

U N C L A S S I F I E D

EXECUTIVE SUMMARY

16 MAR 04

(U) UPDATE - LEISHMANIASIS AMONG US MILITARY PERSONNEL IN SOUTHWEST ASIA. (DASG-PPM-NC) (U). Since 1 Jan 03, three hundred and seventy eight (378) cases of cutaneous leishmaniasis (CL) and two cases of visceral leishmaniasis (VL) have been confirmed among troops deployed to Southwest Asia. CL and VL are found throughout southwest and south-central Asia. Both diseases are transmitted through the bite of infected sand flies. All CL cases have been treated at Walter Reed Army Medical Center (WRAMC), the DOD referral center for treatment of CL. One VL case has been treated at WRAMC and one at the Naval Medical Center in San Diego. Of CL cases for whom a location of likely exposure was known, slightly over half were most likely exposed in central Iraq (especially the area northeast of Baghdad near the Iranian border). About one third were exposed in northern Iraq (Tikrit, Mosul, etc.), and about one tenth in the vicinity of Tallil Airbase in southern Iraq. Definitive treatment of DOD personnel with CL occurs only at WRAMC with sodium stibogluconate (Pentostam™). Liposomal amphotericin B is the preferred treatment for VL. Eight soldiers with CL have failed treatment and require repeated treatment. All personnel deployed to Iraq are deferred from donating blood until 12 months after leaving Iraq. Prevention requires command emphasis on use of personal protective measures against biting insects with DEET-containing repellents, and uniforms and bed nets impregnated with permethrin.

ADDITIONAL INFORMATION

SUBJECT: Leishmaniasis Among Soldiers Deployed to Operation Iraqi Freedom.

1. References.

- a. Defense Intelligence Agency, Armed Forces Medical Intelligence Center, Infectious Disease Risk Assessment: Iraq, October 2002 DI-1812-IRQ-02.
- b. Defense Intelligence Agency, Armed Forces Medical Intelligence Center, Infectious Disease Risk Assessment: Iraq, 18 April 2003 DI-1812-330-03.
- c. Defense Intelligence Agency, Armed Forces Medical Intelligence Center, Infectious Disease Risk Assessment: Kuwait, October 2002 DI-1812-KWT-02.
- d. Defense Intelligence Agency, Armed Forces Medical Intelligence Center, Infectious Disease Risk Assessment: Afghanistan, October 2002 DI-1812-AFG-02.
- e. Armed Forces Pest Management Board Technical Information Memorandum No. 36: Personal protective techniques against insects and other arthropods of military significance, August 1996.

DASG-PPM-NC

SUBJECT: Leishmaniasis among soldiers deployed to OIF/OEF.

f. Centers for Disease Control and Prevention. Health Information for International Travel, 2003-2004. Atlanta, GA: US Department of Health and Human Services, Public Health Service, 2003.

g. Communicable Disease Profile-Iraq, World Health Organization, Communicable Disease Working Group on Emergences, HQ, 19 March 2003.

h. Centers for Disease Control and Prevention. Mortality and Morbidity Weekly Report. Cutaneous Leishmaniasis in US Military Personnel-Southwest/Central Asia, 2002-2003. Vol. 52 (42); 1009-1012. 24 October 2003.

i. Memorandum, MCPO-SA, 21 Oct 03, subject: Medical Advisory –Leishmaniasis.

j. Memorandum, DASG-HSZ, 23 Dec 02, subject: Policy for Diagnosis and Treatment of Leishmaniasis sp. Diseases.

k. Memorandum, DASD (FHP&R), 2 Oct 03, subject: Blood Donor Deferral for leishmaniasis in Iraq.

l. Internal Medicine, Stein – 5th Ed., Jay H. Stein, MD et al, 1998.

m. Memorandum, CJTF7-SG, 25 Nov 03, subject: CJTF-7 Policy on Cutaneous Leishmaniasis Diagnosis and Treatment.

