

**Not for Publication until released by  
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**Statement of**

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## **the House Armed Services Committee**

Chairman Snyder, Representative Wittman, distinguished Members of the Subcommittee, I am pleased to be with you today to update you on Navy Medicine's response to multidrug resistant organisms (MRDOs). As the Navy Medicine Specialty Leader for Infectious Diseases and a practicing infectious disease physician at the National Naval Medicine Center, Bethesda, I can assure you that this issue is vitally important to the Navy Surgeon General, Vice Admiral Adam Robinson, and it has considerable focus at the Bureau of Medicine and Surgery (BUMED) and throughout Navy Medicine.

As the 20<sup>th</sup> century closed, the global medical community became increasingly aware that infectious diseases were far from vanquished. Bacteria that had been evolving for billions of years had been able to adapt to the antibiotics developed in the last 80 years -- leaving us with the reality of MDROs. This complex, worldwide threat has reached such critical proportions that earlier this year the Institute of Medicine of the National Academy of the Sciences sponsored a workshop "*Antibiotic Resistance: Implications for Global Health and Novel Intervention Strategies*" whose findings were released this month in a 440 page summary of the situation and how to address it<sup>1</sup>.

In 2010, treating infections in the setting of widespread bacterial resistance has challenged the Military Health System (MHS) as it has hospitals throughout the US and rest of the world. The difference for the Department of Defense (DoD) has been the concomitant care of thousands of young, injured service members coming from the wars in Iraq and Afghanistan.

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<sup>1</sup> *Antibiotic Resistance: Implications for Global Health and Novel Intervention Strategies: Workshop Summary* Eileen R. Choffnes, David A. Relman, and Alison Mack, Rapporteurs; Forum on Microbial Threats; Institute of Medicine. National Academies Press, Washington, DC 2010.

Increasingly, many of these critically injured patients are colonized or infected with MDROs, especially gram-negative bacteria, that demonstrate resistance not just to first line antibiotics, but to all the major antibiotic classes in our armamentarium. This situation limits treatment options with either second line drugs with greater toxicity or, in some cases, no drugs to which the organism demonstrates sensitivity. As a result, this has led to an extensive search for the source of these multiple drug resistant organisms and how to most effectively treat and control their spread among patients and staff in our hospitals.

An emerging problem with drug resistance organisms in the deployed setting, initially *Acinetobacter baumannii* complex, first became evident on the USNS COMFORT (T-AH 20) during its deployment to the Persian Gulf in 2003. Subsequently, all three Services observed an increase in combat injured patients returning with resistant bacteria and the Services have addressed these problems in a similar fashion. As the two wars have continued, the MDRO problem has evolved from primarily *Acinetobacter* to an expanded problem with gram-negative bacteria producing Extended Spectrum Beta Lactamases (ESBLs) including *Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter cloacae* and *Pseudomonas aeruginosa*, as well as the widely publicized gram positive organism, methicillin resistant *Staphylococcus aureus* (MRSA).

The U.S. Centers for Disease Control and Prevention (CDC) has responded to the problem of MDROs in US hospitals with updated guidelines. DoD military treatment facilities (MTFs) have been following CDC recommendations as well as requirements established by The Joint Commission (TJC) for monitoring and responding to healthcare associated infections (HAI). Additionally, DoD regulation 6025.13R requires MTFs to have a Healthcare Quality Assurance Program that includes a locally constituted Infection Control Committee (ICC). The ICCs of every MTFs have increased their vigilance for these MDRO infections. In addition, the

military medical centers treating combat injured have gone further in establishing screening for MDROs upon hospital admission to identify colonized/infected patients. In 2008, DoD joined the CDC's National Healthcare Safety Network (NHSN) and mandated the use of the NHSN for reporting device-associated infections in critical care areas and HAI. Infection control professionals from MTFs participate in DoD's Infection Prevention and Control Panel (IPCP) to address issues in infection prevention and control including HAI. The IPCP collaboration includes Tri-Service and Office of the Assistant Secretary of Defense for Health Affairs/TRICARE Management Activity (TMA) representatives with responsibility for providing oversight, direction and guidance for Infection Control in the Military Health System. The joint IPCP group meets monthly to discuss infection prevention across the military by Navy, Army and Air Force infection prevention subject matter experts (SMEs). The SMEs and TMA track and report on NHSN data that includes the combat injured as part of the data for individual hospitals.

While most U.S. hospitals have reported these problems among long-term patients, frequently elderly in the Intensive Care Unit (ICU), MTFs experienced a different demographic, with most cases of MDRO infections occurring in younger, combat-injured patients. MDROs began to complicate chronic skin and soft tissue infections, osteomyelitis cases and, in some of the injured, led to increased limb loss, sepsis and death. The infectious diseases (ID) and infection control (IC) communities of the treating MTFs recognized the need for focused efforts in addressing a number of aspects of the MDRO problem in the combat injured. These included:

1. Determining the etiology of colonization/infection: Is the source at time of initial injury, early medical care in theater or from ICUs in the continental US? Are MDROs found in the environment, and how are these organisms related genetically? Bacterial isolates from patients should be maintained in a repository so they can be studied to determine how resistance has spread and to ascertain whether there is a relationship among different isolates.
2. Re-emphasizing standard infection control procedures at each level of care to minimize contamination of injured patients and transmission of MDROs to other patients in the MTF.
3. Making recommendations for antibiotic management to minimize selection of resistant organisms and to best manage established MDRO infections.
4. Investigating outcomes in the combat injury-related infections to determine what medications, techniques, etc., were associated with improved (or worse) outcomes.

