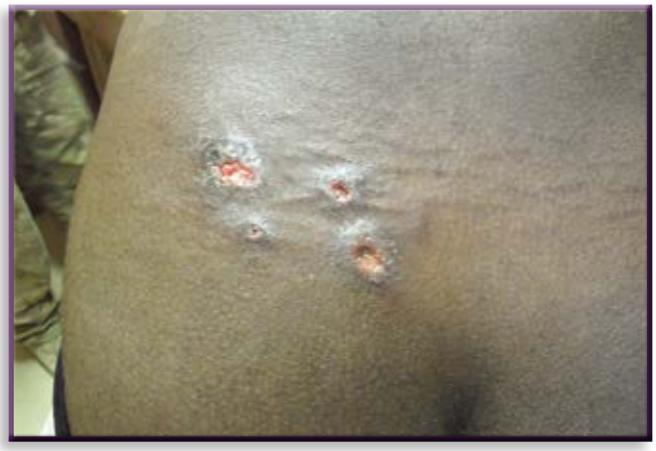
An Ongoing Series on Dermatological Issues of Importance to the Deployed Special Forces

Charles A. Sola, MD; Kristen L. Toren, MD

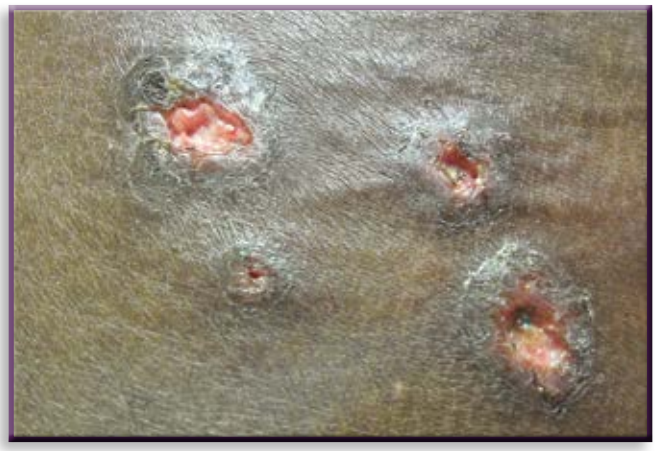
You are deployed with your unit to Afghanistan and your team has been traveling extensively around the country for several months. One of your men complains of a nontender crusted plaque that has developed on his right forearm, as well as four minimally puritic papules on his lower back. He does not recall any history of insect or arthropod bites and he denies any puncture injuries. He notes that the lesion on his arm was the first to appear and is in the same general location where he has had several bouts of cellulitis in the past. His past medical history is otherwise unremarkable. You treat him initially with hydrocortisone 1% cream for what you suspect are bug bite reactions. The patient returns for follow-up and notes that the lesion on the arm is not healing and that the ones on the lower back have now become larger nodules, although they remain relatively asymptomatic. You conduct a thorough examination and note that the lesions on his lower back are in fact larger and he has developed inguinal lymphadenopathy. You decide that the lesions are likely abscesses and choose to treat with a combination of incision and drainage and cefalexin and clindamycin antibiotic therapy. After completing the full course of antibiotics, the lesions fail to resolve, but the lymphadenopathy is no longer present. You prescribe a 10-day course of trimethoprim-sulfamethoxazole, and there is still no improvement. Approximately two months after the initial lesion was noticed, the lesions on his lower back have progressed as illustrated in Figures 1 and 2. The patient is reluctant to leave his unit because he is feeling well despite the presence of these lesions, so you take photographs of the lesions for a consult with the theater infectious disease and dermatology specialists.

Figure 1 Photograph of lesions on the left lower back.



Clinical photograph courtesy of MAJ Brad Starley

Figure 2 Detailed view of lesions on the left lower back.



Clinical photograph courtesy of MAJ Brad Starley

Using the primary lesion definitions outlined in your SOF medical handbook, how would you describe the morphology of these lesions?

What is the differential diagnosis of these lesions?

