Innovations in Wound Infection Prevention and Management and Antimicrobial Countermeasures

The Quadruple Aim: Working Together, Achieving Success

COL Duane Hospenthal, Infectious Disease Consultant to the Army Surgeon General

24 January 2011
**Title:** Innovations in Wound Infection Prevention and Management and Antimicrobial Countermeasures

**Performing Organization:** Army Medical Command, Army Surgeon General, Fort Sam Houston, TX, 78234

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- b. Abstract: unclassified
- c. This Page: unclassified

**Limitation of Abstract:** Same as Report (SAR)

**Number of Pages:** 77
Complex traumatic injuries are often complicated by multidrug-resistant (MDR) bacterial infections and colonization
- Resulting in increased morbidity and mortality
- Increased use of broad spectrum antimicrobials and older and/or more toxic agents (e.g., colistin and aminoglycosides)
MDR bacteria – multidrug-resistant bacteria

MDRO – multidrug-resistant organisms
  – Typically, gram negative rods
    • Acinetobacter, E. coli, Enterobacter, Klebsiella, Pseudomonas
  – Also, gram positive cocci
    • Methicillin-resistant Staphylococcus aureus (MRSA)
    • Vancomycin-resistant Enterococcus (VRE)
Wound Infection Prevention and Management - Solutions

- Prevention
  - Prevention of infection
  - Prevention of colonization

- Management
  - New diagnostic modalities
  - New treatment modalities
Wound Infection Prevention and Management - Solutions

- **Prevention**
  - Prevention of infection
  - Prevention of colonization

- **Management**
  - New diagnostic modalities
  - New treatment modalities

- Epidemiology
- Pathophysiology
Wound Infection Prevention and Management - Solutions

- Prevention
  - Prevention of infection
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- Management
  - New diagnostic modalities
  - New treatment modalities
  - Epidemiology
  - Pathophysiology
  - Epidemiology
  - Pathophysiology
Wound Infection Prevention and Management - Outline

- Current epidemiology
- Prevention efforts
- Management efforts
Wound Infection Prevention and Management

- Current epidemiology
- Prevention efforts
- Management efforts
Wound Infection Prevention and Management - Epidemiology

Combat Hospital - Vietnam

Arnold. Mil Med 1978;143:161

2011 MHS Conference
Association of infection with trauma (Joint Theater Trauma Registry, JTTR)

<table>
<thead>
<tr>
<th></th>
<th>Odds ratio</th>
<th>95% CI</th>
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<tbody>
<tr>
<td>Bomb</td>
<td>9.78</td>
<td>1.81-54.82</td>
</tr>
<tr>
<td>Landmine</td>
<td>4.00</td>
<td>1.29-2.4</td>
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<tr>
<td>ISS score &gt; 29</td>
<td>3.76</td>
<td>2.47-5.73</td>
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<tr>
<td>ISS score 15-29</td>
<td>2.33</td>
<td>1.56-3.50</td>
</tr>
<tr>
<td>Explosive device</td>
<td>1.86</td>
<td>1.04-3.33</td>
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</table>

### Infections associated with combat-injury

#### Trauma Infectious Disease Outcome Study (TIDOS) (NIAID-USU IDCRP)

<table>
<thead>
<tr>
<th></th>
<th>ICU</th>
<th>Ward</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>64 (43.8%)</td>
<td>128 (14.8%)</td>
<td>192 (24.5%)</td>
</tr>
<tr>
<td>Infections</td>
<td>28 (43.8%)</td>
<td>19 (14.8%)</td>
<td>47 (24.5%)</td>
</tr>
<tr>
<td>Bloodstream</td>
<td>12 (18.8%)</td>
<td>6 (3.9%)</td>
<td>17 (8.9%)</td>
</tr>
<tr>
<td>Skin/soft tissue</td>
<td>16 (23.4%)</td>
<td>12 (9.4%)</td>
<td>27 (14.1%)</td>
</tr>
<tr>
<td>Osteomyelitis</td>
<td>8 (12.6%)</td>
<td>6 (4.7%)</td>
<td>14 (7.3%)</td>
</tr>
</tbody>
</table>
Wound Infection Prevention and Management - Epidemiology

- Acinetobacter and other MDR pathogens
  - Hospital-acquired infections in Turkey
  - Ventilator-associated pneumonias in Lebanon
  - Nosocomial bacteremia in Israel
  - ICU infections in Kuwait
- USNS Comfort, March-May 2003
- 211 trauma patients (85% Iraqi) - 56 infected
  - Injury to admission - avg. 4.2 days
  - \textit{Acinetobacter} - 33%
Virulence of MDR *Acinetobacter* (USAISR burn patients). Mortality with bacteremia

