Chapter 40

MULTIDRUG-RESISTANT ORGANISMS AND INFECTION CONTROL PRACTICE IN THE US MILITARY MEDICAL SYSTEM

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INTRODUCTION

The pervasive use of improvised explosive devices, mortars, and rocket-propelled grenades by opposition forces, as well as the helmets and body armor worn by US military personnel, make extremity blast trauma the most common type of injury among soldiers and marines wounded in Iraq and Afghanistan.[1] The mechanism of injury (penetrating trauma) and the nature of the wounds (with devitalized tissue and retained foreign bodies) create a milieu conducive to infection, either by organisms inoculated at the time of injury or subsequently by contaminating bacteria and fungi. Although wound microbiology at the time of injury tends to consist of antibiotic-susceptible, skin-commensal, gram-positive cocci,[2] subsequent infections with multidrug-resistant (MDR) bacteria are common.[3]

There is no standardized definition of multidrug resistance, and criteria vary among organisms and institutions. At Walter Reed National Military Medical Center, a gram-negative bacterium is considered MDR if it is resistant to at least three classes of antibiotics among aminoglycosides, carbapenems, cephalosporins, penicillins, and quinolones. Methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Escherichia coli* (VRE), and the extended spectrum β-lactamase (ESBL) producing gram-negative bacteria are generally recognized as MDR organisms. Additionally, MDR *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, and species belonging to the *Acinetobacter baumannii-calcoaceticus* complex (ABC) are frequently isolated from infected wounds sustained in Iraq and Afghanistan.[4,5] The discordance in wound microbiology at the time of injury versus the nature of the organisms subsequently cultured from infected wounds suggests nosocomial colonization, which has been documented in at least one investigation.[6]

Because wounded military personnel are evacuated by various means (ambulance, rotary and fixed-wing aircraft, and ship) to one of a number of destinations for transient and definitive care (typically combat support hospitals and military medical centers, respectively), it is unlikely that any single location or method of conveyance can be implicated as the sole source of colonization with MDR organisms. The emergence of MDR pathogens, while not a uniquely military phenomenon, poses challenges in the treatment of hospitalized service members with infected war wounds. As organisms become increasingly resistant, the number of available effective antibiotics diminishes, and use of antibiotics to which MDR isolates are susceptible may be limited by untoward side effects or patient allergies. For example, colistin (colistimethate sodium), a polymyxin antibiotic to which many MDR ABC strains are solely susceptible, is nephrotoxic, causing acute renal failure in almost half of patients and severe enough effects in 21% of patients to warrant discontinuation of the drug.[7] Moreover, drug resistance is emerging at a faster pace than drug development, a trend that is unlikely to be reversed in the foreseeable future.[8]

CHEMOPROPHYLAXIS AND THE COMBAT CASUALTY

Two factors contributing to the emergence of MDR organisms are the selective pressure for resistance by prolonged exposure to antibiotics and the tremendous adaptive capability of bacteria owing to high mutation rates and short generation times. While the emergence of antimicrobial resistance is inevitable,[9] the process is accelerated by the injudicious use of antibiotics. Consequently, antibiotic use in the combat casualty should target the likeliest pathogens in the case of prophylaxis or empiric therapy, and should be culture-driven when the pathogen and its susceptibilities are known. In 2008, guidelines for the prevention of infection among combat wounded were published by a panel of experts, convened by the US Army Medical Command (MEDCOM), in various medical and surgical subspecialties.[10] The panel reconvened in January 2011 and published revisions to its guidelines.[11] This chapter is not intended to supplant these guidelines but rather to provide succinct compatible recommendations.

The reader is encouraged to review the guidelines in their entirety at http://journals.lww.com/jtrauma/toc/2011/08002.