2. General.

a. **Leishmaniasis** is a vector-borne parasitic disease spread by the bite of infected female sand flies. The *Phlebotomus papatasi* sand fly, about 1/3 the size of a mosquito, is a noiseless flyer, has a short flight range, and typically bites at night. The sand fly breeds in dark places such as leaf litter, rubble, loose earth, caves and rock holes. It does not leave telltale pain, itch or visible evidence of the bite such as with mosquito bites. Reservoirs for the parasite are humans, rodents, marsupials, and dogs. Leishmaniasis is characterized by a substantially long incubation period of a week to years. The most common forms of leishmaniasis are **cutaneous** (skin sores) with an incubation period of weeks to months, **visceral** (internal organs) with an incubation period of 10 days to years, which, if untreated, can be fatal. Rarely, cutaneous leishmaniasis (CL) strains from the Western Hemisphere (North and South America) may progress to the **mucosal** (mouth and nose) form, if left untreated. Twenty cases of CL and twelve cases of visceral infection were reported in soldiers infected during Operation Desert Storm from 1990 to 1991.

b. In Southwest Asia, the most common parasite species are *Leishmania major*, *L. tropica*, *L. infantum*, and *L. donovani*. *L. major* and *L. tropica* cause cutaneous infection, and *L. donovani* and *L. infantum* cause visceral infections. The twelve cases of 'viscerotropic' *L. tropica* reported during Operation Desert Storm constituted the first time this clinical presentation had been reported. All cases of CL in US servicemembers from Operation Iraqi Freedom are *L. major*. The species causing the two VL cases has not been identified.

c. According to the US Centers for Disease Control and Prevention (CDC), leishmaniasis is found in 90 tropical and subtropical countries around the world, causing about 1.5 million new cases of CL and 500,000 new cases of visceral leishmaniasis each year. More than 90 percent of the world's cases of CL occur in Iraq, Afghanistan, Saudi Arabia, Syria, Iran, Peru, Algeria, and Brazil. More than 90 percent of visceral leishmaniasis cases occur in Bangladesh, Brazil, India, Nepal and Sudan.

3. Leishmaniasis in Iraq. Both cutaneous and visceral forms of leishmaniasis are endemic in Iraq. In 2001, about 3,000 visceral and 625 CL cases were reported among the general population in Iraq. The true incidence of CL in Iraq is thought to be much higher than these data would indicate.

a. CL, due to *L. major*, is primarily found in rural areas of Iraq bordering Turkey and Iran. Transmission peaks from July through September with seasonality running from April through November. Most CL cases in urban areas (Baghdad and Mosul) are attributed to *L. tropica*. In both locations, a high percentage of the adult population appears to have acquired immunity since most clinically apparent cases occur in children.

b. Visceral leishmaniasis is primarily in rural areas (mainly central Iraq) and is caused by *L. infantum* and *L. donovani*. Cases of visceral leishmaniasis among Iraqi residents have been increasing in central and southern Iraq at least since 2002. In southern Iraq, about 700 cases were identified from January through April 2003.

c. Sandfly trapping and PCR testing for leishmaniasis infection was performed by US forces from multiple sites within the theater of operations during the 2003 transmission season. Infection rates ranged from 0% (0/448) at Diwaniyah to 1.44% (183/12,697) at Talil Air Base. A total of 40 pools of *Leishmania*-positive sand flies were tested for presence of visceral *Leishmania* species; two such sandfly pools tested positive for *Leishmania infantum*, indicating potential transmission of visceral leishmaniasis to US servicemembers.

4. Leishmaniasis in Kuwait. In Kuwait, leishmaniasis is a disease of potential risk which warrants force protection emphasis. *L. major* and *L. tropica* cause CL primarily in rural areas of Kuwait. Transmission peaks from July through September with the season running April through November. A limited study from 1990 found CL in 54 patients from the Al Jahra district, west of Kuwait City.