<table>
<thead>
<tr>
<th>Organism</th>
<th>OR</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>P. aeruginosa</em></td>
<td>2.25</td>
<td>0.96 - 5.30</td>
<td>0.061</td>
</tr>
<tr>
<td><em>K. pneumoniae</em></td>
<td>2.71</td>
<td>1.14 - 6.49</td>
<td>0.025</td>
</tr>
<tr>
<td><em>Acinetobacter</em></td>
<td>0.48</td>
<td>0.21 - 1.11</td>
<td>0.084</td>
</tr>
<tr>
<td><em>S. aureus</em></td>
<td>0.79</td>
<td>0.30 - 2.06</td>
<td>0.628</td>
</tr>
<tr>
<td>any MDR</td>
<td>2.78</td>
<td>1.13 - 6.83</td>
<td>0.026</td>
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</table>

### Acinetobacter virulence (extremity trauma)

<table>
<thead>
<tr>
<th>Organisms</th>
<th>Initial</th>
<th>Relapse</th>
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<tbody>
<tr>
<td><strong>Acinetobacter</strong></td>
<td>13</td>
<td>0</td>
</tr>
<tr>
<td><strong>Enterobacter</strong></td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td><strong>Pseudomonas</strong></td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td><strong>E. coli</strong></td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>CoN <strong>Staphylococcus</strong></td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td><strong>Staphylococcus aureus</strong></td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td><strong>Enterococcus</strong></td>
<td>3</td>
<td>0</td>
</tr>
</tbody>
</table>

Fungal pathogens causing invasive infections

WRAMC - 2002-2008

0.4 cases/1,000 admissions (n=6)

Where are all the Acinetobacter and other MDR bacteria coming from?
Theories
- Pre-injury colonization
- Inoculation at time of injury from environment
- Nosocomial transmission
Wound Infection Prevention and Management - Epidemiology

- Pre-injury colonization
  - Fort Sam Houston, 100 Soldiers
    - *Acinetobacter* detected in 17 (17%)
    - Phenotypes/genotypes unlike clinical isolates
    - Repeat study in Iraq detected 0/107 (0%)
  - Fort Sam Houston, 812 Soldiers
    - Community-acquired MRSA detected in 24 (3%)
    - MDRO carried into battle

Griffith. Infect Control Hosp Epidemiol 2006;27:659
Environmental contamination?
- Wound of Soldiers, Baghdad CSH, Iraq
- 49 casualties - 61 wounds
  - 37 of 40 recovered bacteria
    - Gram positive skin flora (including 2 MRSA)
    - No gram negative MDR bacteria recovered

Murray. Mil Med 2006;171:826
Nosocomial transmission?
– Cultures from an deployed CSH (Iraq)

Yun. Mil Med 2006;171:821

2011 MHS Conference
- MDR bacteria recovered from local nationals in both Iraq and Afghanistan at admission
  - Large number of MDR *E. coli* in Afghanistan

Ake. IDSA 2009
Sutter. IDSA 2009

2011 MHS Conference
Wound Infection Prevention and Management - Epidemiology
Wound Infection Prevention and Management - Epidemiology
- **PFGE strains**
  - 66 different strains among 170 clinical isolates
  - 25 different strains among 34 environmental isolates

A strain
- Environmental sample from a CSH Operating room
- 43 patients- 2 Baghdad, 18 Comfort, 6 LRMC, 19 WRAMC

2011 MHS Conference
Acinetobacter recovered from Canadian soldiers treated in Afghanistan after return to Canada

Tien. BMC Infect Dis 2007;7:95

Lane 10 - ventilator air filter (Kandahar)
Wound Infection Prevention and Management - Epidemiology

- **54 Screened in Iraq** - 1 MRSA
  - 0%

- **50 Screened in Germany** (2.8 days) - 1 Acinetobacter
  - 2%

- **32 Screened in the US** (7.9 days) - 1 ESBL-producing *Klebsiella pneumoniae*, 2 MRSA, 3 Acinetobacter
  - 10%

- **9 Infections in the US** (11.6 days) - 1 ESBL-producing *Klebsiella pneumoniae*, 7 Acinetobacter