It has been estimated that the number of bacteria inhabiting the human body outnumber human cells by 10:1,[12] and that 500 to 1,000 different species comprise the human microbiome.[13] Each of these species occupies a niche, and the nature of the microbial flora varies by anatomic location. Strict anaerobes, for example, are much more prevalent in the gut than on skin, where *Propionibacterium* (an aerotolerant anaerobe), *Corynebacterium*, *Streptococcus*, and *Staphylococcus* are the predominant bacterial genera and *Malassezia* is the predominant fungal genus.[14] It makes sense, therefore, that the choice of an initial empiric antibiotic should be driven, in part, by the anatomic location of the wound (Table 40-1). For wounds of skin, soft tissue, and bone (such as extremity wounds), as well as maxillofacial fractures and penetrating chest wounds, an antibiotic

TABLE 40-1

RECOMMENDED EMPIRIC ANTIMICROBIAL THERAPY FOR INFECTION PROPHYLAXIS IN THE COMBAT CASUALTY

Injury	Recommended Agent	Alternate Agent	Duration
Skin, soft tissue, or bone injury	Cefazolin 1 g IV every 8 h	Clindamycin 900 mg IV every 8 h	72 hours
Penetrating chest wound	Cefazolin 1 g IV every 8 h	Clindamycin 900 mg IV every 8 h	24 hours
Maxillofacial fracture	Cefazolin 2 g IV every 8 h (note higher dose)	Clindamycin 900 mg IV every 8 h	24 hours
Penetrating abdominal wound	Cefoxitin 1–2 g IV every 6–8 h or piperacillin-tazobactam 4.5 IV every 6 h	Levofloxacin 750 mg IV daily or ciprofloxacin 400 mg IV every 8–12 h and metronidazole 500 mg IV every 6 h, or moxifloxacin 400 mg IV daily	24 hours after definitive washout
Central nervous system injury	Cefazolin 1 g IV every 8 h. Add cefazolin, penicillin, and gentamicin for gross contamination or metronidazole 500 mg IV every 6–8 h if also an abdominal wound.	Ceftriaxone 2 g IV daily. Add cefazolin, penicillin, and gentamicin for gross contamination. For penicillin allergic patients: vancomycin 1 g IV daily and ciprofloxacin 400 mg IV every 8–12 h	5 days
Eye injury	Erythromycin or Bacitracin ophthalmic ointment 4 times daily for non-penetrating injuries, burns or abrasions	Fluoroquinolone 1 drop 4 times a day	Until epithelium healed
Burns	Mafenide acetate topical each morning and silver sulfadiazine topical each afternoon	Either mafenide acetate or silver sulfadiazine twice daily. Bioprane may be used for partial thickness burns and silver impregnated dressings for limited, clean, full thickness burns.	Until healed or grafted

IV: intravenous
Adapted with permission from: Hospenthal DR, Murray CK, Andersen RC, et al. Guidelines for the prevention of infections associated with combat-related injuries: 2011 update. *J Trauma*. 2011;71(2 Suppl):S214–S215.

targeting susceptible gram-positive cocci is sufficient (eg, cefazolin, clindamycin). Conversely, a broad-spectrum antibiotic such as piperacillin-tazobactam would be indicated for a penetrating abdominal injury with a perforated viscus and fecal spillage. For penetrating injuries of the brain and spinal cord, cefazolin is the preferred agent, with extended coverage (eg, the addition of penicillin and gentamicin) for gross contamination or an antibiotic with anaerobic coverage (eg, metronidazole) if the abdominal cavity is involved. Systemic antibiotics are not recommended for eye injuries; however, a topical antibiotic such as erythromycin or bacitracin is appropriate for ocular burns or abrasions (but not for penetration). Similarly, systemic antibiotics are not recommended for bodily burns.

With respect to the timing of antibiotics, there is sufficient data to suggest that at least for some wounds (eg, extremity wounds) early debridement and administration of antibiotics are associated with lower infection rates, whereas delays in antibiotic administration beyond 2 to 6 hours are associated with higher infection rates.[15] Therefore, when evacuation from the battlefield is expected to be delayed beyond 3 hours, the recommendation for open extremity wounds is a single early dose of a fluoroquinolone (moxifloxacin 400 mg per os [PO], levofloxacin 500 mg PO, or gatifloxacin 400 mg PO); patients with penetrating abdominal injuries, shock , or for those unable to take medication orally should be given ertapenem 1 g IV/IM, cefoxitin 2 g IV/IM, or cefotetan 2 g IV.[16] These antibiotics were chosen by the MEDCOM panel for their spectrum of activity, ease of dosing, and stability during storage.

