Am. J. Trop. Med. Hyg., 57(3), 1997, pp. 309–312
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TREATMENT OF CUTANEOUS LEISHMANIASIS WITH LOCALIZED CURRENT FIELD (RADIO FREQUENCY) IN TABASCO, MEXICO

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Abstract. In Mexico cutaneous leishmaniasis (CL) occurs in 17 of 32 States, and is a serious public health problem. This is a report of treatment of CL patients in the State of Tabasco, Mexico with a localized current field-radio frequency (LCF-RF) device to generate precisely controlled heat as an alternative to prohibitively expensive drug treatment. It was not a controlled clinical trial, but rather an evaluation of the feasibility of this form of treatment for all CL patients encountered in the endemic area. A total of 201 previously diagnosed patients with CL caused by *Leishmania mexicana* were treated with a portable Thermosurgery® LCF-RF generator powered by rechargeable batteries. The ages of the patients ranged from two to 75 years; the sex distribution was 63% males and 37% females. A single device was used in five different municipalities. Lesions were first anesthetized with 1% lidocaine HCl and moistened with normal saline solution. Treatment consisted of a single application that produced 50°C for 30 sec. After four weeks, 122 patients were available for evaluation, of which 95% were totally cured; (even those involving ear cartilage, which respond poorly to antimonials). At eight weeks post-treatment, 191 patients were evaluated, with a total cure rate of 90%. This form of treatment proved to be effective and convenient for use in primary health care facilities in Mexico and has many advantages over traditional forms of therapy.

In Mexico, cutaneous leishmaniasis (CL) occurs in 17 of the 32 states, and in some regions constitutes a serious public health concern with an ever growing number of cases.[1,2] In this situation, treatment has become an increasingly more difficult problem. Pentavalent antimonial compounds, the traditional treatment, and that recommended by the World Health Organization,[3] are so expensive for large numbers of patients that they often exceed the total normal state budget for primary health care facilities. Additionally, the required series of daily injections is inconvenient for the patients and results in a workload that often overwhelms the capabilities of medical facilities. As a consequence, a search for an alternative effective treatment has become a high priority for authorities responsible for health care.[1]

A treatment for CL that uses a localized current field-radio frequency (LCF-RF) device to generate precisely controlled heat beneath the surface of the skin has been approved by the U.S. Food and Drug Administration. This is a patented device based upon technology originally developed at the U.S. Department of Energy National Laboratory (Los Alamos, NM), which delivers precisely controlled localized current field (LCF) heat, generated by radio frequency (RF) energy, making it possible to destroy disease agents and diseased tissue with pinpoint accuracy, while leaving healthy tissue virtually undamaged. The device directs a high-frequency current to a dual-electrode surface probe, or applicator, which is placed in contact with the skin. Due to tissue resistance to current flow, excitation of the molecules in the tissue between the probes creates heat. The stainless steel probes are not heated to transfer the heat to the skin, but the heat is generated within the tissue itself within a range of 42–52°C. One of the arms of the probe contains a thermocouple device that continuously monitors the temperature of the treatment site and controls the electrical circuitry that generates the radio frequency field to maintain the selected temperature with an accuracy of ± 0.25°C.

This treatment has previously been shown to be at least as effective as pentavalent antimonial compounds in a double-blind, placebo-controlled trial in Guatemala.[4] This modality has the advantage of greatly reduced cost and of being effective with a single application in the great majority of cases. Initial trials of the device in Mexico have shown promising results, but the feasibility of this type of treatment for use in primary health care facilities or regional hospitals is unknown. The reliability of the device in the hands of many different physicians treating large numbers of patients, under often difficult conditions, had to be determined before it could be adopted for general use and this was the objective of the present study.

This is a report of treatment of CL patients in the State of Tabasco, Mexico with an LCF-RF device similar to that used in Guatemala, but with some improvements. This study was not designed to be a controlled clinical trial, but rather an evaluation of the feasibility of this form of treatment for all patients with localized cutaneous leishmaniasis (LCL) presenting to primary care facilities and a regional hospital in the endemic area.