*Kaspar. Mil Med 2009;174:899*

2011 MHS Conference
Also, within CONUS within our MEDCENs

22% of patients developed new colonization with MDRO after admission to WRAMC

Weintrob. Infect Control Hosp Epidemiol 2010;31:330
Incidence/prevalence of MDR infections?
- No ICD-9 code for *Acinetobacter* infection
- No ICD-9 codes for MDR Gram negative bacteria infections
- Admission colonization screening
  - BAMC/LRMC/NNMC/WRAMC collaboration
  - Produce potentially actionable data
    - For individual patient care/local infection control
    - For feedback upstream
  - 2003-2008, screening not standardized, *Acinetobacter* only
  - Fall 2008-present, screening standardized, expanded to all MDR bacteria
- 2005-09, 18,560 of 21,272 admits screened
- *Acinetobacter* colonization declined
  – LRMC, 7% to 1%; Level V, 21% to 4%
## Wound Infection Prevention and Management - Epidemiology

- **MDR screening (2009)**

<table>
<thead>
<tr>
<th></th>
<th>LRMC</th>
<th>BAMC</th>
<th>NNMC</th>
<th>WRAMC</th>
<th>Total</th>
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<tbody>
<tr>
<td>Personnel screened</td>
<td>2256</td>
<td>169</td>
<td>193</td>
<td>371</td>
<td>2989</td>
</tr>
<tr>
<td>Personnel MDR positive</td>
<td>78</td>
<td>27</td>
<td>23</td>
<td>43</td>
<td>171</td>
</tr>
<tr>
<td><strong>Colonization rate</strong></td>
<td><strong>3%</strong></td>
<td><strong>16%</strong></td>
<td><strong>12%</strong></td>
<td><strong>12%</strong></td>
<td><strong>6%</strong></td>
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<tr>
<td><em>Acinetobacter</em> species</td>
<td>18</td>
<td>7</td>
<td>11</td>
<td>14</td>
<td>50</td>
</tr>
<tr>
<td><em>Escherichia coli</em> (ESBL)</td>
<td>52</td>
<td>11</td>
<td>10</td>
<td>25</td>
<td>98</td>
</tr>
<tr>
<td><em>Klebsiella</em> species (ESBL)</td>
<td>7</td>
<td>8</td>
<td>0</td>
<td>3</td>
<td>18</td>
</tr>
<tr>
<td>MRSA</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>4</td>
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<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
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### MDR screening (2009)

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<tr>
<td>MRSA</td>
<td>1</td>
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<td>2</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

Hospenthal. ATACCC 2010

2011 MHS Conference
Joint Theater Trauma Registry (JTTR) Infectious Disease module

- Improved clarity to define epidemiology
  - Tool for study of injury-associated infections and best care/interventions
Wound Infection Prevention and Management - Epidemiology

- Multidrug-resistant Organism Repository and Surveillance Network (MRSN)
  - Improved clarity to define epidemiology
    • Phenotypic and genotypic characterization of bacterial isolates
    • Resource for MTF outbreaks
Wound Infection Prevention and Management

- Current epidemiology
- Prevention efforts
- Management efforts
Standardization of care practices

- Guidelines
  - Use on national/international guidelines
  - Development of combat-specific guidelines

- Standardization of theater infection control (IC) program/procedures (SOPs)

- Trained IC officers (ICOs) in theater

Emphasis on IC basics in theater

Clinical microbiology in theater
Wound Infection Prevention and Management - Prevention

- Clinical practice guidelines
  - Consensus conference (Jun07)
  - Production of clinical practice guidelines – “Guidelines for Prevention of Infection after Combat-related Injuries” (Mar08)
  - Basis for JTTS guidelines (Mar10)
  - Update consensus conference (Jan11)
Wound Infection Prevention and Management - Prevention

- Clinical practice guidelines
  - Rapid evacuation to surgical care (irrigation/debridement)
  - Limit antibiotic spectrum/duration around wound management
  - Emphasize basic infection control efforts to prevent spread from other hospitalized patients and to decrease antibiotic pressure selecting for resistant organisms

Hospenthal. J Trauma 2008;64:S211

2011 MHS Conference
Infection control basics
  – Handwashing, cohorting, transmission based precautions (isolation)
Antimicrobial stewardship
  – Preventive and empiric use
Continued study of epidemiology
Innovative strategies and technologies
Wound Infection Prevention and Management - Prevention