5. Leishmaniasis in Afghanistan. CL is endemic in Afghanistan. WHO reported resurgence of CL during 2002 with at least 250,000 cases reported countrywide, and at least 200,000 reported in Kabul alone. The risk period for CL is seasonally March through November. The risk distribution for CL is countrywide including urban areas. Foci of *L. major* have been reported from rural areas in the northern plains of Baghlan, Balkh, Faryab, Jowzjan, Konduz, Samangan, Takhar Provinces, and in the southwestern lowlands. Foci of *L. tropica* have been reported from most towns and cities of Badakhshstan, Ghazni, Herat, Kabul, Kandahar, Kapisa, and Parvan Provinces. In endemic areas where humans live close to the reservoir and vector, a high percentage of the population may have acquired immunity to CL, with clinical cases occurring mostly

in children. Visceral leishmaniasis (VL) is countrywide including urban areas. *L. donovani* and *L. infantum* cause VL infection. The risk period for VL is seasonally March through November. Foci of VL have been reported from Badakhstan, Badghis, Ghazni, Kabul, and Kandahar Provinces.

6. Clinical diagnosis of leishmaniasis. CL may present as non-healing ulcerous lesions, characterized by one or more open, (crater-like) skin sores that develop over weeks to months after a person is bitten by an infected sand fly. This protracted delay in the appearance of characteristic lesions often foils attempts to identify the specific locale of initial infection, due to the mobility of military personnel. This delay, along with the fact that the disease is not indigenous to the US, contributes to delayed diagnosis. Visceral leishmaniasis can be very difficult to diagnose. Symptomatic individuals generally have chronic fever, and may experience weight loss, evidence of an enlarged spleen and liver, anemia, leukopenia, and thrombocytopenia.

7. Confirmed diagnosis of leishmaniasis. Biopsy (punch or skin scraping) and positive culture are required to confirm the diagnosis and to determine the species of *Leishmania*.

8. Leishmaniasis treatment (see reference in para.1 j. and reference in para. 1 m.).

a. While cutaneous infection is non-fatal, the skin sore can be unsightly. Immediate medical evacuation for treatment is not required for all identified leishmaniasis cases. Based on the species and extent of the disease (reference in para. 1 m.), the CJTF-7 Surgeon has written guidance to commanders on the priority and urgency for which Soldiers are evacuated. If the diagnosis is confirmed for *Leishmania major*, there are several options for evacuation:

i) If the lesion is large (greater than or equal to 2.5 cm diameter, three or more lesions, or occurs on the face, ear, hand, foot or joint, then the Soldier will be evacuated to WRAMC for further evaluation and treatment. Thirty-six Soldiers are currently being treated for cutaneous leishmaniasis at WRAMC.

ii) If the lesion is small (less than 2.5 cm diameter) or less than three lesions, and in an area where scarring is not an issue, the Soldier may choose to continue with local assessment and treatment. Even if left untreated, CL is a self-limited infection and may heal spontaneously within weeks or months.

iii) If the diagnosis is confirmed for *Leishmania*, the Soldier will be evacuated to WRAMC.

b. Most CL from OIF due to *Leishmania major* is treated with an antimony-containing compound, sodium stibogluconate, Pentostam™, intravenously for ten days. Larger lesions, lesions on the face, and those that do not respond to initial treatment may require twenty days of therapy. This product is administered voluntarily under an FDA approved Investigational New Drug (IND) protocol at WRAMC, the only DOD facility with the IND exemption protocol, serving all branches of the military. Side effects can include weakness, anorexia, mild, reversible liver function abnormalities, and transient abnormalities of the T wave on ECG testing. Leukopenia and thrombocytopenia may

occur with longer periods of treatment. To date, two Soldiers developed angioedema during treatment (may or may not have been causally related) and treatment was stopped. One additional patient was stopped at three days due to pancreatitis. The approved 10-day protocol has shown essentially equal efficacy, with reduced side effects. Eight Soldiers have failed treatment and require repeated treatment with Pentostam™. Liposomal amphotericin B may be required if the patient does not respond well with Pentostam™. The Pentostam™ treatment has been about 95% effective in soldiers. Thirty-six Soldiers are currently being treated for cutaneous leishmaniasis at WRAMC. Fluconazole and heat treatment of the lesions are also being used as alternative treatments. After completion of treatment, Soldiers are able to return to their unit and are fully deployable.

