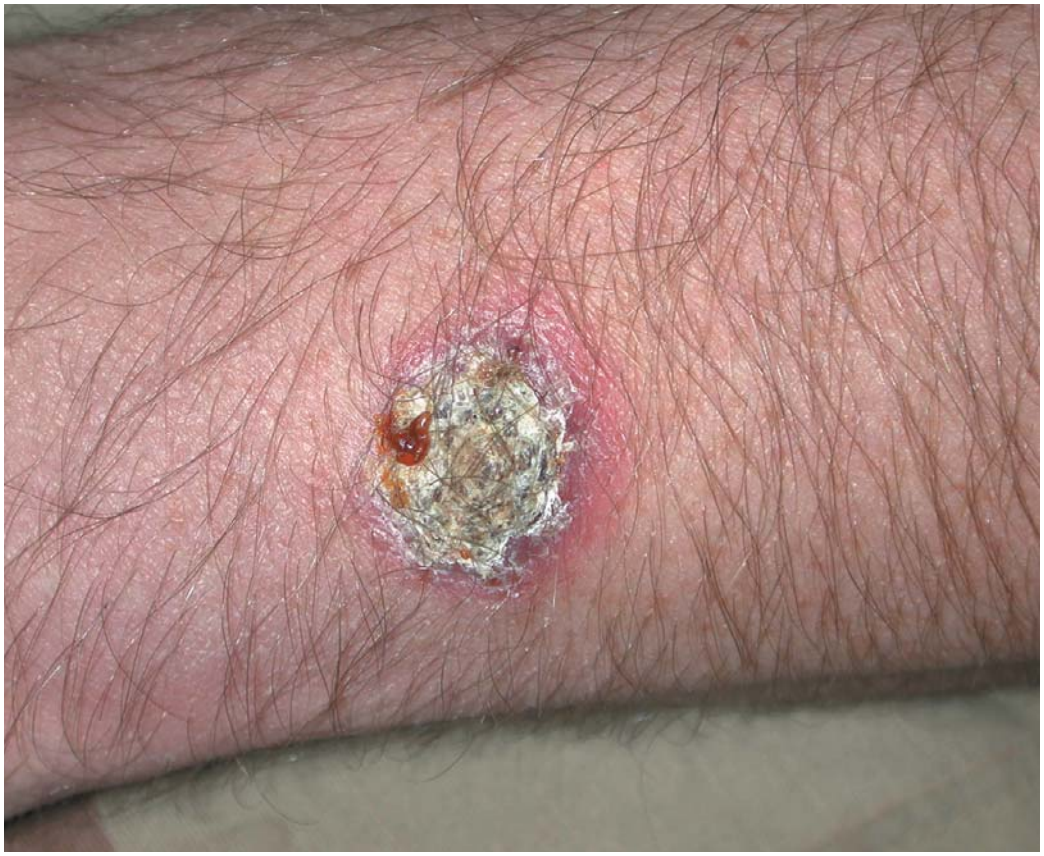
What Is Your Diagnosis?



A 21-year-old man presented with a 2-month history of a nonhealing lesion on his left forearm. Results of a physical examination revealed a 2-cm erythematous plaque with central crusting and a small area of ulceration.

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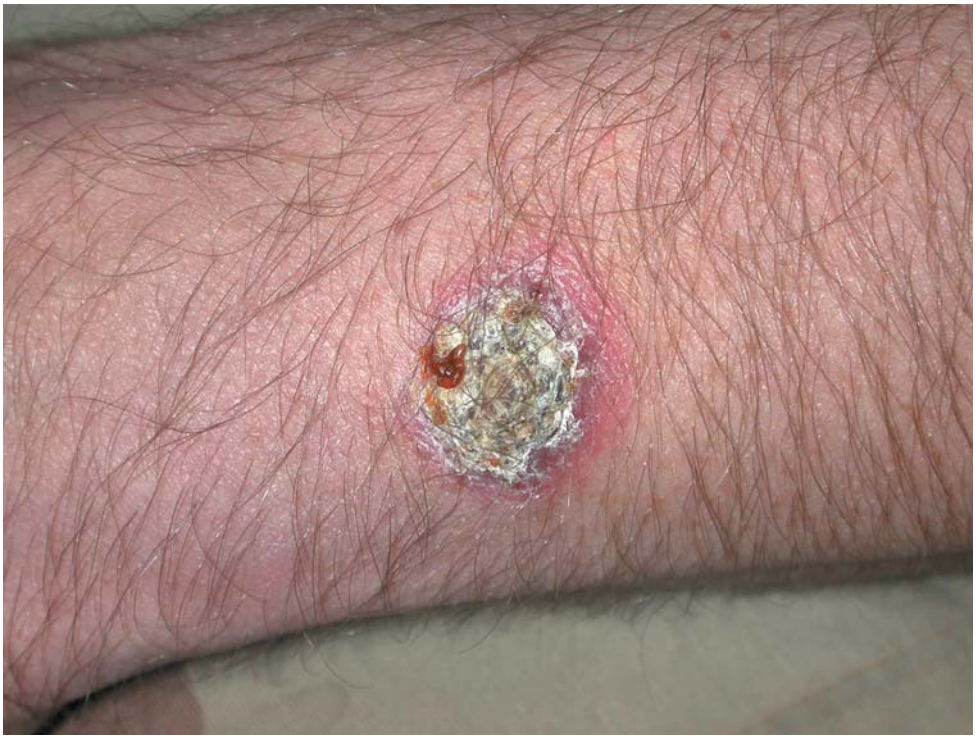
The authors report no conflict of interest.