- Ventilator-associated pneumonia prevention - Air Force Theater Hospital Balad

Landrum. J Trauma 2008;64:S123

2011 MHS Conference
- Rapid discharge of host nation patient to decrease nosocomial MDR spread

Wound Infection Prevention and Management - Prevention

  - Limited availability of trained IC personnel
  - Lack of emphasis on IC basics

Hospenthal. J Trauma 2009;66:S120

2011 MHS Conference
Wound Infection Prevention and Management - Prevention

- Infection control ALARACT (2008)
  - Called for CSH Commander to assess and improve IC programs
- IC teleconsultation service established (2008)
  - infect.cntrl.consult@us.army.mil
Infection Control in the Deployed Setting course developed (2008)
- AMEDD C&S course 6A-F22, "Infection Control in a Deployed Environment"
- 5-day short course for deploying Infection Control Officers (ICOs)
- Nine classes held to date at BAMC
  - 46 USA/USAF graduates
Wound Infection Prevention and Management - Prevention

- HQDA EXORD 328-10 Infection Control Officers In Deploying Combat Support Hospitals (2010)
  - Requires CSH to have trained ICOs at each deployed location
- Deployment IC SOP adopted by USFOR-A (2010)
Wound Infection Prevention and Management

- Current epidemiology
- Prevention efforts
- Management efforts
Wound Infection Prevention and Management - **Diagnostics**

- Study of microbiology and immunological response/pathophysiology
- Predict when wounds can be safely closed
- Predict whether bacteria are contaminating, colonizing, or infecting wounds (who to treat)
Prediction of when wounds can be safely closed

**TABLE V Comparison of Effluent Cytokine Concentrations Between Healed and Dehisced Wounds (N = 50)**

<table>
<thead>
<tr>
<th></th>
<th>Concentration (Mean and Standard Deviation) (pg/mL)</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Healed</td>
<td>Dehisced</td>
</tr>
<tr>
<td>RANTES protein</td>
<td>1372 ± 1056</td>
<td>410.4 ± 350.5</td>
</tr>
<tr>
<td>Amino-procalcitonin</td>
<td>18.0 ± 19.3</td>
<td>169.3 ± 59.8</td>
</tr>
<tr>
<td>IL-13</td>
<td>12.0 ± 14.8</td>
<td>6.00 ± 2.78</td>
</tr>
</tbody>
</table>

*Student t test.

Wound Infection Prevention and Management - Diagnostics

- Bioburden/microbiome studies
- Studies of resistance and virulence genes
- Special media (e.g., CHROMagar)
- PCR-based diagnostics

Wound Infection Prevention and Management - Treatment

- Treatment of contamination or colonization (prevention)
  - Antibiotic timing and delivery (local and systemic)
  - Irrigation timing and pressure
  - Immunomodulation
  - Prevention or disruption of biofilms

- In vitro, animal models, retrospective and prospective clinical trials
Wound Infection Prevention and Management - Treatment

- NIAID-USU Infectious Disease Clinical Research Program (IDCRP)
  - Multicenter clinical trials group
    - DoD-VA Trauma Infectious Disease Outcome Study (TIDOS)
    - Preventive use of chlorhexidine clothes in military trainees

Whitman. Infect Control Hosp Epidemiol 2010;31:1207
2011 MHS Conference
Orthopaedic Extremity Trauma Research Program (OETRP, formerly OTRP) (2006)
- Reduction in wound infection
- Multicenter clinical trials group
  - FLOW (Fluid Irrigation Techniques in Patients with Open Fracture Wounds) study
  - Local therapies to prevent infections and promote wound healing
Major Extremity Trauma Research Consortium (METRC)

- Supported by DoD and OETRP funding, including through PRORP
- Prevention and treatment of acute and chronic Infections
- Multicenter clinical trials group
  - Wound bioburden study
  - Randomized trial of oral versus IV antibiotics for wound infection with hardware in place (POvIV)
Peer Reviewed Orthopaedic Research Program (PRORP)

– DoD CDMRP program
  - Non-invasive thermal ablation of osteomyelitis
  - Novel agents to inhibition of orthopaedic implant infections (e.g., host defense peptides, bacterial collagen-like proteins)
  - Novel agents to prevent biofilms
Wound Infection Prevention and Management - Treatment

- In vitro - antibiotic calcium sulfate pellets
- In vivo (animal)
  - Timing of antibiotics/debridement
  - Use of colistin beads in osteomyelitis
  - Resorbable antibiotic chitosan sponge

Stinner. J Orthop Trauma 2010;24:592

2011 MHS Conference
Clinical, retrospective
- Vancomycin/amikacin dosing in burn patients undergoing continuous venovenous hemofiltration (CVVH)
- Use of external fixation in the combat setting

