to be harmless and useful. Antimicrobials are therefore frequently used for several illnesses, especially for those with any inflammatory reaction. Rational antimicrobial prescription needs good diagnostic approach, including microbiologic diagnosis. Quality of curriculum for professional trainees, etiologic epidemiology information and laboratory supports are necessary. These are frequently insufficient in developing countries. Infectious disease specialists who are competent in guiding rational antimicrobial use are also scanty. In addition, antimicrobial drugs are widely used in animal husbandry without adequate guide or controlled.

In Thailand, inappropriate use of antimicrobial drugs and antimicrobial resistance problems have been concerned. The National Committee on Revising Essential Drug List tried to minimize the antimicrobial items in a National Drug List 2000. National guideline for antimicrobial therapy has been developed since 1994 and revised in 1996. National Antimicrobial Resistant Surveillance Center for monitoring resistance problems in human beings and Center for Antimicrobial Resistance Monitoring in Food-Producing Animals were developed recently. Activities to get people who concern about antimicrobial resistance problems in animals and in human to work and to think together have been organized through the National Committee on Controlling Non-Typhoidal Salmonellosis. Several strategies to improve prevention and treatment of infectious diseases, have been implemented in hospitals and community. Drug utilization reviews in hospital setting are performed for all restricted antibiotics. So far, inappropriate use of antimicrobial drugs and resistance problems in Thailand are still increasing. A strong national policy commitment and support on solving this problem is necessary.

92 Infectious Diseases in Aging Populations

Wednesday, March 27, 10:30 a.m.
Centennial Ballroom IV

93 Foreign Policy and Infectious Diseases

Wednesday, March 27, 10:30 a.m.
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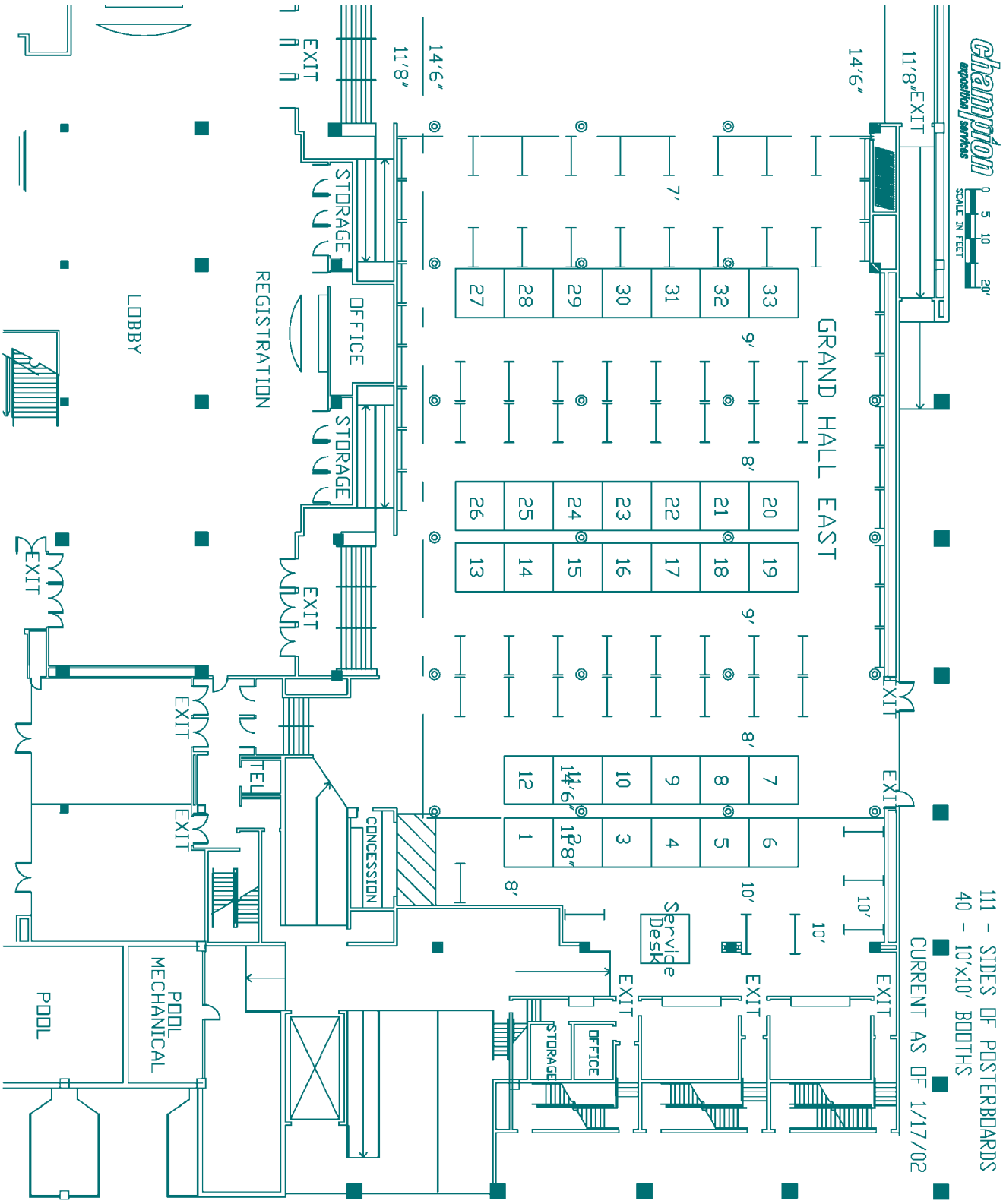

