LEISHMANIASIS
Information for Clinicians

A Collaborative Effort of DHCC, AFIOH/RSR,DHSD, USACHPPM, & WRAMC

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Leishmaniasis is a parasitic disease spread by the bite of infected sand flies. There are several different forms of leishmaniasis. The most common form is cutaneous leishmaniasis, which causes skin sores. Visceral leishmaniasis, which affects some of the body's internal organs, (most commonly the spleen, liver and bone marrow) is the most serious of the infections. Leishmaniasis is endemic to Iraq, Kuwait, Afghanistan, and other places in the Middle East; and poses a health risk to service members deployed there. The sand fly season in Iraq is from April through November and peaks in September/October. While effective treatment is available, prevention remains the best option. Leishmaniasis is not the same thing as Sandfly Fever which is a different disease spread by sand flies.

WHAT ARE THE SIGNS AND SYMPTOMS OF LEISHMANIASIS?

People with cutaneous leishmaniasis have one or more chronic skin lesions where infected sand flies have fed. These lesions are generally unresponsive to antibiotics or topical steroids. The lesions start as a papule that often enlarges and then ulcerates. Some are surrounded by concentric silvery scales; some are raised pink plaques. Scabs may develop. The sores can change in size and appearance over time and some will heal spontaneously. The sores can be painless or painful. Some people have swollen lymph nodes near the sores.

People who have visceral leishmaniasis typically have chronic fever, weight loss, and sometimes an enlarged spleen or liver; usually the spleen is larger than the liver. Some patients have swollen glands. Patients usually have elevated liver function tests or low blood counts, including low red blood cell count, low white blood cell count, and/or low platelet count.

IN WHAT PARTS OF THE WORLD IS LEISHMANIASIS FOUND?

Leishmaniasis is found in about 88 countries. Approximately 350 million people live in these areas. Most of the affected countries are in the tropics and subtropics. Leishmaniasis is found in areas ranging from rain forests in Central and South America to deserts in West Asia. More than 90% of the world's cases of visceral leishmaniasis (VL) are in India, Bangladesh, Nepal, Sudan and Brazil. VL is found in Iraq as well. Cutaneous leishmaniasis (CL) is the most common form, however. Leishmaniasis is endemic to the Middle East and poses a potential health threat to service members deployed to that region.

HOW IS LEISHMANIASIS SPREAD?

Leishmaniasis is spread by the bite of some types of infected blood-sucking sand flies. Sand flies become infected by biting an infected animal (for example, a rodent, dog or person). Sand flies make no noise when they fly or jump, so people may not realize they are being bitten. Sand flies are very small and may be hard to see; they are only about one-fourth the size of typical mosquitoes. Sand flies are most active from dusk to dawn. They are less active during the hottest times of the day. Rarely, leishmaniasis is spread from a pregnant woman to her unborn baby. Leishmaniasis can also be spred by blood transfusions or contaminated needles.

HOW SOON MIGHT LEISHMANIASIS SYMPTOMS APPEAR AFTER INFECTION?

People with cutaneous leishmaniasis usually develop skin sores within a few weeks (sometimes as long as months) of when they were bitten. People with visceral leishmaniasis usually become sick within several months (rarely as long as years) of when they were bitten. Because it is a parasitic disease, if left untreated, reactivation can occur long after initial signs and symptoms resolve.

WHAT WILL HAPPEN IF LEISHMANIASIS IS LEFT UNTREATED?

The skin sores of cutaneous leishmaniasis may heal on their own, but this can take months or even years. The smallest lesions (under 10 mm) may not require treatment, just "watchful waiting." The sores can leave ugly scars. If not treated, infection that started in the skin can rarely spread to

the nose or mouth and can cause sores there (mucocutaneous leishmaniasis), which can be quite disfiguring. This is seen in some of the types of Leishmaniasis found in Central and South America.

Visceral leishmaniasis can cause serious illness (enough to require hospitalization) but does not usually cause death in people with healthy immune systems and good nutrition. In some, visceral leishmaniasis can be a milder illness. On the other hand, individuals with degraded immune system functioning are at higher risk for serious or even fatal illness.

HOW IS LEISHMANIASIS DIAGNOSED?

There is no effective laboratory screening tests for leishmaniasis. Therefore, diagnoses involves a combination of compatible symptoms, objective signs, and laboratory findings.