PATIENTS, MATERIALS, AND METHODS

Study zone. La Chontalpa is a large area situated in the northeast part of the State of Tabasco at altitudes between 0 and 25 meters above sea level, and is divided into seven municipalities. The climate is classified as tropical wet savannah [5] with a median annual temperature of 26°C, varying from 40°C for the major season of the year to 20°C in December and January, with an annual precipitation of approximately 1,600 mm.[6] In this region, the prevalence of CL caused by *Leishmania mexicana* is the highest in the country due to the intimate location of habitations close to, or within, the cacao plantations which form a virtual domestic forest of cacao trees (*Theobroma cocoa*) where the vectors and reservoirs thrive, although their specific identity is not yet known.

Patients. A total of 201 patients from five health jurisdictions with CL lesions caused by *L. mexicana* were treated.

TABLE 1
Sex distribution and time of evolution of lesions treated

Time	Male	Female	No. (%)
<1 month	16	9	25 (12.43%)
2–5 months	48	33	81 (40.29%)
6–11 months	27	14	41 (20.40%)
1–2 years	24	13	37 (18.40%)
3 or more years	3	4	7 (3.48%)
Not specified	8	2	10 (4.97%)
Total	126	75	201 (100%)

TABLE 2
Location of lesions treated by localized current field (radio frequency)

Site of lesion	Male	Female	No. (%)
Ear	19	4	23 (11.0%)
Neck	4	1	5 (2.3%)
Face	16	13	29 (13.6%)
Trunk	11	4	15 (7.0%)
Upper extremities	57	27	84 (39.4%)
Lower extremities	13	26	39 (18.3%)
Mixed	4	0	4 (1.9%)
Not specified	2	0	2 (0.9%)
Total	126	75	201 (100%)

Diffuse cutaneous leishmaniasis (DCL) cases were not included. The sex distribution was 175 males (63%) and 75 females (37%). Ages ranged from two to 75 years and the time of evolution of lesions ranged from less than one month to three or more years (Table 1). Lesions were located in diverse sites, but the majority (41.8%) were on the upper extremities (Table 2). It is of interest that 23 (11%) involved cartilage of the ear (chiclero ulcer), which is very difficult to treat with drugs. Although a few patients had previously received treatment with pentavalent antimonial compounds, none had been treated within 60 days of LCF-RF treatment. Cultures were inoculated with aspirates from lesions of 23 patients, of which 18 resulted in successful isolation of the parasites. All isolates were identified as *L. mexicana,* although some differences between proteins of cell membranes were detectable by Western blots between LCL and DCL parasites, suggesting that some taxonomic differences exist (Arguello C, Lira R, Cervantes C, Centro de Investigacion y Estudios Avanzados, Mexico DF, unpublished data).

Ethical review for the project was accomplished by the established procedure in the office of the Director General of Health. All treatments were elective and patients were made aware of the procedure and its consequences.

Treatment. A single portable Thermosurgery™ LCF-RF generator (Thermosurgery Technologies, Inc., Phoenix, AZ) powered by rechargeable batteries was used in a regional hospital and in health care centers in five health jurisdictions to treat previously diagnosed patients. The treatments were carried out in a total of five sessions conducted between April 23 and May 20, 1994, with the device being transported between the various treatment facilities by automobile. Because a temperature of 50°C is painful, lesions were first anesthetized with 1% lidocaine HCl and moistened with normal saline solution. A single treatment at 50°C for 30 sec was administered. Since heat is completely localized and produced only between the two electrodes of the applicator (an area approximately 3 × 4 mm), repeated applications were necessary in each treatment to ensure complete coverage of the entire lesion. Those cases in which incomplete healing was observed or suspected were given a second treatment. A total of 11 patients received the additional treatment.