It is worth noting that antibiotics are one of several interventions recommended for the prevention

of infection in the combat casualty; the others include prompt wound irrigation, debridement, and coverage, as well as stabilization of fractures. As soon as tactically feasible, wounds should be copiously irrigated (1–3 L) with normal saline or sterile water (or less ideally, potable water) under low pressure to remove gross contaminants. However, removal of deeper foreign bodies such as fragments is best left to a surgeon. Once the wounds have been irrigated, a sterile bandage should be applied and, in the case of extremity wounds, bony fractures should be splinted. In addition to protecting the limb, splinting reduces the risk of infection by reducing the risk of vascular injury, which may lead to limb ischemia and tissue necrosis.

MULTIDRUG-RESISTANT ORGANISM SURVEILLANCE

Historically, surveillance of microbial pathogens was limited to only those organisms with epidemic potential such as *Mycobacterium tuberculosis* or *Salmonella typhi*. Over time, standardization and accreditation of clinical laboratories, as well as the ease of data acquisition and analysis afforded by the computer, has led to more widespread monitoring. However, most surveillance data is still collected and shared only locally (eg, to determine local rates of antimicrobial resistance), and only a minuscule fraction of data is accessible to researchers or clinicians outside the immediate environs of a particular hospital.[17] In a summary statement to the US Congress, the Infectious Diseases Society of America recognized antimicrobial resistance as "one of the greatest threats to human health worldwide" and called for a federally funded network of sentinel sites "to evaluate rapidly emerging resistance in a variety of clinically important organisms and infections, and to develop, implement, and evaluate prevention strategies."[18]

In response to the proliferation of infections caused by MDR gram-negative bacteria among hospitalized military personnel, the Walter Reed Army Institute of Research (WRAIR) stood up the Multidrug Resistant Organism Repository and Surveillance Network (MRSN) in July 2009.[19] Conceived as a performance improvement mandate from MEDCOM, the purpose of the MRSN is to create a repository of targeted MDR organisms accompanied by relevant clinical and demographic information, and to perform antibiotic susceptibility analysis and other testing. Under the mandate, Army hospitals are required to submit specimens, and hospitals from other services are invited to do so. The MRSN submits reports to hospital commanders and consultants to the surgeon general; this data will eventually be available for clinicians as well on the MRSN website.[20] For the deployed provider with access to little or no microbiology assets, the advantages conferred from submitting bacterial isolates to the MRSN include generation of a facility-specific or regional antibiogram and, in the case of a suspected outbreak, comparison of isolates by molecular biology techniques. Information on submitting specimens to the MRSN is available on its website. Other ways in which the military is collecting data on MDR organism infections among war wounded service members include the addition of an infectious disease module to the Joint Theater Trauma Registry,[21] and collaborating with the National Institutes of Health Infectious Disease Clinical Research Program on the Trauma Infectious Diseases Outcome Study.[22]

INFECTION CONTROL FOR THE DEPLOYED PROVIDER

Infection control in a combat environment can be challenging for the deployed provider. However, certain rudimentary practices can be readily implemented which, if adhered to, are proven effective in reducing the risk of nosocomial pathogen transmission. These practices can broadly be categorized as either individual or institutional interventions. Included among the former are standard precautions and isolation precautions (ie, contact, droplet, and airborne precautions). The latter include patient cohorting, disinfection protocols, and antibiotic stewardship.

Individual Interventions

Perhaps the simplest yet most effective infection control practice is handwashing.[23] In fact, the greatest limitation of handwashing's impact is noncompliance or improper technique rather than the use of an ineffective soap.[24] The World Health Organization (WHO) recommends handwashing prior to patient contact, prior to a procedure, and after body fluid exposure, patient contact, or contact with a patient's surroundings.[25] Alcohol-containing sanitizers are an effective alternative to soap and water, especially in the deployed setting where running water may not be available. However, limitations of these products include their lack of activity against spore-forming bacteria (such as *Clostridium difficile*) and decreased effectiveness when the hands are grossly dirty.[26] Of note, while glove use is an important component of infection control, wearing them does not obviate the need for handwashing because gloves often have small invis-

ible tears, and hands routinely become contaminated while removing them.[27,28]

Isolation precautions are categorized according to the three major routes by which nosocomial pathogens are transmitted: contact, droplet, and airborne spread. Contact precautions are indicated for patients colonized or infected with MDR bacteria (such as MRSA and VRE) or *Clostridium difficile*, and for patients with various other conditions easily transmitted by person–person or person–fomite contact (eg, scabies). Contact precautions consist of donning gloves and gowns and, when possible, the use of dedicated medical equipment for individual patients. Although strict contact isolation may be difficult to implement in an austere setting, adaptations include separating patients by empty beds or clearly delineating a designated area for those patients on contact isolation.[29]