Possley. J Trauma 2010;69:S135
Wound Infection Prevention and Management - Way Forward

- Way forward
  - Source of MDR bacteria colonization and infection requires additional study
  - Infection control measures across the Military Health System (MHS) need to be continually improved and emphasized
  - Better understanding of the pathophysiology of wound infections is needed
  - Improved diagnostic and therapeutic modalities are needed
2011 Military Health System Conference

DoD RDT&E Investments in Wound Infection Prevention & Management

The Quadruple Aim: Working Together, Achieving Success

COL Julia Lynch, Director Military Infectious Diseases Research Program, JPC2 Chair

24JAN2011
FY08
- Joint Force Health Protection, GDF report (Guide for Development of the Force)
  - Aim: address prevention, diagnosis, treatment, and mitigation of deployment-related injuries and psychological health concerns
  - Outlined validated gaps deemed likely addressable by increased investment in military medical R&D
- “War Supplemental”
  - One-time appropriation of Congressional Special Interest funding
RDT&E for countermeasures to treat & manage wound infections

- **MIDRP Program Area W – ASAALT established FY10**
  - Strategic Plan: Conduct research leading to the development of measures to prevent wound infections and sepsis and nosocomial transmission of bacteria.
  - FY10 Research Objectives:
    - Determine mechanisms of biofilm formation in wounds and evaluate in-vitro methods of mitigation
    - *In-vitro* analysis of novel therapies for wound infections
    - Characterize basic pathophysiologic mechanisms of Gram negative bacteria
    - Develop methods to understand the dynamics of microbial communities in infected & healing wounds
• Defense Health Program enhancement (DHPe)
  – New, sustained program initiated in FY10
  – Based on GDF gaps
• Objectives:
  – To discover and explore innovative approaches to protect, support, and advance the health and welfare of military personnel, families, and communities
  – To accelerate the transition of medical technologies into deployed products
  – To accelerate the translation of advances in knowledge into new standards of care for injury prevention, treatment of casualties, rehabilitation, and training systems that can be applied in theater or in the clinical facilities of the Military Health System (MHS)
RDT&E for countermeasures to treat & manage wound infections

- **Infectious Diseases DHPe TASKS Areas:**
  - Wound Infection Prevention and Management
  - Antimicrobial Countermeasures
  - Rapid Screening of Fresh Whole Blood
  - Diagnostic Systems for Infectious Diseases
  - Acute Respiratory Disease
  - Innovative Immuno-Chemo Prophylaxis
RDT&E for countermeasures to treat & manage wound infections

- **Wound Infection Prevention & Management:** Fundamental & applied research to develop tools & practices that prevent infections and/or guide clinical wound management decisions.

- **Expected Outcomes:**
  - Discovery & characterization of host immune response biomarkers associated with infection to inform clinical wound-management decisions (e.g., optimal wound closure time)
  - Development of tools for:
    - early detection of multidrug-resistance organisms (MDROs),
    - identification of nosocomial pathogens,
    - characterization of antimicrobial resistance patterns
RDT&E for countermeasures to treat & manage wound infections

- **Wound Infection Prevention & Management:**

- **Expected Outcomes:**
  - Development of novel environmental treatments to prevent/eliminate pathogen contamination from military medical settings.
  - Development of an *in vivo* model for polytrauma/blast wound infection

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**Staphylococcus aureus**

**Confocal image of osteoblast cells attaching on silicon-substituted hydroxyapatite nanocrystals**
RDT&E for countermeasures to treat & manage wound infections

- **Antimicrobial Countermeasures**: Fundamental & applied research to develop therapies to treat wound infections
  - Acinetobacter baumannii, Pseudomonas aeruginosa, methicillin-resistant Staphylococcus aureus, extended-spectrum beta-lactamase producers, & Klebsiella pneumoniae.

- **Expected Outcomes**
  a) Identification & characterization of microbial virulence factors & other potential therapeutic targets of metabolic or signaling pathways associated with wound infection & biofilm processes.
Antimicrobial Countermeasures:

b) Identification of novel therapeutics (e.g., drugs) to mitigate wound infection & biofilm processes.

c) Preference is for discoveries applicable to polymicrobial infections & topical treatment approaches.
FY10 DHPe Funding profile: Wound Infection Prevention and Management task area

Intramural Extramural

<table>
<thead>
<tr>
<th></th>
<th>WRAIR</th>
<th>UC Davis, School of Medicine</th>
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<tbody>
<tr>
<td>NRL</td>
<td>NMRC</td>
<td>AFIP</td>
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</tbody>
</table>

