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MEMORANDUM ON DOD'S RESPONSE TO MULTIDRUG-RESISTANT INFECTIONS IN MILITARY HOSPITALS

FROM: Subcommittee on Oversight and Investigations

The Oversight and Investigations Subcommittee conducted a review that culminated in a hearing on September 29, 2010, on the Department of Defense's (DOD) response to outbreaks of multidrug-resistant infections that occurred in military hospitals over the past several years, particularly in personnel wounded in Iraq and Afghanistan, and whether effective surveillance, control and prevention, and research and development programs are in place to manage the infection problem going forward.

Summary

The U.S. military has been extremely effective in providing rapid, high quality health care for service members wounded in Iraq and Afghanistan. However, many of these personnel unexpectedly developed harmful infections caused by multidrug-resistant bacteria. One of the pathogens with the most notoriety is *Acinetobacter baumannii* (sometimes referred to as Iraqibacter), a group of opportunistic bacteria which are capable of accumulating antibiotic resistance relatively quickly. The only effective treatments available to fight the infections, in some cases, are highly toxic, older drugs that can cause additional and severe harm to a patient's health. According to DOD, over 3,300 service members developed *Acinetobacter* infections during the 2004-2009 timeframe. While *Acinetobacter* is found in the natural environment, evidence suggests that the source of infections was in the military hospitals where wounded personnel were treated, sometimes alongside local nationals. Contamination in these hospitals placed other patients with compromised immune systems at risk; some of them contracted infections as well.

Outbreaks of *Acinetobacter* and other multidrug-resistant infections have created management challenges for the military. For example:

- When infections first began to appear in 2003, there was little known about the epidemiology of *Acinetobacter* and other bacteria causing the infections;
- Determining the nature and extent of the problem took time, in part because infections did not typically show up in patients until days after an injury, and the military's screening and surveillance capabilities were limited;
- Identifying the source of infections was difficult because wounded personnel typically were (and are) evacuated through several levels of treatment facilities before reaching a final medical center in the United States;
- Implementing infection control and prevention measures in combat hospitals was not easy given the harsh physical conditions and limited infrastructure available, and the frequent influx of casualties that can occur over short periods of time; and
- The lack of infection control expertise at these facilities, as well as limited experience in how to treat multidrug-resistant infections, further compounded the struggle to manage the outbreak.

In the past two years, the number of infections in military hospitals has decreased significantly, in part, because the total number of casualties from Iraq and Afghanistan has gone down, but also because DOD and the services have implemented a number of measures to strengthen infection screening, control, and prevention in the military healthcare system. For example:

- Steps have been taken to promote awareness and basic infection control procedures such as using new gloves and gowns with each patient;
- Guidelines for isolating patients with suspected multidrug-resistant infections and more targeted use of antibiotics were implemented;
- Additional infection control training is now provided to deploying medical personnel;
- Standardized screening for multidrug-resistant bacteria has been instituted at the major military medical centers; and
- Several research studies and projects have been conducted which have led to a better understanding of the risks, interventions, treatments, and outcomes associated with multidrug-resistant infections.

While DOD and the services have made considerable progress in controlling *Acinetobacter* and other drug-resistant infections, the problem has not been fully solved and new outbreaks will be a continuing challenge. According to some service officials, there is still a need for (1) more comprehensive surveillance capabilities to identify and monitor infections throughout the military health care system; (2) enhanced expertise in infection control procedures; and, (3) a coordinated and sustained approach to research and development activities.

The incidence of drug-resistant infections is a national and global problem that has grown

dramatically over the past decade in civilian hospitals. According to the Centers for Disease Control and Prevention (CDC), almost one hundred thousand Americans die each year from hospital-acquired infections. Health experts warn that the problem could get worse in the next several years, because there are few new antibiotic treatments expected from the drug research pipeline. Because patients with severe injuries are most susceptible to multidrug-resistant infections, and military personnel are at risk of being wounded in combat, DOD and the services must remain vigilant in their efforts to monitor and prevent these infections.

