Watch for Cutaneous Leishmaniasis in Soldiers

Symptoms can take 4-6 months to appear, so soldiers may return from Iraq with dormant infection.

BY DAMIAN McNAMARA
Miami Bureau

MIAMI BEACH — Some American soldiers are returning from Iraq with a dormant pathogen in tow: cutaneous leishmaniasis. Symptoms of the infection can take 4-6 months to appear after a bite from an infected sand fly, and some unknowingly infected military personnel return to their communities before the lesions develop. This puts community dermatologists in the position of having to treat this tropical infection.

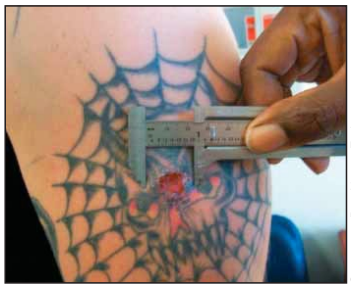
There is a seasonal variance to this protozoan parasitic infection that corresponds with the activity of sand flies in the Middle East. During the 2003-2004 season, localized cutaneous leishmaniasis was frequently diagnosed in U.S. military personnel, with most infections caused by *Leishmania major*, according to a presentation at the annual meeting of the American Society of Tropical Medicine and Hygiene.

There have been more than 500 reported cases since January 2003 among soldiers from Operation Enduring Freedom and Operation Iraqi Freedom, according to U.S. Army medical research data.

Experience with 300 soldiers treated at Walter Reed Army Medical Center in Washington demonstrates that there are multiple presentations for localized cutaneous leishmaniasis. Of the infected patients, 98% were male, 96% were in the U.S. Army, and 91% were enlisted personnel. Almost three-quarters (73%) were white; 16% were African American, 6% were Hispanic, and 5% were from other ethnic groups.

"Patients with lighter skin were overrepresented in our cohort," said Naomi E. Aronson, M.D., professor of medicine and director of the infectious diseases division, Uniformed Services University of the Health Sciences, Bethesda, Md.

Cutaneous leishmaniasis manifests after the multiplication of the organism in phagocytes in the skin. The mean number of skin lesions per patient was 3, and the range was 1-47. The mean time between appearance of a lesion and initiation of treatment was 13 weeks.



COURTESY DR. NAOMI E. ARONSON

Soldiers may get bitten on exposed tattoos, Dr. Naomi E. Aronson said.

Papules often appear first, followed by ulcerative lesions. Lesions commonly appear in pairs. Nodules are uncommon in leishmaniasis. A rare presentation is a large psoriasiform-type plaque containing several small lesions. "I've seen about 10 cases of this form," Dr. Aronson said. Facial lesions, including those on the lips or pinna of the ear, tend to be more inflammatory, Dr. Aronson commented.

Leishmaniasis lesions do not typically feature purulent drainage; if the lesion is tender with pus, it is likely a bacterial superinfection, Dr. Aronson explained. Both the lesions and the resultant bacterial infection may require concurrent treatment courses.

Sand flies are attracted to bright colors, so soldiers are sometimes bitten on exposed tattoos, she said. "A common complaint in our clinic is 'the sand fly messed up my tattoo.' " The cutaneous form of the disease is ultimately self-healing, although disfiguring scars can remain. The visceral and mucosal forms of leishmaniasis are often more serious and sometimes fatal. Educate patients that not all treatments are 100% effective, Dr. Aronson suggested. "It is important to give patients realistic expectations that leishmaniasis may not be gone, but it should improve."

There are no leishmaniasis treatments that have been approved by the Food and Drug Administration. Topical treatments include heat therapy and cryotherapy. Some lesions will respond to treatment with ThermoMed (Thermosurgery Technologies, Inc.) but others only partially respond, Dr. Aronson reported. A clinical trial investigating the technology is underway at Walter Reed Army Medical Center. Cryotherapy with liquid nitrogen is another treatment strategy.

Standard therapy for all forms of the disease is pentavalent antimony of sodium stibogluconate (Pentostam, GlaxoSmithKline) or meglumine antimonate (Glucantime, Aventis). The usual parenteral regimen of sodium stibogluconate, for example, is 20 mg/kg per day for 20 days.