Morphology

The lesions shown are described as a grouping of four discrete, well-demarcated, annular ulcers (loss of epidermis and at least part of the dermis that results in scarring) with moist, yellow-pink bases and hyperpigmented hyperkeratotic scaly margins.[1]

Differential Diagnosis

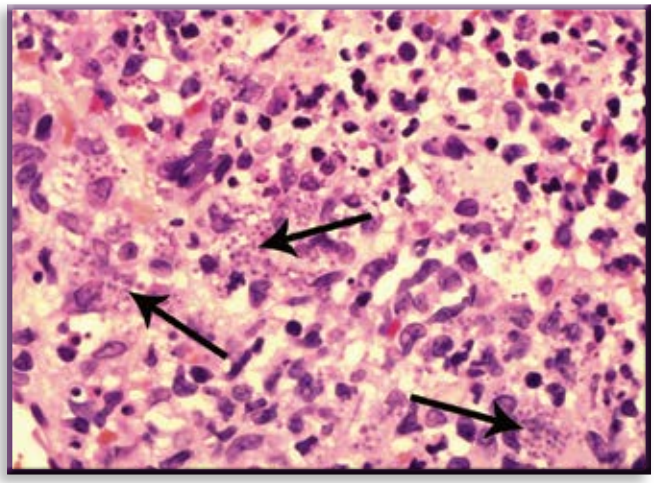
The differential diagnosis for the lesions shown is very broad and includes both infectious and noninfectious processes. Specific entities in this differential are insect bite reaction, furuncle, carbuncle, ecthyma, anthrax, orf,

milker's nodule, tularemia, swimming pool granuloma, tuberculosis cutis, syphilitic gumma, yaws, sporotrichosis, blastomycosis, dracunculosis, metastases, cutaneous lymphoma, and leukemia cutis.[2]

Course

The patient is transported to be seen by dermatology and infectious disease specialists in theater. They order a complete blood count (CBC), comprehensive metabolic panel (CMP), syphilis rapid plasma reagin (RPR), and HIV testing. Additionally, the dermatologist performs several punch biopsies from the edge of the ulcerations. The tissue is sent for hematoxylin and eosin (H&E) stain and mycobacterial, bacterial, fungal, and acid-fast bacillus (AFB) cultures. The CBC and CMP results are within normal limits, and the RPR and HIV results are negative. All cultures eventually return with no growth. The pathology report confirms leishmaniasis and indicates the presence of abundant *Leishmania* amastigotes within the dermis of the submitted sample (Figure 3).

Figure 3 *Leishmania* amastigotes within the cytoplasm of the cells (*black arrows*) (hematoxylin and eosin staining; ×100 original magnification).



Courtesy of LTC Michael Licata

Cutaneous Leishmaniasis

Etiology

The term "leishmaniasis" refers to a parasitic infection caused by the protozoan *Leishmania*. The parasite is dimorphic, with the stage depending on the current host. In mammalian reservoirs (primarily dogs and rodents), *Leishmania* exists in the nonflagellated, intracellular amastigote stage. Female sandflies of the genera *Phlebotomus* and *Lutzomyia* (Figure 4) serve as vectors, acquiring the parasite by ingesting the infected blood of a reservoir host. Once inside the sandfly, *Leishmania* transforms into the flagellated promastigote. The promastigotes are injected into a new host along with the sandfly's saliva during subsequent feedings.[3,4] Figure 5 is a graphic depiction of this process.

Figure 4 Photo is of single sandfly of unknown genus. Female *Phlebotomus* sandfly. From World Health Organization website: www.who.int/leishmaniasis/vector/en/index.html.

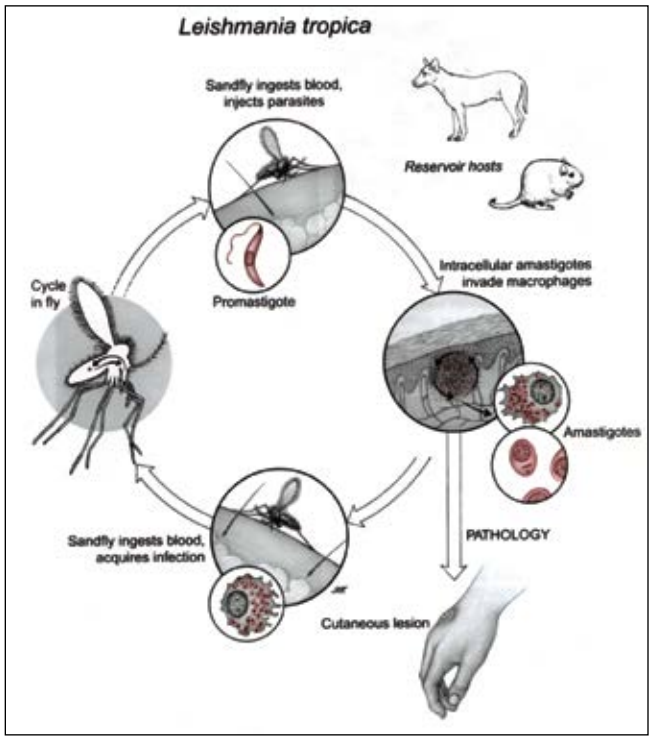
promastigotes are injected into a new host along with the sandfly's saliva during subsequent feedings.[3,4] Figure 5 is a graphic depiction of this process.