Background

Historically, infections were a common problem for military personnel wounded in combat. Since World War II, however, the incidence of combat-related infections has decreased significantly with the introduction and increasing use of antibiotics, as well as better hygiene and casualty care practices. Despite these improvements, the prevention and control of infections can be a formidable challenge for combat casualty care providers. Although the U.S. military has provided rapid, highly effective medical care for casualties in Iraq and Afghanistan, infection outbreaks caused by multidrug-resistant organisms (MDROs) emerged as a problem early on during military operations.[1]

MDRO infections first came to light aboard a U.S. Navy hospital ship (*USNS Comfort*) treating American and Iraqi casualties in 2003. Medical doctors on board saw a number of unexplained infections in wounded patients. Eventually, through consultation with military infectious disease specialists in the United States, it was determined that the infections were caused by a type of gram-negative bacteria called *Acinetobacter baumannii*.[2] *Acinetobacter* organisms are found in the environment (in soil and water), particularly in warm climates such as parts of Iraq. The bacteria are not generally harmful to healthy individuals and can reside on human skin or environmental surfaces. Individuals with open wounds or compromised immune systems, however, are at significant risk of contracting infections from the bacteria. Some strains of the bacteria are highly resilient and able to quickly accumulate resistance to cleaning detergents and antibiotics. Although some common *Acinetobacter* infections are not life-threatening and can be effectively treated with common antibiotics, the bacteria found among military patients in Iraq caused serious infections (e.g., to the bloodstream and lungs) and were resistant to almost all known antibiotic treatments.

Soon after the initial discovery of *Acinetobacter*, the incidence of infections grew dramatically at

[1] MDROs are microorganisms, predominantly bacteria, that are resistant to one or more classes of antimicrobial agents. Certain MDROs are resistant to only one agent, such as *Methicillin Resistant staphylococcus aureus* (MRSA), but many of these pathogens, such as *Acinetobacter baumannii*, are resistant to most available antimicrobial agents. In addition, over time, bacteria can adapt (sometimes quickly) and acquire drug-resistance genes. The widespread use of antibiotics, especially broad-spectrum antibiotics, is believed to play a significant role in the emergence of resistant bacteria.

[2] Bacteria are classified as gram-negative because of their reaction to a gram stain (biochemical) test which is used to classify bacteria. Gram-negative bacteria have an outer membrane that protects them from antibiotics and detergents.

several military treatment facilities. In addition to Acinetobacter, other gram-negative MDRO infections, including extended-spectrum β-lactamase (ESBL)-producing *Escherichia coli* (E-coli) and *Klebsiella pneumonia*, were seen in facilities, but to a lesser extent. Over time, most infections were seen in the major medical centers that received the majority of wounded military personnel evacuated from Iraq and Afghanistan—Landstuhl Regional Medical Center (Germany); Walter Reed Army Medical Center, National Naval Medical Center, and Brooke Army Medical Center. Upwards of 20 percent or more of the patients admitted to these medical centers during the worst of the outbreaks were found to be "colonized" with the bacteria, but not all patients contracted infections. According to available data from the Department of Defense, approximately 3,300 service members that were treated in military treatment facilities during 2004-2009 had *Acinetobacter* infections (see Table 1).

Table 1: Incidence of *Acinetobacter* Infections in among Service Members treated in DOD Medical Facilities, 2004 - 2009

Year	Army	Navy	Marines	Air Force	Total
2004	379	51	210	23	663
2005	503	58	185	29	775
2006	472	63	181	35	751
2007	287	29	84	25	425
2008	274	45	73	22	414
2009	154	43	54	28	279
Total	2,069	289	787	162	3,307

Source: Office of the Assistant Secretary of Defense for Health Affairs[3]

Managing the problem of *Acinetobacter* bacteria and infections was difficult for military medical personnel. Initially the source of the infections was unknown and it took several years before studies and investigations began to identify their origins. There were three potential sources considered: (1) the bacteria were already present on the skin of military personnel prior to being injured; (2) the bacteria were introduced at the time of injury; and, (3) patients acquired the bacteria after injury during treatment at a medical facility. Although the source of the infections has not been fully explained, military studies provided strong evidence that the primary source was the military treatment facilities where the wounded were treated. Military medical experts believe that patients contracted infections through "nosocomial" transmission—that is, the bacteria was introduced into the facilities, and patients acquired it through contact with other contaminated patients, medical personnel, and treatment facility rooms, equipment, and instruments. It is also thought that wounded U.S. personnel may have been initially contaminated from non-U.S. patients being cared for in deployed medical treatment facilities. Colonization of