Pentavalent antimonials are available only through an Investigational New Drug (IND) protocol from the Centers for Disease Control and Prevention. Investigational agents require a lot of paperwork—and institutional review board approval—before they are available for use, Kenneth R. Dardick, M.D., said during a separate presentation at the meeting. Pharmacists need to be educated about storage requirements and nurses instructed to handle the agents as they would a chemotherapy drug. Informed consent is required from patients.

It is possible that physicians working in a community hospital will see only one or two cases of this rare disease. Physicians unfamiliar with use of pentavalent antimonials should consult military and/or CDC infectious disease experts, suggested Dr. Dardick, a family physician at Mansfield Family Practice, Windham Hospital, Storrs, Conn.

The IND requirements "can be novel for a community hospital," Dr. Dardick added. "But cutaneous leishmaniasis can be successfully diagnosed and treated in a community hospital with appropriate index of suspicion." ■

Lack of Penicillin Allergy Skin Test Antigen Poses a Problem in Many Clinical Settings

BY KATE JOHNSON
Montreal Bureau

Skin testing for penicillin allergy has ground to a halt because the most important antigen that is used in the test has been pulled off the market, creating costly problems that have far-reaching impact, according to Steven Grabiec, M.D.

"We are left with a situation where we can't skin test for penicillin adequately because we don't have one of the major antigens we need. If you can't prove a patient is not allergic, you are either obligated to give them a nonpenicillin drug, or you must go through the process of desensitizing them—both options being more costly than simply giving them penicillin," said Dr. Grabiec, who is a clinical associate professor of pediatrics at the State University of New York at Buffalo.

With a complete panel of skin test reagents, more than 90% of patients who report a history of penicillin allergy could be declared nonallergic.

About 10% of the U.S. population reports a history of penicillin allergy, but if they could be tested with a complete panel of penicillin skin test reagents, more than 90% of them could be declared nonallergic, according to the American Academy of Allergy, Asthma, and Immunology.

The main antigen that is used in penicillin skin testing, benzylpenicilloyl polylysine (commonly known as Pre-Pen) is being phased out by the manufacturer. The orphan drug application for another antigen, penicillin minor determinant mixture (MDM), has been on file with the Food and Drug Administration since 1987, Eric Macy, M.D., chair of the AAAAI Committee on Adverse Reactions to Drugs and Biologicals, explained in a written statement (www.aaaai.org/members/academynews/2004/07/penicillin.stm).

The supply of Pre-Pen worldwide ran out in August 2004 when the most recent batch expired. As a result, "the AAAAI has become involved because the free market system in the United States has not worked to fill this critical need," the statement said.

The AAAAI is working to find a manufacturer for the complete set of penicillin skin-testing reagents. "Ideally both materials would be sold together as a single penicillin allergy skin test reagent set," according to the statement.

"Penicillin as an antibiotic has a lot of indications, and removing that from consideration increases the cost of medicine. This is a serious situation, not just for allergists, but for the medical community in general," Dr. Grabiec said in an interview.

"If a complete set of commercial, FDA-approved, penicillin skin test materials were available, allergist-immunologists would be able to safely skin test a much higher fraction of the 10% of the population that carries a history of penicillin allergy," Dr. Macy said.

"This would help promote the more appropriate use of antibiotics and avoid some of the development of antibiotic resistance driven by inappropriate avoidance of penicillins," he added in the statement. ■

Unvaccinated Teen With Rabies Lives

A teenaged girl who contracted rabies from a bat and received experimental therapy recovered and was discharged from the Children's Hospital of Wisconsin (Wauwatosa).

The girl is the first known person to survive rabies without receiving a vaccine. The bat bit the girl on Sept. 12, 2004. She reportedly thought that the bite was just a scratch, and she and those with her assumed, incorrectly, that only healthy bats could fly, so she did not see a doctor for a vaccine.

She presented to Children's Hospital on Oct. 18 with symptoms of rabies, including slurred speech and fluctuating consciousness. The doctors induced a temporary coma and treated her with antiviral drugs to boost her immune system and allow her natural immunity to fight the virus. The details of the treatment were being kept under wraps while the doctors prepared to publish their account of the case.

The girl was discharged in early January, according to a hospital press statement. Although her physicians declared her medically sound, she will continue therapy to refine her speech and regain strength.

A rabies vaccine prevent the disease if given within days of exposure, but is useless in saving the patient's life in advanced cases.

—Heidi Splete