Of the more than 300 species of *Leishmania,* approximately 20 species are known to cause disease in humans. The disease is divided into three major clinical syndromes: cutaneous leishmaniasis (CL), in which the parasite replicates in the dermis; mucosal leishmaniasis (ML), in which it affects the mucosa of the nasooropharynx and rarely the eyes or genitalia; and visceral leishmaniasis (VL), in which it replicates in the reticuloendothelial system. Cutaneous leishmaniasis is further broken down into Old World cutaneous leishmaniasis (OWCL) and New World cutaneous leishmaniasis (NWCL), based on the geographical distribution. OWCL is found primarily in the Near East, Southwest Asia, Africa, the former USSR, and the Mediterranean rim.[2] NWCL is found primarily in the Western Hemisphere and is endemic in Mexico, Central America, Brazil, and Bolivia.[2]

Epidemiology

Worldwide, an estimated 1.5–2 million new cases of CL occur annually.[5] The disease is present in more than 80 countries and on every continent except Antarctica and Australia. Afghanistan, Iran, Saudi Arabia, Syria, Brazil, and Peru combine to account for more than 90% of CL cases.[3] Due to increased conflicts in these regions, CL is of significant concern to the military. Between 2001 and 2006, the Army Medical Surveillance Activity (AMSA) reported 1287 cases of leishmaniasis among

Figure 5 *Leishmania tropica* lifecycle. Illustration by John Karapelou, courtesy of www.microbeworld.org.



U.S. military personnel deployed in support of Operation Iraqi Freedom or Operation Enduring Freedom. Of those, two cases were VL and the remaining cases were CL. Of those infected, 96% were male, 96% were Army Servicemembers, 80% were on active duty, and 62% were under the age of 30. Geographically, 90.3% had served in Iraq, 5.1% had served in Afghanistan, and 4.6% had served in both countries.[6]

Clinical Presentation

The clinical presentation of CL is variable depending on the species of *Leishmania*. The incubation period is typically two to four weeks, but can be longer than one year. Initially, in the localized cutaneous form, an erythematous papule forms at the site of the sandfly bite. The lesion grows in size and begins to crust in the center. Eventually, an ulcerated nodule develops with raised borders. The lesions will continue to grow for several months and will persist for six months or longer. Multiple lesions, widespread involvement, lymphangitis, lymphadenopathy, and mucosal invasion are possible depending on the species.[2]

Diagnosis

The gold standard for diagnosing CL is detecting the parasite in either stained smears or tissue biopsy. Smear specimens can be obtained by injecting the margin of the lesion with sterile saline and aspirating the contents. The same procedure can be used to obtain fluid for culture in Nicolle-Novy-MacNeal (NMN) medium. NMN culture is time consuming and has a low sensitivity. Serologic tests are unreliable due to variable sensitivity and specificity.[7] Polymerase chain reaction is the most common method of species-specific diagnosis and is 100% sensitive and specific.[3,5] The Montenegro skin test (MST) is occasionally used for epidemiologic studies and vaccine trials.[7]

Treatment

Several treatment options exist for CL, including observation, topical treatment, heat therapy, oral chemotherapy, and parenteral chemotherapy. Indications for treatment of CL include those infections acquired in South or Central America, cosmetically or functionally important lesion location, nonhealing lesions (longer than six months), multiple lesions or large lesions (greater than 4–5cm in diameter), evidence of local dissemination of infection, and the immune status of the patient.[8]

Sodium stibogluconate (a pentavalent antimonial agent) is the standard therapy for CL. It is not licensed in the United States but is available from the Centers for Disease Control and Prevention as an investigational new drug (IND). For military personnel, the medication is available from the Walter Reed National Military Medical Center (301-295-4611) and the Brooke Army Medical Center (210-916-4141).[9] The dosing is 20mg/kg administered intravenously for 10–20 days, and allopurinol is occasionally used as an adjunct.[3,8] Alternative treatment regimens include intralesional injections of sodium stibogluconate, cryotherapy or thermotherapy, topical paromomycin, parenteral amphotericin B, parenteral pentamidine, oral mitefosine, oral ketoconazole, and oral fluconazole.