Giemsa-stained tissue samples remain the most commonly used technique in the world today for diagnosis. A local pathologist should review the results first. Confirmation of results can be obtained from the Leishmania Diagnostic Laboratory at WRAIR. Contact information is at the end of this information sheet. Serum antibody detection (serology) can prove useful in diagnosing visceral leishmaniasis but is of no use in cutaneous disease. Other diagnostic techniques exist that allow parasite detection and species identification by special culture and microscopy, biochemical (isoenzymes), immunologic (immunoassays), and molecular (PCR) approaches.

Cutaneous leishmaniasis is diagnosed by sampling the skin lesion, usually with a biopsy or scraping. In visceral leishmaniasis, diagnosis requires invasive samples (bone marrow, liver, lymph nodes) and parasitological diagnosis can be challenging. The rK39 *Leishmania* serology may have a role as a first line test for visceral leishmaniasis in patients with consistent signs and symptoms. Bone marrow aspirate and biopsy (BMA) remains the most definitive diagnostic test but spleen aspirate and liver biopsy are also sometimes used although there is greater risk associated with those procedures. In difficult to diagnose cases, Leishmania PCR of the whole blood may be ordered. Specialized diagnostic support, such as culture and PCR, are available from the Walter Reed Army Institute of Research Leishmania Diagnostic Laboratory. WRAIR will provide test equipment and detailed instructions upon request.

HOW IS LEISHMANIASIS TREATED?

Liposomal amphotericin (AmBisome®) is the drug of choice to treat visceral leishmaniasis in the U.S. but it does not yield high skin concentrations and is not used for treatment of cutaneous leishmaniasis. Pentavalent antimonial (Sb^v) drugs such as sodium stibogluconate (Pentosam®) have been used for six decades to treat both visceral and cutaneous leishmaniasis. It is given intravenously for 20-28 days and has predictable but reversible side effects. Sodium stibogluconate (Pentostam®) is not approved by the Food and Drug Administration (it is made and licensed in Great Britain) and must be given under an investigational new drug (IND) protocol. Walter Reed Army Medical Center (WRAMC) in Washington DC and Brooke Army Medical Center (BAMC) at Fort Sam Houston Texas offer leishmaniasis treatment to military beneficiaries, including reservists no longer on active duty. WRAMC offers treatment to those east of the Mississippi River and BAMC offers treatment to those west of the Mississippi River. The CDC Drug Service provides sodium stibogluconate for civilians. Physicians may consult WRAMC, BAMC, or CDC at the contacts listed at the end of this document to obtain information on how to treat leishmaniasis.

The Department of the Army uses a protocol for treatment with Pentostam® (sodium stibogluconate), which requires service members to be referred to WRAMC or BAMC for treatment. Depending on the severity, the current regimen is for 10 to 20 days of treatment for cutaneous leishmaniasis, and 28 days treatment for mucocutaneous or visceral forms. Sodium stibogluconate is the second line treatment for the visceral form of leishmaniasis. Liposomal amphotericin B (AmBisome®) remains the first line treatment for visceral leishmaniasis and is approved for use by the FDA.

Two other treatment modalities for cutaneous lesions are cryotherapy with liquid nitrogen and the use of localized current field radiofrequency heat.

It has also been proposed that fluconazole may decrease the healing time of *Leishmania major* species infection. After biopsy has determined that this species is the causative agent, a six-week course of this medication may be ordered for treating this species only.

HOW SHOULD I WORK UP A SUSPECTED CASE OF LEISHMANIASIS?

Cutaneous leishmaniasis is suspected in cases where the patient presents with a chronic, often painless, 'clean' ulcer, and/or has plaque-like or nodular lesions occurring with a history of sand fly bites coming from a geographic area where leishmaniasis occurs.

Individuals with suspicious lesions identified during deployment or through post-deployment surveillance should be evaluated on redeployment. Priority for evaluation and treatment is for those lesions that are large (greater than 2.5 centimeters) or occur on the face, or ear, or hand, or over joints, or when there are many in number.

Individuals with unconfirmed infections may be evaluated at their home station MTF in consultation with the Infectious Disease Service at WRAMC or BAMC and referred for evaluation and treatment based on the consultation. Contact information is listed at the end of this document.