[3] Data were provided to the Oversight and Investigations Subcommittee from the Office of the Assistant Secretary of Defense for Health Affairs. The data are derived from DOD's Composite Health Care System (CHCS). According to DOD officials, there are limits to what data are captured in CHCS; for example, medical tests performed at outside or reference laboratories are generally not included.

bacteria increased within the military healthcare system as patients were transported from deployed treatment facilities in the combat theater where they received initial care, to overseas hospitals in Germany where more definitive surgical care was provided outside the combat theater, and finally to one of the major military medical centers in the U.S. where longer term care and rehabilitation was available. Other non-wounded patients receiving care in these facilities were also exposed to the bacteria and some contracted infections as well.

Acinetobacter infections were also difficult to identify in patients because colonization of the bacteria often did not appear in patients until several days after exposure. Many patients were exposed to the bacteria before they reached a medical treatment facility where screening and diagnostic testing were performed. However, the lack of standardized screening and laboratory testing at these facilities presented further complications. For example, medical personnel employed different screening protocols because medical knowledge about the bacteria and how best to screen for it on a patient was limited. Also, laboratory testing could take several days to complete and results were not available in some cases until after a patient was transferred to another medical treatment facility. Moreover, while standard infection control precautions were utilized as much as possible, the ability to control and prevent MDRO infections in deployed military treatment facilities was difficult, given the physical structure of the facilities, environmental conditions, and availability of basic supplies.

Treatment options were also challenging due to the severe nature of many patients' injuries and the drug-resistance exhibited by the bacteria. The use of broad spectrum antibiotics routinely given at the time of injury may have inadvertently contributed to the drug-resistance acquired by the bacteria. Military doctors found that only a few older, but very toxic antibiotics proved effective in fighting the infections. One of these drugs, colistin, had largely gone out of medical use in the 1970s because of its harmful effects. In addition, when colistin was first introduced over 60 years ago, it was not subjected to the regulatory tests required of more modern drugs, and no standardized dosing of the drug was established. As a consequence, when it was brought back into use to fight *Acinetobacter* infections, optimal dosing of the drug was unknown. Therefore, it had to be administered with a great deal of caution. Further complicating efforts to treat patients was that infections in some cases would appear to go away only to re-appear later, causing additional health problems in patients.

Issues

When the outbreak of *Acinetobacter* infections began to appear in wounded military personnel, DOD and the services implemented a number of actions which proved effective, but it took several years to bring the problem under control. The ability to mitigate the infection problem more quickly may have been hindered by the lack of effective surveillance capabilities, infection control and prevention measures, and treatment options. A reliable, comprehensive surveillance system is needed in order to be able to determine the nature and extent of infections; help frame what guidelines and treatments are needed to respond to them; evaluate whether treatments are working; and inform new research and development activities. While DOD and the services have

enhanced their medical surveillance capabilities since the outbreak of infections occurred, a comprehensive system is not yet in place to actively monitor MDROs throughout the military health care system. In addition, DOD and the services have strengthened infection control and prevention practices in military treatment facilities, but further expertise, particularly within deployed facilities, may still be needed. Furthermore, while many individual studies and projects were undertaken to increase the military's understanding of the epidemiology of MDROs and how best to treat them, knowledge gaps remain. Various research and development projects continue to be conducted, but DOD does not have a coordinated and sustained research and development program established to support ongoing MDRO-related research.

MDRO Infection Surveillance: When the *Acinetobacter* outbreak first occurred, DOD and the services did not have a comprehensive screening and surveillance system in place to identify and track MDRO colonization and infections in deployed and non-deployed military treatment facilities. Over time, the four major military medical centers that receive wounded patients from Iraq and Afghanistan established active screening programs to monitor their patient populations. Three of the centers—Brooke, Walter Reed, and National Naval--began screening newly admitted patients for *Acinetobacter* bacteria in 2003, and the fourth center—Landstuhl Regional—began screening in 2005. According to service officials, the screening protocol used to assess patients at each center varied, and it was not until 2009 before a standardized protocol was instituted. Based on data collected through the screening efforts, rates of colonization of *Acinetobacter* bacteria among patients at admissions to the three U.S.-based centers declined over the five-year period 2005-2009: 2005-21%, 2006-21%, 2007-15%, 2008-13%, and 2009-5%.[4] Rates at Landstuhl in Germany also declined over the same period: 2005-7%, 2006-6%, 2007-2%, 2008-2%, and 2009-1%. Screening at the four centers was expanded in 2009 to include all MDROs, and six percent of patients at admissions were found to be colonized with organisms.