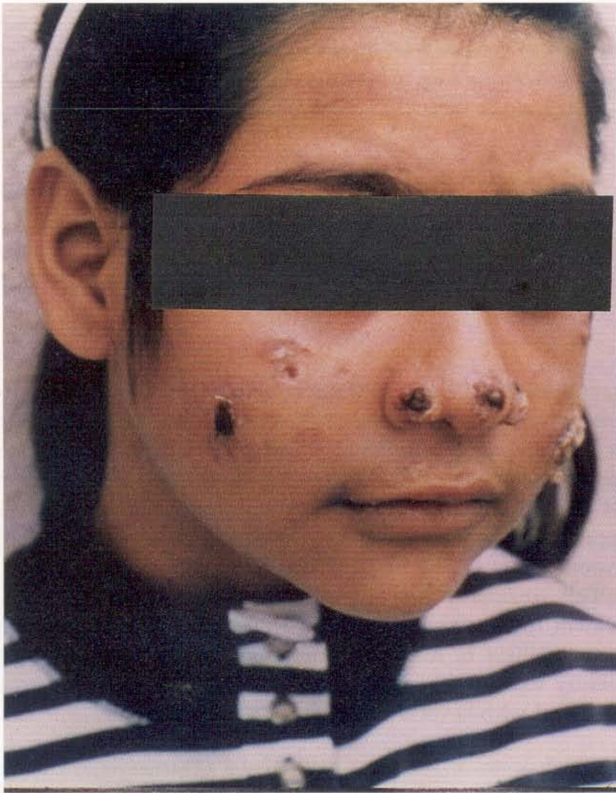
RESULTS

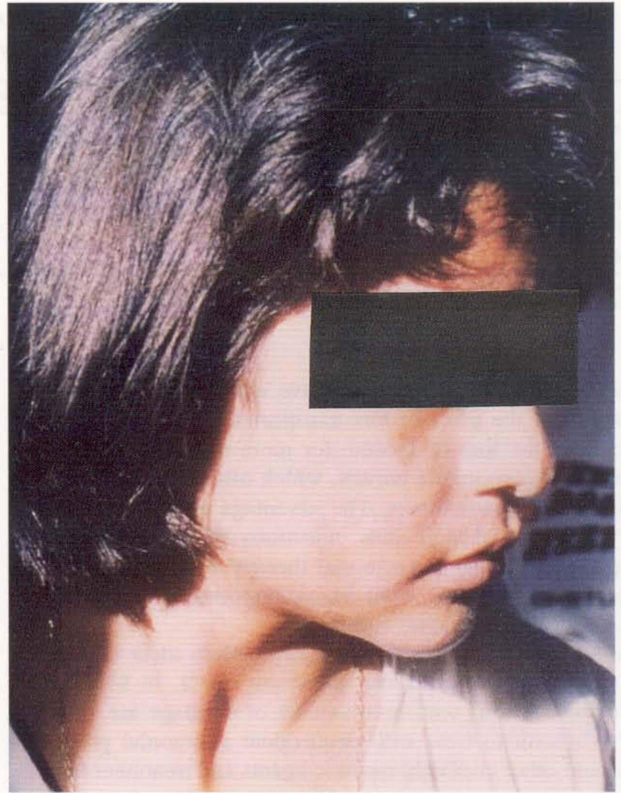
After four weeks, 122 patients were available for evaluation; of these, 95% of the LCL lesions were totally cured. No significant adverse collateral effects were observed. Intensive efforts resulted in locating 191 patients eight or more weeks post-treatment for final photographs and evaluation. Of the 11 patients who showed a poor response upon initial evaluation and received a second treatment, only three resulted in complete cure. Of the eight treatment failures, five had lesions in the form of multiple plaques > 10 cm in diameter and two of these evolved into DCL. The other three failures were patients with multiple nodular lesions, all of which also evolved into DCL.