These efforts involved coordination among the Services as well as among their respective surveillance, research and clinical activities. Additional information on these efforts includes:

**Source of MDRO Infection/Colonization in the Combat Injured:** The initial source of the bacterial contamination of these patients continues to be studied and is likely multifactorial. It is increasingly recognized that even healthy people may be colonized with MDROs that uncommonly become a problem for a healthy individual. The clearest demonstration of this is MRSA that, like methicillin sensitive *Staph aureus*, may colonize the nose and skin of healthy adults. In the vast majority it causes no illness, but even an inconspicuous skin break may subsequently become infected. The extensive injuries

experienced by the combat wounded are therefore readily infected by bacteria that may be colonizing a previously healthy warfighter. Conversely, MDRO gram negative bacteria are generally not found colonizing normal adults (who do not work in a health care setting) and the source of these infections has been attributed to either the initial injury (i.e. a contaminated environment at time of injury as many of these organisms are soil and water contaminants, albeit usually not as MDROs) or more likely, as being transmitted nosocomially in the health care setting. Nosocomial infection may occur from initial contact in the field, at hospitals in theater, during transit, or while being cared for at intermediate stops at Landstuhl or at Level V care in CONUS facilities (tertiary medical facilities). As Colonel Duane Hospenthal, Medical Corps, United States Army and DoD colleagues published this year in the *Journal of Trauma*, it does appear that cross contamination from host nation nationals, who often are kept at facilities in theater for weeks to months, may have occurred<sup>2</sup>. These findings prompted a change in practice where these patients were cohorted separately from coalition patients who would be rapidly moving on to other DoD facilities.

**Reemphasizing standard infection control procedures at each level of care:** As combat injured patients move from theater-based treatment facilities to our medical centers, recognition that early identification of MDRO colonized or infected patients is critical in successful infection control of these bacteria. Establishment of MDRO colonization screening on admission to the major MTFs receiving the war injured (Landstuhl Regional Medical Center, Walter Reed Army Medical Center, National Naval

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<sup>2</sup> *Response to Infection Control Challenges in the Deployed Setting: Operations Iraqi and Enduring Freedom*. DR Hospenthal, HK Crouch, JF English et al. *Journal of TRAUMA Injury, Infection and Critical Care* 2010;69(1):S94-S101

Medical Center Bethesda, Brooke Army Medical Center) was first established at NNMC Bethesda in 2003. Initially this was designed to screen only for *Acinetobacter*, but as additional resistant bacteria were identified this program was expanded to include all MDROs at all four of the major MTFs caring for the combat injured. Patients are not released from contact precautions/isolation until their cultures are negative. Results from this screening are collated, reviewed, and reported by monthly rates that may be discussed by the IPCP. This provides near real-time monitoring of rates and epidemiology of MDRO colonization and infection and rapid identification of problems from a specific treatment facility. The DoD Global Emerging Infection Surveillance and Response System (GEIS; a division of the Armed Forces Health Surveillance Center (AFHSC)) has supported the clinical laboratories performing this admission screening through funding of molecular-typing equipment to further enhance epidemiological study of the recovered MDRO. Further characterization of the bacteria responsible for these infections can now also be performed through the repository capacity of the Trauma Infectious Disease Outcome Study (TIDOS) and the MDRO Repository and Surveillance Network (MRSN) system of the Walter Reed Army Institute of Research (WRAIR). These two projects, both inaugurated in the last year, will complement each other and allow for resistance phenotypes and molecular analysis of infecting and colonizing strains to determine relationships and common sources of these infections (as well as non MDRO and fungal organisms).

The Army, Navy and the Air Force have re-emphasized the need for basic infection control efforts in deployed settings whether on ships, in facilities in theater or in CONUS through clinical practice guidelines based on those of the CDC that have been

adapted for use in the deployed setting. The Army has spearheaded efforts that have subsequently been utilized by the Navy and Air Force. Specific efforts undertaken include:

- a. Assessing prevention and infection control practices in theater by conducting on-site reviews of infection control practices by infectious diseases (ID) and infection control (IC) leadership.
- b. Providing prevention and infection control training for individuals prior to deployment and ensuring identified infection control expertise is available at facilities in theater.
- c. Establishing an internet based system for inquiries regarding ID/IC that have been established for providers in theater to have ready access to these professionals in CONUS.