Other military treatment facilities also screen for *Acinetobacter* bacteria in patients to varying extent, but there is no department-wide surveillance system in place to capture and bring together MDRO-related information from these facilities. To obtain more comprehensive surveillance coverage, the Army established a new system in 2009 called the Multidrug-resistant Organism Repository and Surveillance Network (MRSN). The MRSN is intended to be an Army-wide surveillance system, as well as a central repository for collecting and analyzing strains of MDROs. The repository receives strains directly from military treatment facilities and determines their biological/genetic characteristics and susceptibility to different antimicrobial treatments. Clinical and demographic information on patients are also collected and analyzed. The Army plans to eventually make MDRO data available to the wider military medical community on a regular basis through a secure web-based database. The Army has also discussed expanding the MRSN over time to encompass all military treatment facilities in DOD's healthcare system, but there are no formal plans to do so at this time. To date, MRSN has

[4] Hospenthal, D.R. et al, *Multidrug-resistant Bacterial Colonization of Combat-injured Personnel at Admission to Medical Centers Following Evacuation from Afghanistan and Iraq*, (Paper presented at the Advanced Technology for Applications and Combat Casualty Care conference, August 19, 2010).

been limited to Army facilities and supported largely through research funding for overseas contingency operations, and it does not have a permanent funding program established.

DOD has a number of other medical surveillance systems in place, but they are largely geared towards collecting and reporting information on major medical events that pose a significant threat to the health and readiness of the force, and generally do not focus on MDROs. The Global Emerging Infections Surveillance and Response System (GEIS), which is a component of the Armed Forces Health Surveillance Center, is the primary department-wide surveillance system for emerging infections.[5] GEIS covers about 70 reportable medical events. A joint working group, consisting of representatives from the military services and Office of the Secretary of Defense for Health Affairs, determines which medical events are reportable. To be included as a reportable event, the disease must have a clear case definition, laboratory criteria for diagnosis, and an associated International Classification of Diseases, 9th revision (ICD-9) code.[6] The majority of reportable events are well-defined diseases that have been of concern to the military for many years such as malaria, cholera, hepatitis, and smallpox. In 2009, the joint working group updated the list of reportable medical events to include a category called "disease outbreak," which is defined as unspecified infectious and parasitic diseases that may include MDRO-related infections. Because MDRO infections are diverse and complex to characterize, ICD-9 codes have not been established for tracking them.

DOD also has extensive healthcare datasets on patients treated in the military healthcare system which have been used to conduct analyses about medical events of interest, including *Acinetobacter* and other MDRO-related infections. The Navy and Marine Corps Public Health Center, for example, has identified cases of Acinetobacter infections by using existing patient data records to identify individuals with wounds and then comparing them with other electronic data that contain patient laboratory test results. The Center currently maintains the ability to conduct such analyses and respond to inquiries from the military medical community. Some of DOD's key data systems, however, cannot be linked directly to other military data systems, making it difficult to conduct analysis and report timely information. The inability to link with Department of Veterans Administration data systems has also been a long-term issue.

In addition, DOD is in the process of implementing CDC's National Healthcare Safety Network (NHSN) reporting system. NHSN is designed to track healthcare-associated infections from a large sample of private and public healthcare facilities in the United States, including infections caused by MDROs. NHSN is a voluntary internet-based surveillance system for hospitals and state health departments. Currently, about half the hospitals in the nation (about 2,500 hospitals) participate in the network. Data collected through the network are used to estimate the magnitude of infections that occur and the extent to which healthcare practices to mitigate infections are

[5] GEIS is a consortium of surveillance and response assets from across DOD, including the Army Center for Health Promotion and Preventive Medicine, Army Medical Research Institute of Infectious Disease, Naval Health Research Center, Naval Environmental Health Center, and Air Force Global Surveillance Office.