Droplet precautions consist of wearing a face mask and should be implemented for patients with confirmed or suspected infections caused by *Neisseria meningitidis* (bacterial meningitis), *Bordetella pertussis* (whooping cough), *Haemophilus influenzae* or *Mycoplasma pneumoniae* (atypical pneumonia), *Corynebacterium diphtheriae* (diphtheria), *Yersinia pestis* (plague), group A streptococcus, or various droplet-borne viruses (rhinovirus, influenza, rubella, mumps, adenovirus, respiratory syncitial virus, and parvovirus B19). Because droplets remain suspended only briefly, it is probably unnecessary to wear a mask beyond 3 to 6 feet from the patient.[30]

Airborne precautions are indicated for infectious agents that remain suspended in the air for a long time. Examples included rubeola virus (measles), varicella virus (chickenpox), and *Mycobacterium tuberculosis*. Ideally, a patient on airborne precautions would be placed in a negative pressure isolation room with special air handling and ventilation capability, and healthcare workers entering the room would wear an N95 mask or respirator. Because such resources are unlikely in the deployed setting, the transmission risk can be mitigated by masking the patient, placing the patient in a private room with the door closed, and providing healthcare workers N95 masks or respirators before entering the room.

Institutional Interventions

At the facility level, a number of interventions can be implemented to reduce the risk of nosocomial pathogen transmission. One such intervention is patient cohorting, which entails grouping people colonized or infected with the same drug-resistant bacterium. Because patients with recent prior hospitalizations or those who have been hospitalized for more than 72 hours are more likely than newly admitted patients to be colonized with nosocomial pathogens, separating these two cohorts can also reduce transmission risks.[31]

Environmental cleaning, disinfection, and sterilization are other simple methods proven to reduce the transmission of nosocomial pathogens.[32] Cleaning refers to the removal of foreign material from objects and is typically accomplished with water and detergents. Disinfection and sterilization both refer to the elimination of microbes from inanimate objects. However, the former (usually accomplished with chemicals) does not eliminate bacterial spores, while the latter (by means of steam, heat, pressure, or gas) does. Sterilization is usually accomplished by autoclaving or by using ethylene oxide gas or chemical sterilants (eg, 2% glutaraldehyde-based products, 6% stabilized hydrogen peroxide, peracetic acid). Some examples of chemical disinfectants include sodium hypochlorite, ethyl or isopropyl alcohol, phenolic and iodophor solutions, and quarternary ammonium germicidal detergents. Although maintaining a clean environment and sterile medical devices may be challenging for deployed providers (especially those in more austere environments), the importance of doing so cannot be overstated.

The perseverance and ubiquity of microbes are testimony to their tremendous adaptive capability. This adaptability means that prolonged exposure to any antibiotic will almost inevitably culminate in resistance to that drug. Hence, the injudicious use of broad spectrum antibiotics has the unintended consequence of selecting for organisms with multidrug resistance. This risk can be mitigated by selecting an empiric antibiotic that targets the likeliest pathogens and then tailoring and narrowing coverage based upon culture data and local antibiograms. Preprinted admission or preoperative orders prescribing broad spectrum antibiotics for all patients should be avoided. Additionally, the duration of antibiotic use should be limited to the shortest effective length of time.[33]

After reviews in 2008 and 2009, a number of measures were put in place addressing infection control practices and challenges in theater hospitals. Among these was a mandate that all deploying combat support hospitals should have a designated infection control officer (ICO), and also the creation of a formal infection control course taught at the Army Medical Department Center and School (AMEDD C&S) at Fort Sam Houston, Texas. The purpose of this 5-day instruction is to provide training for military personnel who will be performing the duties of an ICO or overseeing an infection control program within Role 3 hospitals.[34] The course consists of a pre-test to assess attendee baseline knowledge, 18.5 hours of didactics, and a post-test. Topics include combat theater infection control overview and principles; clinical micro-

biology; preventing transmission of infectious agents; hand hygiene; principles of cleaning, disinfection, and sterilization; special patient populations (surgical, burn); healthcare acquired infections; blood and body fluid exposure management; program management; and infectious disease threats. Additional information about this course can be found on the AMEDD C&S website.[35]

INFECTIONS RELEVANT TO THE DEPLOYED PROVIDER

Just as extremity blast trauma and traumatic brain injury are the signature injuries of the combat in Iraq and Afghanistan, certain infections have also come to define the medical experience in these theaters. In addition to those caused by MDR bacteria, common infections are caused by protozoa belonging to the genera Leishmania and Plasmodium, causative agents of leishmaniasis and malaria, respectively.