The Diagnosis: Cutaneous Leishmaniasis



The *Leishmania* parasite can cause multiple clinical diseases in humans. These include cutaneous leishmaniasis (CL), mucocutaneous leishmaniasis, and visceral leishmaniasis or kala azar.

CL is endemic in 88 countries located in the tropics, subtropics, and southern Europe. There are an estimated 12 million cases worldwide with 1 to 1.5 million cases of CL reported yearly. A sharp increase in recorded cases has been reported over the last 10 years.[1]

The arthropod vectors of all forms of leishmaniasis are female sand flies. They are small, hairy, mosquitolike insects 1.5 to 4 mm in length. Their small size allows them to pass through ordinary mesh screens and mosquito netting. Sand flies are widely found throughout the tropics and subtropics in a variety of habitats, including deserts, rain forests, and highlands. The disease is transmitted in the Old World by flies of the genus *Phlebotomus* and in the New World by the genus *Lutzomyia*.

The cutaneous afflictions of leishmaniasis have been known since antiquity. Descriptions of the cutaneous disease in the Old World are found from the first century AD. Illustrations on New World pottery from Peru and Ecuador dating from 400 to 900 AD show faces afflicted with lesions consistent with leishmaniasis.

CL can be divided into *Old World* and *New World* forms. Old World CL (also known as Aleppo, Baghdad, or Delhi boil; Kandahar, Lahore, or Oriental sore; and Biskra button) is found in widely scattered parts of Asia, Africa, and Europe and in much of the Middle East, especially in the Jordan Valley, Sinai Peninsula, Iran, Iraq, and eastern Saudi Arabia. Old World CL is caused by several *Leishmania* species, including *Leishmania major*, *Leishmania tropica*, and *Leishmania infantum*. The progression of the disease is similar for these species. The first sign is a small erythematous papule that may appear immediately following a bite from a sand fly but usually appears 2 to 4 weeks later. The papule slowly enlarges over a period of several weeks and assumes a more dusky violaceous hue. The lesion eventually becomes crusted in the center. When the crust is removed, there is a shallow ulcer, often with a raised and indurated border. The ulcer is typically painless. After approximately 2 months, the peripheral spreading stops, and the

ulcerated nodule remains the same size for another 3 to 6 months. The lesion will then heal leaving a slightly depressed scar. In some cases there may be multiple lesions where multiple sand fly bites have occurred.

New World CL (also known as chiclero ulcer, uta, pian bois, and bay sore) is found as far north as Texas and as far south as Brazil, including Mexico and Central America. The disease progression is similar to that of Old World CL. Although the lesions can develop on any part of the body, in Mexico and Central America, sores characteristically involve the pinna of the ears. This is the classic chiclero ulcer.[2,3]

The key to diagnosis of CL is awareness of military and travel histories. A significant portion of the American military service in the Middle East consists of reservists. These are patients who will subsequently return to the United States and receive their healthcare from civilian physicians. In general, people also are taking more adventurous journeys to countries where CL is endemic. It is imperative for physicians to have a high index of suspicion in patients who have had significant exposure and are at risk.

The laboratory diagnosis of CL is challenging for several reasons. First, CL lesions have a very low parasitic burden. Second, histopathologists in nonendemic countries are relatively inexperienced with CL. The 3 traditional diagnostic techniques include microscopic examination of a Giemsa-stained smear from the ulcer border or from a biopsy specimen, culture from the ulcer aspirate or skin biopsy specimen (takes approximately 4 weeks), and histopathologic examination of a biopsy specimen taken from the border zone of the ulcer or nodule. Polymerase chain reaction testing on aspirate fluid or biopsy specimens has been studied in multiple clinics around the world and has been shown to be the single most reliable test.[4] Experienced histopathologists in a tropical dermatology center compared polymerase chain reaction with the combined results from the 3 traditional diagnostic techniques and found no significant difference in sensitivity. However, polymerase chain reaction has the highest sensitivity when used as a single diagnostic procedure.[5] In our patient, the diagnosis was made by histopathologic examination of a shave biopsy specimen taken from the border of the plaque.

Physicians have used many treatments for CL including physical methods of cryotherapy, heat therapy, and photodynamic therapy. Also, topical formulations of ointment containing 15% paromomycin (an aminoglycoside); intralesional infiltration with pentavalent antimony; and multiple oral medications including fluconazole, amphotericin B, and allopurinol have been used. Fluconazole 200 mg/d for 6 weeks showed promising results against *L major* (Old World CL). Healing of lesions was complete for 79% of patients (63/80) at the 3-month follow-up in the treatment group but only for 34% of patients (22/65) in the placebo group.[6] Photodynamic therapy has shown promising results but has only been used in small studies.[7]

Since 1978, military personnel with potential cases of CL have been referred to Walter Reed Army Medical Center (WRAMC) for evaluation and therapy with the pentavalent antimonial compound sodium stibogluconate BP. Although treatment of cases of CL with pentavalent antimonial compounds has been considered the standard of care for over half a century, they are still not licensed for use in the United States. WRAMC treats patients with sodium stibogluconate BP under Investigational New Drug (IND) protocols that the Surgeon General of the Army holds with the US Food and Drug Administration (FDA).[8] Currently, every patient diagnosed with CL at Landstuhl Regional Medical Center in Germany, including our patient, is sent to WRAMC for treatment using the sodium stibogluconate BP IND protocol. The US Centers for Disease Control and Prevention has a separate IND protocol with the FDA for providing this drug to civilians.

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