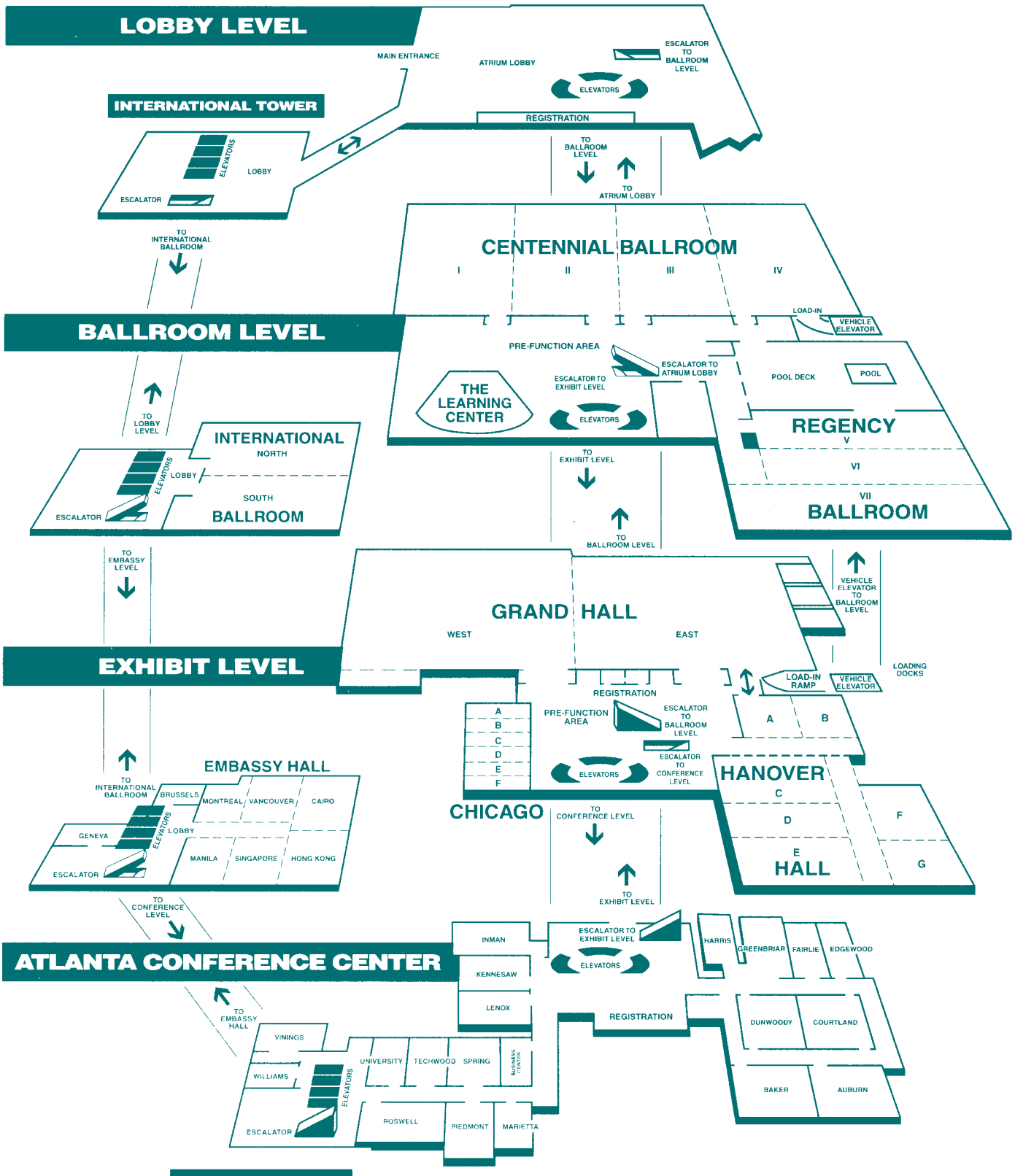

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