Malaria

Although malaria, typically caused by chloroquine-sensitive *P vivax*, occurs with a very low prevalence in Iraq, both *P vivax* and, to a lesser extent, *P falciparum* are highly endemic in Afghanistan, with one case report describing 38 cases of *P vivax* among a 725-soldier Ranger Task Force that deployed to eastern Afghanistan between June and September 2002.[36] The US Army Central Command has articulated a policy on malaria chemoprophylaxis for deploying units.[37] Among its key features is the requirement for mandatory glucose-6-phosphate dehydrogenase (G6PD) deficiency screening prior to deployment with results annotated either in Defense Department form 2766 or the service-specific immunization database. The policy also dictates that doxycycline be used as the primary malaria chemoprophylactic agent, with mefloquine and atovaquone/proguanil (Malarone [GlaxoSmithKline, London, UK]) as second and third alternatives, respectively, for those with a contraindication to doxycycline. Personnel should be cautioned that doxycycline should be taken with food or water and not within an hour of lying down to mitigate potential side effects. They should also be advised to avoid taking the drug with milk or antacids, which may impair absorption. When chemoprophylaxis with mefloquine is being considered, it is important to exclude any history of depression, anxiety disorders, psychosis, or other psychiatric disorders as well as cardiac conduction defects.

Service members should deploy with sufficient malaria chemoprophylaxis in hand to cover the preexposure period (2 days for doxycycline and Malarone, 2 weeks for mefloquine); the period of exposure; and the terminal prophylaxis period (4 weeks for doxycycline and mefloquine, 1 week for Malarone). Deploying personnel are not required to hand carry primaquine because terminal chemoprophylaxis with primaquine will occur after redeployment (return to garrison). Providers should be aware that primaquine dosing recommendations often refer to the base ingredient (primaquine phosphate) and that 26.3 mg tablets contain 15 mg of primaquine base. According to the policy, malaria prophylaxis is indicated year round for Afghanistan, Pakistan, and Yemen and from May through October in Tajikistan. An exception applies to individuals whose deployment is restricted exclusively to the months of January and February.

Leishmaniasis

In contrast to malaria, leishmaniasis is endemic to both Iraq and Afghanistan; unlike malaria, which is transmitted by mosquitoes, this protozoan infection is typically transmitted by the bite of an infected sand fly. The nature of the infection depends upon the particular Leishmania species. In Iraq, where *L major* predominates, most infections are restricted to the skin, with occasional lymphadenitis. Lesions are typically painless, dry, and ulcerated, and may have an overlying eschar (Figure 40-1). A purulent discharge is not typical and may represent a secondary bacterial infection. In Afghanistan, where other Leishmania species are also found (eg, *L tropica* and *L infantum-donovani*), visceral

Figure 40-1. Typical lesion caused by Leishmania major. Note the lack of erythema and pus.

disease may rarely occur and has been documented among deployed soldiers.[38] The clinical presentation of visceral leishmaniasis varies but classically consists of fever, pancytopenia, hepatosplenomegaly, and cachexia.

The diagnosis of cutaneous leishmaniasis is made by confirming the presence of the amastigote in a skin biopsy or scraping. The diagnosis of visceral leishmaniasis is made by demonstration of amastigotes in biopsy specimens of bone marrow, lymph node, liver, or spleen. Additionally, serologic assays such as the rK39 immunochromatographic assay (Inbios International, Seattle, WA) and the *Leishmania* immunofluorescence assay (Centers for Disease Control and Prevention) are sensitive for systemic infection with Leishmania. Testing, by means of culture, histopathology or polymerase chain reaction (PCR) amplification is done at the WRAIR Leishmania Diagnostic Laboratory in Silver Spring, Maryland. With prior arrangement, samples can be sent for testing via commercial delivery services. The laboratory can be contacted via e-mail or 24 hours a day by telephone (301-573-3763), and additional instructions can be found at the WRAIR website.[39] Supporting documentation including a patient information sheet and specimen collection procedures are provided as Exhibits 40-1 and 40-2, respectively. On June 6, 2011, the US Food and Drug Administration approved a rapid diagnostic (SMART Leish PCR) for the diagnosis of cutaneous leishmaniasis.[40] The assay, developed in partnership among WRAIR, the Army Medical Materiel Development Activity, and a commercial partner (Cepheid, Inc, Sunnyvale, CA), utilizes real-time PCR to amplify *Leishmania major*-specific DNA sequences from skin scrapings. It is anticipated that this assay will be used at the Leishmania Diagnostic Laboratory at WRAIR and perhaps eventually by deployed medical assets.