c. In the Eastern Hemisphere, *Leishmania donovani* is the usual agent causing visceral leishmaniasis. It is treated by the use of liposomal amphotericin B (AmBisome™) as the drug of choice with Pentostam™ as an alternative therapy. It is important to note that *Leishmania donovani* may also cause cutaneous leishmaniasis without visceral involvement.

9. Current Actions.

a. Additional treatment facilities and alternative treatments for cutaneous leishmaniasis are currently being investigated.

b. Troop and Health care provider information (see reference 1. i.). Laminated, wallet-size information cards were produced and distributed to deployed troops. These cards contain information on leishmaniasis including contact information, diagnostic support and treatment. A website has been developed by the DOD Deployment Health Clinical Center (<http://www.pdhealth.mil/leish.asp>) to provide troops, family members, REFRAD reservists and health care providers information on this disease.

c. Blood donor deferral. (see reference, para. 1. k.). Although no cases of transfusion-acquired leishmaniasis have been reported in the US, all US personnel deployed to Iraq will be deferred from donating blood for 12 months after departure from Iraq. Persons diagnosed with leishmaniasis are permanently deferred. These deferrals are in conjunction with the donor deferrals in effect for malaria risk in Afghanistan and Iraq.

d. Commanders of units deploying to Iraq should ensure that personnel have adequate supplies of DEET, permethrin and bed nets and are trained and disciplined in their appropriate use.

e. Due to the delay in onset of symptoms and signs of CL and visceral leishmaniasis, new cases are expected to emerge among troops currently deployed, and those recently returned from Iraq for several months after the end of the sand fly transmission season in Iraq in November 03.

f. The potential for introduction into the US of leishmaniasis by soldiers returning from Southwest Asia is remote. It is possible that one or more of the US mammalian biting sand flies could harbor and transmit Old World leishmaniasis. However, the risk of

DASG-PPM-NC

SUBJECT: Leishmaniasis among soldiers deployed to OIF/OEF.

L. major being introduced into the US by infected soldiers coming back from Iraq is negligible. Humans are not an effective reservoir for *L. major* because in humans the parasites are restricted to the lesion site. Sand flies could ingest parasites only if they feed directly on the lesion, which is very unlikely. Keeping lesions covered with a dressing would insure that no sand flies could become infected. Another Old World species of Leishmania, *L. infantum* also occurs in Central and South America, and has been reported in the US among dogs in 21 states. However, no human cases have been reported in the US, even among the dog handlers.

10. Preventive measures for leishmaniasis. There are neither vaccines nor medication effective for prevention of leishmaniasis. Prevention of leishmaniasis is accomplished by (1) suppressing the reservoirs including dogs and rodents, (2) suppressing the vector (sand fly) which is critical to preventing exposure in stationary troop populations and (3) command emphasis on personal protective measures (PPM). Effective PPM measures include all of the following: a) application of repellent lotion containing N, N diethyl-m-toluamide (DEET) in an extended use formulation (NSN 6840-01-284-3982) to exposed skin, b) proper wear of the US military battle dress uniform (BDU), preferably Permethrin treated, with sleeves rolled down and pants tucked into boots, and, c) use of Permethrin treated bed nets and screened enclosures.

Mr. Paul Repaci/DASG-PPM-NC/681-2949
Approved by COL Robert DeFrait