Visceral leishmaniasis should be suspected in any patient presenting with non-specific, chronic, febrile illness from a geographic area where leishmaniasis is present, such as SW Asia. This is especially true if the patient has a history of sandfly bites, and has splenomegaly, hepatomegaly, anemia, elevated liver function tests, or other cytopenias.

If tests are negative and objective exam signs are absent or minor but symptoms persist, a period of "watchful waiting" should be pursued rather than aggressive lab testing. Watchful waiting involves a follow-up visit and directed history and exam in search of objective signs of progression. No general screening tests exist for the disease.

Biopsy is required for diagnosis of cutaneous, muco-cutaneous and visceral forms of leishmaniasis. This may be done locally if leishmania diagnostic capability and trained personnel are available. If not available, the patient should be referred to WRAMC or BAMC.

Diagnostic help is available upon request from the Walter Reed Army Institute of Research (WRAIR). POC for the diagnostic help is LTC Peter Weina at 301.319.9956 (telephone), 301.319.7360 (fax), or peter.weina@NA.AMEDD.ARMY.MIL (e-mail). He would prefer to be contacted through e-mail, if possible.

Complete instructions for obtaining help from WRAIR are available at http://www.pdhealth.mil/downloads/Leishmaniasis_DS_04272004.pdf.

WHAT SHOULD I TELL MY PATIENT WITH SUSPECTED OR CONFIRMED DISEASE?

Patients may be reassured that effective treatment is available. Give an explanation of the referral process so that the patient will know what to expect. Answer basic questions about the diagnostic work-up and possible treatments. Confer with a consultant for more complicated questions. Patients should be referred to additional information such as the DHCC web site at www.pdhealth.mil and the CDC web site at http://www.cdc.gov/ncidod/diseases/submenus/sub_leishmania.htm. The patient should always be offered ongoing follow-up to monitor progress during and after evaluation and treatment to ensure continuity of care in accordance with the DOD/VA Post Deployment Health Clinical Practice Guideline.

BLOOD DONATION

Service members who have been in areas such as Southwest Asia where leishmaniasis is endemic should be advised that they may not donate blood for one year after redeployment. Service members diagnosed with leishmaniasis may not donate blood for the rest of their lives.

LEISHMANIASIS: PREVENTIVE MEASURES

The best way to prevent leishmaniasis is to prevent sand fly bites by instructing service members to:

- Stay in air conditioned tents from dusk to dawn whenever possible
- Stay in well-screened tents if air conditioned tents are not available
- Wear long sleeved shirts, long pants, and socks when going outside. Tuck undershirts into pants and pants into boots. Insect repellent should be applied liberally on uncovered skin and under the ends of sleeves and pant legs. The military controlled-release lotion containing 33% DEET is effective for 4 to 12 hours depending on the climate. Repeat as directed.
- Clothing should be treated with permethrin-containing insecticides. The military IDA kit treats one uniform and lasts through approximately 50 washings. Uniforms treated with permethrin in an aerosol spray can must be retreated every 5 to 6 washings.
- If sleeping in areas without air-conditioning or adequate screening, use a fine mesh bed net (at least 18 holes per inch) if possible and tuck it under the mattress. The bed net should be soaked or sprayed with permethin since the sand flies are small enough to pass through the mesh.
- Avoid dogs or rodents near sleeping areas.

Where can I get more information?

Leishmania Treatment at Walter Reed Army Medical Center

LTC Glenn Wortmann, COL Naomi Aronson
Commercial: 202.782.1663/8695/8691
DSN: 662.663/8695/8691

Leishmania Treatment at Brooke Army Medical Center

LTC Duane Hospenthal, COL David Dooley, CPT Timothy Kaiser
Commercial: 210.916.5554/4355
DSN: 429.5554/4355

Walter Reed Army Institute of Research (WRAIR)

LTC Peter Weina at 301.319.9956 (telephone), 301.319.7360 (fax), or peter.weina@NA.AMEDD.ARMY.MIL (e-mail). He would prefer to be contacted through e-mail, if possible.

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http://www.pdhealth.mil/downloads/Leishmaniasis_DS_04272004.pdf

DoD Deployment Health Clinical Center at Walter Reed Army Medical Center

Phone: 866.559.1627 European Toll-Free Phone 0800.8666.8666 Internet URL: http://www.pdhealth.mil/

Center for Disease Control and Prevention's Leishmaniasis web page at:
http://www.cdc.gov/ncidod/dpd/parasites/leishmania/default/htm

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