With respect to treatment, patients with leishmaniasis are managed differently depending on whether they have cutaneous or visceral disease. Infection with *L major* is usually self-limiting, and watchful waiting is reasonable in many cases. For patients who need more immediate treatment (eg, those with large facial lesions), options include cryo- or thermo-therapy, topical paromomycin, azoles, pentavalent antimonies, and a lipid formulation amphotericin. The Army surgeon general holds the investigational new drug approval for pentavalent antimony, and this drug, as well as topical paromomycin, are solely given at Walter Reed National Military Medical Center. Because visceral leishmaniasis is life threatening, systemic therapy is always indicated and should be done under the direction of or in consultation with an infectious diseases specialist.

Other Common Infectious Diseases in Theater

In addition to those already discussed, the deployed provider should be aware of other infectious diseases endemic to the Middle East and Southwest Asia. A detailed discussion of each of these is beyond the scope of this paper, and ample reviews have been published[41,42]; however, a few relevant comments are appropriate here . According to the WHO, Afghanistan has a high burden of tuberculosis, with an incidence in 2009 of 187 cases per 100,000 persons. During the same year, the WHO reported an incidence of 67 cases per 100,000 persons in Iraq.[43] In line with Department of the Army Personnel Policy Guidance for Overseas Contingency Operations,[44] personnel deploying to either country require tuberculin skin testing (TST) within 12 months prior to deployment and again upon redeployment for soldiers considered to have been at high risk for exposure. High risk exposure is defined as indoor exposure to local people or third country nationals of greater than 1 hour per week in a region with greater than 25 cases per 100,000 persons annually (for the purpose of this policy, both Iraq and Afghanistan are considered to be high risk tuberculosis incidence areas). Individuals with previous positive tuberculin skin tests do not require TST. Interferon-gamma release assays such as the QuantiFERON-TB Gold (Cellestis,Inc, Valencia, CA) may be considered for those individuals with indeterminate TST results or for foreign-born individuals vaccinated with the Bacillus Calmette–Guérin (BCG) vaccine. Although the results of interferon-gamma release assays appear to decline after treatment for latent tuberculosis infection, and more significantly after treatment for active tuberculosis, there is insufficient data to support using these assays to monitor response after treatment for latent tuberculosis infection.

Q fever, a zoonotic disease caused by the Rickettsia-like bacterium *Coxiella burnetii*, is another infectious disease threat to deployed troops. Reservoirs include ruminants (as well as other mammals, birds, and arthropods), and humans become infected after inhalation of aerosolized bacteria or consumption of unpasteurized dairy products. Acutely infected individuals classically present with fever, atypical pneumonia, and hepatitis, and some will develop chronic disease including culture-negative endocarditis. The true risk to deployed personnel is unknown, but a recent study of banked sera from soldiers deployed to Iraq showed a 10% seroconversion rate, indicating exposure to the bacterium.[45] Because *Coxiella burnetii* is both fastidious and highly infectious, the diagnosis of Q fever is usually made by serology from acute and convalescent sera. This testing is cur-

EXHIBIT 40-1

WALTER REED ARMY INSTITUTE OF RESEARCH LEISHMANIASIS PATIENT INFORMATION SHEET

Leishmaniasis Patient Information Sheet
Soldier completes Part A; Clinical provider completes Part B