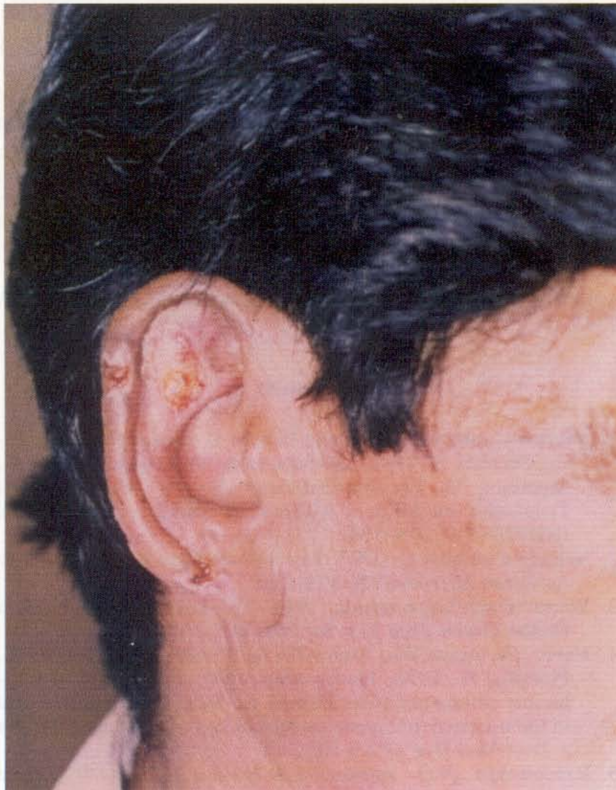
One to five patients were lost to follow-up in four of the five treatment localities (Table 3). Of the 191 patients observed after eight or more weeks, all but 10 had complete healing as judged by repithelization and lack of induration and discoloration (Figure 1). This corresponds to a cure rate of 90% (Table 3). However, reliable information was received from several other patients, which indicated that the patients who never returned for follow-up and were not observed had not returned because their lesions were completely cured. Assuming that this information is correct, and all those who did not return had healed lesions, the cure rate would be 95%. It is of special interest that all of the chiclero ulcers were observed to be healed, including some with very extensive involvement of cartilage. Several ear lesions were seen four weeks post-treatment, and these had responded even more rapidly than the strictly cutaneous lesions (Figure 2).

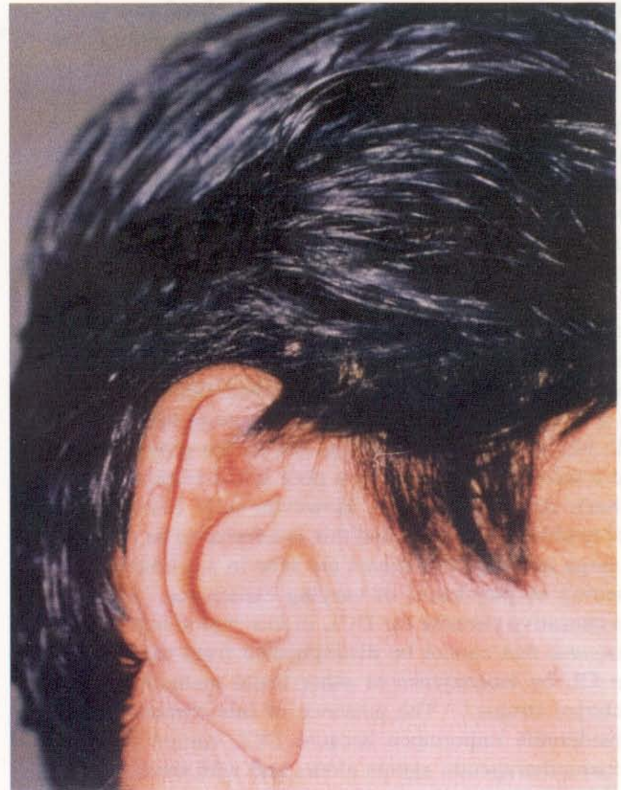
DISCUSSION

It is a commonly held belief that CL caused by *L. mexicana* spontaneously heals in a few months, and this belief has been perpetuated by repetition in the literature. In the past, this belief has often been the basis for a policy of nontreatment with toxic (and expensive) antimonial preparations, which were considered to be inappropriate because the disease is not life-threatening. Although self-healing undoubtedly occurs in a small proportion of lesions, observations in Mexico over more than 40 years with hundreds of cases of CL with this etiology indicate that this is not the rule. (Velasco O, INDRE, Colonia Santo Tomas, Mexico DF, unpublished data) This is seen particularly in persons who accept the infection as a natural event and allow the lesions to heal spontaneously. Although small ulcerations tend to heal spontaneously in less than two years, the same is not true of large ulcerations or nodular or vegetative lesions, and particularly with lesions of any type involving cartilage, which tend to become chronic and mutilating. It is not rare to encounter mutilations of the pinna with active leishmaniasis and a history of 40 years of evolution. Nontreatment can no longer be considered an acceptable option for CL.