FY10 $:

\[
\begin{align*}
\text{Intramural} & : 77\% \\
\text{Extramural} & : 23\%
\end{align*}
\]

\text{Total} ~$4.5 \text{ M} + ~$1.3 \text{ M} = ~$5.8 \text{ M}
FY10 DHPe Funding profile: Antimicrobial Countermeasures task area

<table>
<thead>
<tr>
<th>Intramural</th>
<th>Extramural</th>
</tr>
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<tbody>
<tr>
<td>WRAIR</td>
<td>Aridis Pharmaceuticals, LLC</td>
</tr>
<tr>
<td>ISR</td>
<td>North Carolina State University</td>
</tr>
<tr>
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<td>University of Pennsylvania</td>
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<tr>
<td>Iasis Molecular Sciences</td>
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<tr>
<td>University of Michigan</td>
<td></td>
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<tr>
<td>Mote Marine Laboratory</td>
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</tr>
<tr>
<td>Colorado State University</td>
<td></td>
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<tr>
<td>University of MD; Biotechnology Institute</td>
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<tr>
<td>Akebia Therapeutics</td>
<td></td>
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<tr>
<td>University of Toronto</td>
<td></td>
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<tr>
<td>New Mexico Institute of Mining &amp; Technology</td>
<td></td>
</tr>
</tbody>
</table>

FY10 $69% Intramural: ~$6.5 M
31% Extramural: ~$14.1 M
Total $20.6M
Key Accomplishments

- **WRAIR**: Developed a *novel osteomyelitis model* to study effects of MDR bacteria infection on osteoblast differentiation
  - Model will facilitate study of gene expression changes during bone differentiation in the context of infection, and provide a system for the study of therapeutic effects of agents.
  - May accelerate development of treatment & management options for osteomyelitis due to MDRO

- **NRL**: Antimicrobial Resistance Determinant Microarray (ARDM)
  - New technology for rapid screening of microbial or clinical samples for a broad range of antibiotic resistance genes
  - Promising as a useful tool for clinicians in selecting the best antibiotic therapy before the resistance phenotype is available
Key Accomplishments

**WRAIR, WRAMC, JHU: Arbekacin Treatment-IND**
- Arbekacin, approved for use in Japan, has recently been demonstrated by WRAMC to be effective against several MDR bacterial species.
- A collaborative effort between researchers at WRAIR, WRAMC, and JHU is preparing a treatment IND for submission to FDA in 2011.

**WRAIR: Recombinant human PON1 (quorum sensing molecule) inhibits formation and/or disruption of bacterial biofilms *in vitro***
- PON1 (100 mg/ml) *inhibited* the formation of biofilms
  - *A. baumannii* & *P. aeruginosa*
- Human PON1 worthy of investigating as an anti-biofilm agent for treating chronic wound infections.
**Key Accomplishments**

- **WRAIR**: Iron chelator (VK28; human use approved for other treatment) is effective against MDR bacteria \textit{in vitro}.
  - Works in synergy with conventional antibiotics.
  - Converted \textit{Acinetobacter baumannii} once resistant to kanamycin & gentamicin to susceptibility.
  - Compound in Phase I clinical testing.
  - Iron chelators may prove useful in treating MDROs \textit{in vivo}, & maybe even biofilms.

- **The Scripps Research Institute**: Synthetic derivatives of arylomycin (inhibitor of bacterial type I signal peptidase) display broad-spectrum antibiotic activity.
  - Arylomycin-based drugs may reduce virulence while simultaneously killing bacteria.
RDT&E for countermeasures to treat & manage wound infections

- DHPe-sponsored Wound Symposium
  - 2-4 MAY 2011; San Antonio, TX
  - Program planning coordinated with AFIDS
  - Goals:
    - Assess Progress: FY10 DHPe + FY08 War Supplemental
    - Facilitate collaboration: intramural and extramural
    - Re-assess research gaps
- Anticipate second round of DHPe funding in FY12
Thank you for your attention....
Joint Program Committee (JPC2):
- Army Representative on JTCG-2 (Chair of the committee and Director RAD-1)
- Navy representative on JTCG-2
- Air Force representative on JTCG-2
- ID consultant to USA SG
- ID consultant to USAF SG
- ID consultant to USN SG
- MIDRP Program W Research Coordinator
- USAMMDA
- AMEDD C&S
- AFHSC
- NIH
- OSD[HA]
- ODATSD (CBD/CD)
- VA
- IDCRP (NIAID/USUHS)