PART A – SOLDIER

Patient Name: _____ SSN: _____ Rank/ Service: _____

Blood type_____ Weight _____ Med Allergies _____ Age _____ DOB: _____

Unit: Company _____ BN _____ BDE/BCT _____ DIV _____

Date soldier arrived in Theater: _____ in Iraq: _____

Places/dates lived in Iraq: (e.g., *FOB Murphy, 10 Jun – 15 Jul 03*) _____
_____

Were rodents present around bivouac area? Y / N   Were dogs in the area? Y / N

Places You Slept	# Weeks or N/A	Screens Or Windows? (Y/N)	A/C (Y/N)	Use Bednet (Always/ Sometimes/Never)	Use Repellent (Always/ Sometimes/Never)	Insect Bites Per Night? (<5, 5-20, >20)
Vehicle or Ground						
Tent						
Building						

Your Use of Insect Repellents	Product Was Not Available to Soldier	Product was Available to Soldier			
		Did Not Use	Used Only After Insect Bites – After how many bites? (<5, 5-20, >20)	Used Every Night	Used Other Times *Describe When*
Bed Net, Treated w/ Permethrin					
Bed Net w/o Permethrin					
Permethrin Treated DCUs					
DEET (green tube) on Skin					
Commercial Insect Repellent *If Yes, List in Box*					

PART B – CLINICAL PROVIDER (*Send form with slides and biopsy*)

Lesion Location & #: _____ Duration? _____

Antibiotic Treatment (type/dose/length): _____

Photos Taken?   N / Y   If Yes, sent to WRAIR?   N / Y
Procedures Done: Scrape Biopsy: N / Y   Punch Biopsy: N / Y   Touch Prep: N / Y
            Culture: N / Y   Preserved Tissue: N / Y   PCR: N / Y

Date Eval: _____ MTF: _____ POC: _____ Phone: _____

                                            E-mail(POC): _____

Clinician Name   E-mail (Provider): _____
(stamp) ══
     Results: (POS / NEG) _____
Notes: _____

For questions regarding Leishmaniasis, contact the Leish Diagnostic Lab (peter.weina@us.army.mil)

version 12Apr04

EXHIBIT 40-2

WALTER REED ARMY INSTITUTE OF RESEARCH LEISHMANIASIS SCRAPING AND BIOPSY PROCEDURES

DEPARTMENT OF THE ARMY
WALTER REED ARMY INSTITUTE OF RESEARCH
503 ROBERT GRANT AVENUE, ROOM 2S04
SILVER SPRING MARYLAND 20910-7500

Leishmania Scraping & Biopsy Procedures

1) Criteria for scraping or biopsy:
- Any patient who has had a non-healing lesion (does not have to be an open, weeping ulcer) for greater than 3 to 4 weeks needs to be suspected of having leishmania.
- These patients need to be placed on a course of antibiotic therapy for 7 to 10 days with an antibiotic, which has proven activity in Iraq (recommendation is Augmentin 875mg BID for 7 to 10 days).
- At the conclusion of therapy, the patient should be seen by the same practitioner and a decision needs to be made if there was any efficacy to the course of antibiotics. If the lesion has persisted or worsened, a scraping or biopsy should be performed.
- Photos of the lesion prior to scraping or biopsy being done should be accomplished if the practitioner has the capability. E-mail these photos to WRAIR since this may help in the diagnosis (peter.weina@us.army.mil).

2) Scraping procedure:
- Clean area with alcohol pads and allow to dry.
- Anesthetize with lidocaine 1% or 2% with epinephrine 1:100,000 (unless the epinephrine is contraindicated due to anatomic site).
- 2 tissue smears are performed by horizontally scraping (lightly enough to elicit an exudates, but not vigorously enough to cause bleeding) the base of the underlying ulceration with a #15 blade (this often requires removal of the overlying crusted debris). The dermal tissue is then thinly applied in a circular fashion to a dime to nickel sized area in the center of the slide. Minimize blood, epithelium (keratinocytes), and purulence on the specimen.
- Additionally, material from the scrapings (and even the overlying crusted debris) should be inserted into a small vial of 95-100% ethanol for PCR analysis.
- Ensure slides are labeled per the format of your affiliated pathology department and submit per their protocol. If pathology services unavailable locally, ship per address below. Work closely with pathologists to verify adequacy of tissue smear samples.

2) Biopsy/touch prep-impression smear procedure:
- An area of the lesion needs to be cleaned thoroughly with alcohol pads and dried.
- The anticipated area of biopsy should be anesthetized as described above.
- A 4 mm sterile disposable punch or sterile scalpel (#15, #11, or #10) should to be used to remove a piece of tissue approximately 3 to 4 mm in circumference and approximately 1 mm deep from the edge of the lesion (see photo for preferred area of biopsy). Lesions on the face, anterior of the neck, and near larger vessels and/or nerves need to be biopsied with extreme caution and a simple surface scraping (described above) may be preferred to a true biopsy.
- The biopsy should be placed on a sterile, clean, dry gauze 2X2 briefly to absorb excess blood on the tissue that may interfere with the reading of the touch preparations.