**Antibiotic Management:** Recommendations for appropriate antibiotic stewardship are critical in both the treatment of those infected with MDROs but also in diminishing the selection of these organisms. Emphasizing the need to avoid overuse of the most broad spectrum antibiotics in an empiric setting has been addressed through education of the providers in theater and in the provision of improved laboratory capacity for obtaining cultures and sensitivities in theater. This has limited the need for use of multiple broad spectrum agents in critically ill patients in whom resistance organisms are likely to be selected. Frequent clinical conferences among ID staff at the major tertiary care MTFs in CONUS (WRAMC, NNMC Bethesda and BAMC) regarding treatment of the most highly resistant MDROs has been helpful in treating these patients and has led

to research protocols assessing the use of drugs such as colistin and arbekacin to treat the most highly resistant infections.

**Clinical Outcomes:** The interest that infections with MDROs have generated is related to the poor outcomes associated with these organisms. Persistent infections, prolonged hospitalizations, more numerous and extensive surgical procedures and loss of limb and life have been attributable to MDROs. The goal of those caring for the combat injured is to restore them to health as quickly as possible with as few complications as possible but addressing care for combat related infections has been lacking. Published or unpublished collections of anecdotal reports (from US and foreign, civilian and military hospitals) have led to challenges in how combat trauma should best be addressed.

Clearly, assessing what aspects of a patient's care have been associated with a better or worse outcome are critical in establishing better practices for everything from management of the initial injury, up to procedures performed at a tertiary referral center. This has prompted DoD clinicians to develop a program that will yield evidence-based strategies for the best care for combat-associated infections including MDROs. The Trauma Infectious Disease Outcomes Study (TIDOS) has been carefully designed to combine surveillance, laboratory and clinical data of combat injured patients identified in the DoD MTFs and follows them through their transition to the VA system. The capacity for DoD ID clinicians to work together in developing this needed project was made possible through the Uniformed Services University's (USU) Infectious Diseases Clinical Research Program (IDCRP). The IDCRP was developed and funded through an Inter Agency Agreement between USU and the National Institute of Allergy and Infectious Disease (NIAID) to perform clinical studies of infectious diseases of military importance, requires additional support for large projects.

The TIDOS effort has been funded primarily by BUMED and integrates the US Army Institute for Surgical Research's Joint Theater Trauma Registry (JTTR) through a specially designed Infectious Disease module. The TIDOS project began enrollment in June 2009 and addresses questions related to infection-specific incidence estimates, risk factor analyses, trends over time, and factors associated with treatment failure and success. During the June-August 2009 period, there were 356 Level IV trauma admissions at Landstuhl RMC with 192 (53.9%) of these patients transferred to WRAMC, BAMC or NNMC Bethesda. A relatively high proportion of the TIDOS cohort (40%) have left active duty service and registered for care in the Veterans Administration Medical Center system within one year of their injury. Infectious complications have been relatively common, 60% of patients experienced at least one infection and 22% developed an additional infection post-hospitalization. The overall incidence rate for infections (through hospitalization) was 2.0 per 100 person-days. Of the patients with infections, 50% had 2 or more separate infections and 10% experienced  $\geq 4$  separate infections. The most common infections were wound infections (34.6%), bloodstream infections (17.3%), and osteomyelitis (bone infection) (16.5%).

The TIDOS project is the first prospective evaluation of infectious disease complications/outcomes, among wounded military personnel, using predefined standardized methodology combined with analysis of clinical management, surgical and medical care (i.e. antimicrobial therapy), and clinical microbiology results across levels of care, medical facilities, and outpatient follow-up. At present, enrollment is over 500 combat-injured personnel and recent approval from the Veterans Administration was obtained to expand TIDOS follow-up to include patients as they transition to the VA. This first of its kind study for the DoD and VA is unique in providing for collection of data from combat-injured patients for five years (or

potentially longer). A gratifying aspect of the TIDOS study is the enrolled patients' recognition that what can be learned from their misfortune may lead to changes in practice and improvements in the care of future warriors who are injured in combat.

In summary, the response of the DoD Infectious Diseases and Infection Control communities to the threat of MDROs in our MTFs, especially among the combat injured, has been an effort coordinated among the Services while maintaining the requirement for site and service-specific guidelines at different MTFs. The coordination of surveillance, treatment and research efforts regarding infections in the combat injured has taken years to develop and is only in the last year coming to fruition. Given the continuing operational tempo of our overseas contingency operations, we can expect that injuries and infections with MDROs will continue in our facilities at all levels, however, our level of preparation to identify and treat these infections is at a much higher level than it was in 2002. Furthermore, military medicine is unique in its ability to collect the data and follow our patients and their infections in a manner that will permit a greater understanding of the epidemiology, prevention, control and treatment of MDRO infections. Our efforts will continue to be critical in supporting our world-wide force health protection mission.

Again, I appreciate the opportunity to update you on our efforts in support of protecting our Sailors and Marines against MDROs. We are making progress; however, we recognize there is much more to do. Please be assured that Navy Medicine, in conjunction with DoD and the Army and Air Force, is confronting this challenging issue directly and will continue to devote the expertise and resources to protect the health of our service members. That is our greatest responsibility. I look forward to your questions.