



## The Unexpected Enemy: Chronic Infections from Military Deployment

Military deployment is a unique form of travel medicine. First, combat activities result in intense high-risk exposure of non-immune individuals to foreign environments containing novel infectious agents. Present military deployments are also in countries where medical and public health systems are in disarray, resulting in further risk from interactions with ailing local populations and their living conditions. Secondly, unlike the average vacation, a typical tour of duty is 6-12 months, increasing the probability for unusual infectious exposures. Although acute and self-limited infections are common throughout the deployment, those agents with longer incubation periods or an indolent disease course can be overlooked in healthy soldiers by family physicians upon their return (1). This article will summarize the three most documented chronic infections seen in U.S. military personnel participating in Operations Iraqi and Enduring (Afghanistan) Freedoms (OIF and OEF respectively) that have presented after returning to North America.

Body armour is now standard military equipment, shifting injuries from torso to extremities, which are mainly the result of explosive devices and readily contaminated (2). Despite rapid surgical debridement and prophylactic antibiotics, gram negative bacteria continue to cause post-operative wound infections (3). A well recognized outbreak with multi-drug resistant (MDR) *Acinetobacter baumannii* complex has been occurring in U.S. soldiers returning to North America and Europe, with either skin colonization or infection. The U.S. army has reported its preliminary experience from OIF and OEF combat personnel from 2002-2004 (4). Eighty five cases of blood stream infections were recorded at major military ICUs (Landstuhl Regional and Walter Reed Army Medical Centers) after receiving recently injured soldiers from various field hospitals. Two thirds of the cases were identified within 48 hours of transfer. This spike in clinical cases was 3.5 times the baseline nosocomial rates for both hospitals and prompted further investigation. The *A. baumannii* isolates collected from combat soldiers between 2002 and 2005 revealed that resistance to all common antibiotic classes

was wide spread, with one third susceptible only to carbapenems (3). Fortunately, this has not translated to increased morbidity or mortality in the average healthy soldier. In a case series of extremity infections (predominantly osteomyelitis), with over half due to multi-drug resistant strains, all patients showed sustained clinical improvement with various antibiotic regimens (5). With 15% of hospitalized soldiers colonized, the real concern has been ongoing nosocomial spread within military medical facilities. Walter Reed Army Medical Center has reported 53 cases of soldier to patient transmission, leading to four deaths amongst immunocompromised patients (2,3). Genetic analysis has linked clinical isolates to field hospital environmental strains, where acquisition of broad resistance from long standing antibiotic exposure and dissemination from lax hand washing/infection control procedures during mass casualty situations is believed to have occurred (2).

reliable preventative measures for travellers include regular chemoprophylaxis (tailored to local drug resistance) and insect repellent (e.g. N, N-diethyl-3-methylbenzamide (DEET) and permethrin). However, for long-term travellers (soldiers) this can become bothersome (e.g. drug side-effects) or difficult to remember daily (e.g. during combat activities). A Special Forces unit illustrated how unreported lapses in personal protective measures could delay the recognition of a *P. vivax* outbreak (8). In 2002, the 725 man unit patrolling in Eastern Afghanistan (on mefloquine prophylaxis) reported 38 cases, but the median time to diagnosis (by thin & thick smears) was 233 days. Three quarters of the cases were not formally diagnosed until their return to the USA, almost 290 days post Afghanistan deployment. A survey of the unit revealed that only a third of the soldiers correctly took the recommended chemoprophylaxis and only 20% used DEET as instructed.

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Malaria is a prevalent travel related infection transmitted by the night time biting female *Anopheles sp.* mosquito. *Plasmodium falciparum* causes a rapidly life-threatening disease in the non-immune traveller, but other *Plasmodium* species (*P. vivax* and *P. ovale*) manifest as indolent and/or relapsing non-specific febrile illness. Because they cause lower degrees of parasitemia and dormant hepatic stage that can reactivate months after returning from abroad, the diagnosis of non-falciparum malaria is not commonly considered. Although both Iraq (certain provinces) and Afghanistan (below 2000 metres elevation) are endemic areas, cases have only been seen in soldiers serving in Afghanistan (2,6). In 2004, 56 cases of malaria (25% due to *P. vivax*) were reported in U.S. troops, taking up to 20 months to establish the diagnosis by thick and thin blood films (7). At present,

Leishmaniasis is a protozoan parasitic disease transmitted by the bite of an infected sand fly and is endemic to both Iraq and Afghanistan. With its common clinical forms, cutaneous or visceral, prolonged illness results from lack of access to treatment (especially amongst the endemic population) or failure to recognize the subtle disease (9). The latter has resulted in an outbreak of cutaneous leishmaniasis, due to *L. major*, amongst U.S. service personnel initially deployed in OEF and OIF. Overall, approximately 0.25% of all deployed U.S. forces were affected from 2003 to 2005, with a peak of 522 cases occurring between August and November 2003 (3). Although Afghanistan is considered one of the world's most endemic areas for cutaneous leishmaniasis (200,000 cases in Kabul alone),

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virtually all cases have been in soldiers serving in Iraq (10, 1). The self-limited cutaneous disease is generally recognized as a slowly expanding, painless, scaly skin lesion that commonly ulcerates and rarely disseminates. Diagnostic confirmation comes from visualization of amastigotes in Giemsa stained skin scraping or biopsy with culture or PCR permitting speciation (3). Treatment varies from observation, cryo- or heat therapy, topical paromomycin, pentavalent antimonials or oral azoles. In contrast, there have been 5 cases of visceral leishmaniasis (kala-azar) in U.S. soldiers due to *L. infantum-donovani* complex,

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with 4 cases from Afghanistan (2,3). Despite a variable incubation period, life threatening systemic disease (fevers, wasting, bone marrow and reticuloendothelial involvement) has been seen up to 14 months after returning from deployment. The laboratory diagnosis is similar to cutaneous disease but requires reticuloendothelial tissue (e.g. liver, spleen, bone marrow) biopsy for histopathological confirmation of the amastigotes (3). Intravenous therapy with liposomal amphotericin B or pentavalent antimonials (e.g. sodium stibogluconate) is used to control disease symptoms but may not eradicate the intracellular organisms.

The eventual recognition of chronic and indolent infections resulting from OIF and OEF deployment has led the U.S. military to adapt its delivery of healthcare to lessen the disease impact on its personnel. Currently, improved soldier education, case surveillance, better living conditions, and insect control programs have been success-

ful in combating sand fly and mosquito vectored disease. This has been coupled with re-enforcing time tested personal protective measures, such as DEET, permethrin impregnated field uniforms, malaria chemoprophylaxis and avoiding exposed skin (e.g. pant cuffs tucked into boots and sleeves worn down; 12). With these interventions in place, improvements in the rates of cutaneous leishmaniasis have already been realized compared to the initial case load seen in 2002-04 (13). With respect to MDR *A. baumannii* complex, awareness of how soldiers acquire the organism have allowed for steps to prevent transmission. Universal screening and isolation of all transferred injured

soldiers, strict hand washing and prudent use of antimicrobials is underway to combat further nosocomial spread (2,5). As military operations in Iraq and Afghanistan continue to unfold, the potential for novel infections amongst soldiers related to the unpredictable nature of military activity will exist. Persistent medical vigilance for these exotic diseases, both abroad and at home, will be necessary to safeguard the men and women from these unexpected enemies. ♦

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