[6] The International Classification of Diseases is published by the World Health Organization and used worldwide to code and classify diseases for health statistics, healthcare reimbursement systems, and medical decision-making.

implemented. DOD began participating in HNSN in 2009, and now has 33 military treatment facilities providing information to the surveillance network. The Department hopes to bring additional military treatment facilities into the system in the future and begin using it as another means to monitor MDRO infections.

Incidence of MDROs in non-DOD hospitals: MDRO infections, including *Acinetobacter*, have been a growing public health problem in the U.S. and globally over the past few decades. According to researchers at CDC, a total of 1.7 million hospital-acquired infections occur annually in the United States, leading to almost 100,000 deaths.[7] A majority of these infections and deaths are caused by MDROs. Other data from CDC's National Healthcare Safety Network indicate that gram-negative bacteria are responsible for about 30 percent of the hospital-acquired infections that occur. They are one of the major causes of infections in hospital intensive care units and are prevalent in cases of ventilator-associated pneumonia and urinary tract infections. Similar data and trends are reported in civilian hospitals in many other parts of the world. In Europe, for example, gram-negative infections are believed to cause 25,000 deaths annually.

The Department of Veterans Affairs (VA) currently does not have a surveillance system to identify and track MDRO infections in its medical facilities, but according to the Congressional Research Service[8] the VA is exploring the logistical and technological requirements needed to develop such a system. The VA developed a national surveillance and prevention system several years ago to track and respond to Methicillin-resistant *Staphylococcus aureus* (MRSA) bacteria and infections. This system has been effective and the VA plans to use it as a basis to develop a similar system for other MDRO infections.

According to DOD officials, there are no formal coordination efforts between DOD and VA pertaining to the surveillance, prevention, and treatment of MDRO infections. However, the two departments initiated a collaborative research project in 2009 to study interventions and outcomes in combat-wounded patients who develop MDRO infections over the next five years.

Infection control and prevention in military treatment facilities: The military's response to the outbreak of *Acinetobacter* infections included concerted efforts to enhance infection control and prevention practices in all military treatment facilities. Emphasis was placed on basic infection control measures, such as hand hygiene, proper use of gloves and gowns, and the disinfection or sterilization of patient care equipment and rooms. Patient isolation precautions were also taken in facilities where infections were likely to occur. And, antibiotic control policies were established to limit the use of broad-spectrum antimicrobial agents. Much of the emphasis on improving infection control practices was achieved through education and training. Raising awareness about infection control practices was promoted through briefings by military medical experts to their leadership and to deploying commanders and personnel. In addition, the military services and

[7] Klevens, R.M., et al, "Estimating health care-associated infections and deaths in U.S. hospitals, 2002", *Public Health Report* (2007:122:160-166).

[8] Information provided to the Oversight and Investigations Subcommittee by the Congressional Research Service, July 2010.

CENTCOM issued formal communications to medical personnel and treatment facilities, emphasizing the need for mandatory use of basic infection control practices.

In 2007, Army medical experts took the initiative to convene a committee of subject matter experts from across DOD to review and strengthen infection control guidelines and management strategies for the care of combat casualties. The committee produced new infection control guidelines that were published in the *Journal of Trauma* in 2008, based on evidence derived from a review of existing medical literature and a consensus of expert opinion.[9] Army experts also visited deployed treatment facilities in 2008 and 2009, to assess the effectiveness of infection control practices being used. The experts found that while various infection control practices were being implemented, facilities would benefit from having standardized infection control procedures and guidelines. It was also determined that increased infection control expertise, including trained infection control officers, should be deployed to each military treatment facility.

To help strengthen the coordination of infection control guidelines and practices department-wide, DOD established an Infection Prevention and Control Panel in 2009. The panel is comprised of infection control experts from the services and representatives from the Office of the Secretary of Defense for Health Affairs. The Panel issued more detailed guidelines in October 2009 to enhance the standardization of infection control and prevention programs in deployed treatment facilities. Infection control guidelines were also issued as a CENTCOM Joint Theater Trauma System Clinical Practice Guideline.

Additional infection control training was also established in 2008 as part of the Joint Forces Combat Trauma Management Course at Fort Sam Houston, Texas for medical personnel being deployed to combat support hospitals. Furthermore, a five-day course was established to train infection control officers who are responsible for infection control programs within these hospitals. According to Army officials, the course has been offered on an ad hoc basis, but efforts are underway to make it a required course for infection control officers being deployed.