(**Exhibit 43-2** *continues*)

Exhibit 40-2 *continued*

- The tissue should be grasped with forceps and impression smears made on clean slides (4 for each biopsy) by rubbing the tissue gently across the surface of the slide in a circular motion.
- Dry thoroughly. Fix with methanol if available.
- The tissue biopsy (after the impression smears are made) should then be placed in a very small amount of ethyl alcohol (just enough to cover the specimen) in a leakproof vial (such as a "nunc" transport tube).
- The slides and the vial with the tissue should be shipped per your local pathology section protocol or via DHL or Federal Express to the address below. The container should be labeled as diagnostic specimens and no shipping permit is required (all MTFs have personnel and resources to ship diagnostic specimens correctly).
- **PLEASE LABEL WITH PATIENT NAME, SPECIMEN SOURCE, DATE, AND MATERIAL TRANSPORTED IN** (formalin, ETOH, etc.).
- Complete the patient information sheet (attachment #2 below) and include with the specimen for each patient biopsied.
- Procedural inquiries should be made to COL Peter Weina at (301) 319-9956.

SHIPPING ADDRESS

Colonel Peter J. Weina, PhD, MD
Director, Leishmania Diagnostic Laboratory
Division of Experimental Therapeutics
503 Robert Grant Avenue
Walter Reed Army Institute of Research
Silver Spring, Maryland 20910-7500

Preferred biopsy area:

Biopsy should just catch edge of most affected tissue and should have relatively intact tissue adjacent to the lesion for at least one half of biopsy

rently unavailable in the deployed setting. However, a diagnostic utilizing real-time PCR with a rugged deployable platform is being developed.[46] Guidelines promulgated by the Armed Forces Infectious Diseases Society TriService Q Fever Working Group recommend empiric therapy with doxycycline, 100 mg twice a day for 21 days, for patients suspected of having acute Q fever.[47] The working group also recommends sending serum for testing to the US Air Force School of Aerospace Medicine at the time of presentation and again in 2 weeks. If a patient has positive serologic testing for acute Q fever, a transthoracic echocardiogram (TTE) should be performed to document any baseline cardiac valvular abnormalities, and infectious diseases consultation should be obtained. However, the guidelines do not recommended medical evacuation exclusively for the purpose of obtaining a TTE unless there are clinical signs suggesting more urgent evaluation is indicated.

Like *Coxiella burnetii*, species belonging to the genus Brucella (in particular, *B melitensis*) cause acute and chronic infections in humans, have a reservoir in ungulates, and are transmitted via aerosols or contaminated dairy products. Brucellosis is a common cause of fever of unknown origin, and the clinical presentation may be nonspecific. However, well-described complications include sacroiliitis, epididymo-orchitis, meningitis, endocarditis, and hepatic abscess. The diagnosis is made by culture (*B melitensis* is a potential hazard to laboratory workers, and the laboratory should be notified when brucellosis is suspected), serology, or PCR. Although *B melitensis* is endemic worldwide, including the Middle East, only a few cases have been reported among redeploying troops.[48,49] However, brucellosis should be considered in an individual with chronic fever and past exposure to ungulate animals or consumption of raw dairy products. Treatment involves a prolonged course of multiple antibiotics and should be done under the direction of or in consultation with an infectious diseases specialist.

SUMMARY

The deployed provider can expect to encounter patients with infectious and noninfectious conditions. Orthopedic injuries are common among the latter, while among the former, gastroenteritis and upper respiratory infections predominate. While the preponderance of infections are the same as those encountered stateside, deployments present special challenges for the healthcare provider. In addition to the commonplace infections are those endemic to the region. Moreover, prevention of infection, both combat associated and nosocomial, can be difficult even under ideal conditions. A useful asset available to any military provider with Internet access is the remote consultation service offered by infectious diseases specialists assigned to stateside military medical centers. Providers can submit case presentations and solicit advice via e-mail (id.consult@us.army.mil) and expect thoughtful, comprehensive replies typically within several hours.

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