FIGURES 1 AND 2. **1 (top left)**, multiple facial lesions that had not resolved after treatment with pentavalent antimonial; **(top right)**, same patient eight weeks after a single localized current field (radio frequency) treatment. **2 (bottom left)**, chiclero ulcer with extensive involvement of cartilage; **(bottom right)**, same patient four weeks after a single localized current field (radio frequency) treatment.

TABLE 3
Results of localized current field (radio frequency) treatment of cutaneous leishmaniasis patients

Locality	Treated	Cured	Lost to follow-up	Not cured	% cured*	% cured†
Jalpa de Mendez	8	7	1	0	87.5	100
Huimananguillo	20	18	0	2	90.0	90.0
Cunduacan	63	59	2	2	93.6	96.8
Comalcalco	34	29	2	3	85.2	91.2
Cardenas	76	68	5	3	89.4	93.4
Total	201	181	10	10	90.0	95.0

* Based upon observed healing 20 or more weeks post treatment.
† Assuming all patients not returning for follow-up were cured.

The great majority of patients have very limited financial resources and the price of bus transportation to a treatment facility plus the loss of income for more than a week constitutes an unsupportable burden, which often causes the patient to opt for nontreatment. The advantage of a single treatment over the repeated daily injections for long periods, which is required with traditional therapy with pentavalent antimonial compounds, is of major importance to the patients, as well as to health authorities.

The surprisingly rapid response of chiclero ulcer was an unexpected bonus to LCF-RF treatment of CL in Mexico. Leishmanial lesions with involvement of cartilage are notoriously difficult to treat with pentavalent antimonial preparations and other chemotherapeutic agents and treatment failure is frequently encountered with chiclero ulcer. It is presumed that the poor response is due to lack of vascularity in cartilage, which prevents delivery of effective drug concentrations to the amastigotes. In contrast, LCF-RF often appears to be even more effective in chiclero ulcer than in CL in other anatomic locations. Complete healing was seen in as little as two weeks in some cases. Since involvement of cartilage of the pinna of the ear in a relatively large proportion of cases is a feature of CL in Mexico, this advantage is of major significance, although the reason for it is unexplained at this time.

It is of interest that the greatest prevalence of DCL in Mexico, and possibly in the hemisphere, also occurs here (Velasco C, Instituto Nacional de Diagnostico y Recursos Epidemiologica, Mexico DF, unpublished data). In retrospect, a review of the patient forms suggests that most, if not all, of the eight treatment failures in the group that received a second treatment after a poor initial response might have been classified as DCL. However, early cases are not always readily recognized, and this is a factor to be expected when large numbers of patients are seen in a primary health care setting by physicians of varying experience.

The causative parasite for DCL in this region is a form of *L. mexicana* that cannot be distinguished from that causing simple CL by isoenzymes or other usual methods used to characterize strains.[1,2] The presence of this clinical form is of considerable importance because DCL cannot be cured with chemotherapeutic agents alone, and with these patients the lesions could be expected to eventually evolve into disseminated disease after the initial favorable response to antimonials. However, DCL responds well to heat and complete cures with adjunct local heat delivered by electric heating pads have been reported in patients from the Dominican Republic[7] and Tabasco, Mexico. (Neva FA, National Institutes of Health, Bethesda, MD, unpublished data). The use of LCF hyperthermia could possibly be a better means for initial treatment of early small lesions that are incipient DCL. However, these data also show that a more aggressive approach is needed for more advanced lesions if LCF (RF) hyperthermia is to be effective.

This treatment modality proved to be feasible and convenient for use under conditions existing in primary health care facilities in Mexico, providing cure rates higher than usually expected with antimonials drugs at much reduced cost, and with several other important advantages.

Acknowledgments: We thank Gene Hedin (ThermoSurgery Technologies, Inc., Phoenix, AZ) for providing the LCF-(RF) instrument with logistical support and technical assistance and Dr. Jose Rodriguez-Dominguez (Director General of Preventive Medicine) for official sanction and administrative support, without which this study would not have been possible.

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