Infection control expertise in deployed treatment facilities was further enhanced by providing medical personnel access, via telecommunications systems, to infection control experts at the military medical centers in the United States. According to Army medical experts, while this service is beneficial, it would be more effective to have medical personnel with infection control expertise assigned to each deployed facility and an infection control consultant assigned to each combat theater to coordinate efforts and establish specific practices and policies that may be needed. At the subcommittee's hearing, Army officials testified that there was a shortage of well-trained infection control officers in part because combat support hospitals were often split into multiple treatment facilities, operating at different locations rather than as a single hospital unit. While an overall hospital did have a trained infection control officer, each treatment facility component did not. In September 2010, the Army established a requirement to assign a trained

[9] Hospenthal, D.R. et al, "Guidelines for the Prevention of Infection after Combat-Related Injuries", *Journal of Trauma* (2008: 64:S211-S220).

infection control officer to each location that provides inpatient care.

Research and Development: DOD and the services have supported a number of intramural and extramural research and development studies and projects in response to the outbreak of infections. These efforts were instrumental in helping to determine the characteristics and source of the bacteria and infections, protocols to test for colonization of bacteria, and effective infection control and treatment options. Individual studies and projects were funded through various DOD and service research and development programs related to infectious diseases, casualty care, deployment-related medical care, and medical technologies. Research organizations and programs that have supported MDRO research and development include:

- Defense Medical Research and Development Program (DMRDP)
    - DMRDP Defense Health Program Enhancement (DHPe)
- Military Infectious Diseases Research Program (MIDRP)
    - Wound Infection Program and Diagnostics Program
- Infectious Disease Clinical Research Program (IDCRP)
- Deployment-related Medical Research Program
- Defense Threat Reduction Agency, Transformational Medical Technology Program
- Congressional Special Interest Projects on Wound Infection
- SBIR Projects on Wound Infection & Diagnostics
- Army Combat Casualty Care Research Program
- Navy Wound Infection & Diagnostics

In 2006, DOD established a joint program effort with NIH (National Institute of Allergy and Infectious Diseases) to investigate infectious diseases facing the military. The program, called the Infectious Disease Clinical Research Program, is headquartered at the Uniformed Services University of the Health Sciences and involves a network of military hospitals and military research facilities. In the past few years, this program has initiated several studies on wound-related infections focusing on the epidemiology, prevention, and management of MDRO infections. Funding for these studies comes from existing DOD and service research and development programs, such as the Navy's Bureau of Medicine Wounded Warrior Initiative and the Army's Medical Research and Medical Command's research programs. One major study is a collaborative effort with the VA to follow and assess patient outcomes at several military and VA treatment facilities over the next several years, with the intent to develop recommendations for preventing and managing MDRO infections. Other studies funded through the IDCRP are assessing new diagnostic methods and treatments for MDRO-related infections.

In the Department of Defense, MDRO-related research is an emerging area that must compete for funding with other disease and infection programs that are well-established. According to DOD and service officials, funding for MDRO-related research has been intermittent and a more coordinated, sustained MDRO-related research program is needed. For example, the DMRDP

Defense Health Program Enhancement, which is administered by the Office of the Secretary of Defense for Health Affairs, established a research area pertaining to wound infections and antimicrobial countermeasures, but funding commitments for the research field have been lacking. DOD programmed about $14 million for 18 research projects in this area in fiscal year 2010, but only requested $2 million in fiscal year 2011 to carry forward the projects started the previous year. Funding for new research projects was not available; however, the Department has proposed reprogramming $9 million of excess fiscal year 2010 operations and maintenance funding for additional MDRO-related research.

Ongoing Actions

The House Armed Services Committee will continue to conduct oversight on the Defense Department's ongoing efforts to control and prevent multidrug-resistant infections in military hospitals.

In addition, to further strengthen its ability to manage multidrug-resistant infections, the subcommittee recommends that DOD: (1) consider expanding the Army's Multidrug-resistant Organism Repository and Surveillance Network to monitor MDROs throughout the military health care system; (2) determine whether sufficient infection control expertise is available in deployed military treatment facilities and, if not, take steps to address the shortage; and (3) ensure there is a coordinated, sustained program in place to support ongoing MDRO-related military research needs.