Lesions should show decreased inflammation and a two-thirds reduction in size by six weeks after therapy. If no improvement is observed after six to eight weeks, an alternative therapy should be considered. Relapses are possible, and the patient should follow up at six-month intervals for one year.[8] Scarring, as well as hypopgimentation or hyperpigmentation, is common.

Prevention

The Department of Defense is currently taking measures to decrease the risk for CL among U.S. military personnel in Southwest and Central Asia. Some of these measures include improving the living conditions of deployed personnel, heightening awareness of leishmaniasis among personnel deployed in endemic areas, emphasizing the importance of using personal protective measures (permethrin-treated clothing, bed nets, insect

repellent containing 30%–35% DEET), and enhancing vector control activities.[10] Through the implementation of these measures, the hope is that fewer Soldiers will return from deployment with cutaneous leishmaniasis.

References

1. Schissel, D. (2008). Skin: Introduction to Dermatology. In Special Operations Forces Medical Handbook (2nd ed.). Washington, DC, U.S. Government Printing Office, Part 4, Chapter 6, pp. 4–39–4–40.
2. Fitzpatrick, T., Johnson, R., Wolff, K., Suurmound, D. (2001). Color Atlas & Synopsis of Clinical Dermatology (4th ed.). New York, McGraw-Hill, pp. 851–857.
3. Machado-Pinto, J., Azulay, R. (2006). Leishmaniasis. In Tropical Dermatology. Philadelphia, Elsevier, Chapter 5, pp. 41–48.
4. Despommier, D., Gwadz, R., Hotez, P., Knirsch. (2000). Introduction to the Leishmania & cutaneous leishmaniasis: Leishmania major Leishmania tropica Leishmania Mexicana. *Parasitic Diseases* (4th ed.). New York, Apple Trees Productions, Chapter 4, pp. 13–22.
5. Pavil, A., Maltezou, H. (2010). Leishmaniasis, an emerging infection in travelers. *International Journal of Infectious Disease*. 14:e1032–e1039.
6. Army Medical Surveillance Activity. (2007). Leishmaniasis in relation to service in Iraq/Afghanistan, U.S. Armed Forces, 2001–2006. *Medical Surveillance Monthly Report*. 14(1):2–4.
7. Reithinger, R., Dujardin, J. (2007). Molecular diagnosis of Leishmaniasis: Current status and future applications. *Journal of Clinical Microbiology*. 5(1):21–25.
8. Murray, H. (2012). Review: Leishmaniasis in the United States: Treatment in 2012. *American Journal of Tropical Medicine and Hygiene*. 86(3):434–440.
9. Leder, K., Weller, P. (2009, Dec. 22). Treatment and prevention of cutaneous leishmaniasis. Retrieved September 26, 2012, from UpToDate website. Website: (http://www.uptodate.com/contents/treatment-and-prevention-of-cutaneous-leishmaniasis?source=search_result&search=leishmaniasis&selectedTitle=3%7E70).
10. Centers for Disease Control and Prevention. Parasites—Leishmaniasis. Retrieved September 28, 2012, from CDC website. Website: (http://www.cdc.gov/parasites/leishmaniasis/).

LT Charles Anthony Sola is a 2008 graduate of the Uniformed Services University of the Health Sciences. He completed a transitional internship at Naval Medical Center San Diego in 2009. In 2010, he completed his training and certification as an Undersea and Diving Medical Officer. He then served two years at the Naval Health Clinic Charleston. Currently he serves at Naval Special Warfare Group 4.

Dr. Kristen Toren is a board-certified dermatologist and an Active Duty servicemember in the United States Army. She attended Emory University School of Medicine. She then completed a transitional internship at Tripler Army Medical Center in Honolulu, Hawaii, and her residency in dermatology at Walter Reed Army Medical Center, Washington, DC. She is currently deployed as the Operation ENDURING FREEDOM Theater Consultant for Dermatology and, when at her permanent duty station, serves as the Chief of Dermatology at McDonald Army Health Center, Fort Eustis, Virginia. Dr. Toren has published multiple scientific articles in peer-reviewed journals and has presented at both national and international professional meetings. Her current research interests include the use of simulation in dermatologic surgery.