

Survey of 259 cases of American cutaneous leishmaniasis in Nicaragua

E. Missoni and R. Morelli

Health Center 'Fidel Ventura', Waslala and Health Center 'Mauricio Abdalah', Rio Blanco, Nicaragua

Summary

The clinical aspects of mucocutaneous leishmaniasis in Nicaragua are examined for the first time. Data regarding 259 cases were collected by the authors in two health centres of a central region of the country. On the basis of clinical observations the multiple aetiology (i.e. *L. mexicana* complex and *L. braziliensis* complex) of the lesions is suggested. The problem is of increasing importance in Nicaragua because of greater public awareness and new settlements in the endemic area and so it deserves further research.

Introduction

Cutaneous and mucocutaneous leishmaniasis seem to be a relevant medical problem in Nicaragua today, nevertheless no clinical description of its local characteristics is available.

The disease, which was known to exist in the country in 1977 (WHO 1980) and probably before (Woke 1947), but which at those times was still considered infrequent or absent by many writers (Müller 1954), was first reported to WHO by the Nicaraguan Health Authorities in 1980 (493 cases) (WHO 1983) after the revolutionary war and after the institution of the National Unified Health System (1979). Since then a progressively increasing number of cases of the disease has been notified to the local health authorities (Nicaragua 1984, unpublished data), showing characteristics of endemicity at least in some areas of the country (Table 1).

Correspondence: E. Missoni, Via Valdagno 26, 00191 Roma, Italy.

Table 1. Number of notified cases and incidence rate in the region of Matagalpa (Health Region VI), 1980-1983

Year	Notified cases	Incidence rate
1980	143	44/100 000
1981	620	177/100 000
1982	2107	593/100 000
1983	1154	230/100 000

Note: a change in most of the staff in rural Health Centers, the new staff being less sensitized to the problem, is probably the reason for the reduction of notified cases in 1983.

The aetiology of leishmaniasis in Nicaragua is not known; it is assumed to be due to *L. braziliensis* (Urcuyo & Zaias 1982; UNDP/World Bank/WHO 1983).

This is the first attempt to describe the main clinical features of cutaneous and mucocutaneous leishmaniasis in Nicaragua.

Materials and methods

Data referring to 259 patients were collected in the rural health centres of Waslala and Rio Blanco situated in the central mountainous region of Nicaragua (Figure 1). This is a humid climate zone, between the isohyetes of 2250 and 2500 mm of annual rainfall, with abundant vegetation typical of the rainforest. The areas within the jurisdiction of the two health centres are contiguous and have altogether a population of approximately 100 000. The area considered is part of the administrative region of Matagalpa (VI region) where cutaneous leishmaniasis is showing up to be a major cause of morbidity.

The diagnosis was exclusively clinical in most of the cases and was based on: the typical

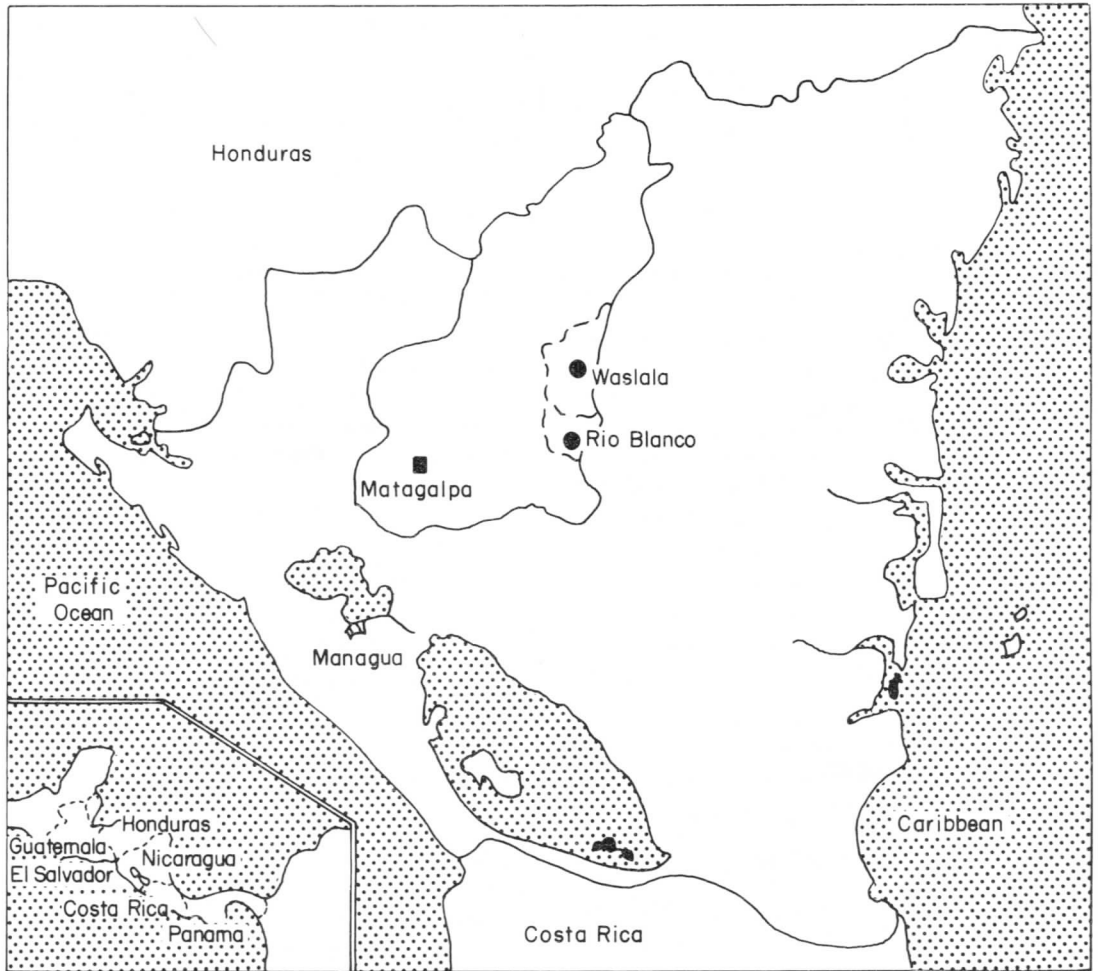


Figure 1. Map of the Republic of Nicaragua to show: — limits of Health Region VI and - - - - limits of the area served by the Health Centers of Waslala and Rio Blanco.

appearance of the lesion, as commonly described in the literature (Kerdel Vegas 1975, Manson-Bahr 1982, Haghghi & Rezai 1977); the exclusion of similar lesions caused by other agents by epidemiological, clinical and available laboratory means. In addition wherever possible confirming evidence was sought by: the use of the Montenegro skin test, randomly executed in 42 cases using leishmanin of Venezuelan strain, 0.1 ml injected subcutaneously with readings at 24 and 48 h. Results were only considered positive when an area of infiltration and erythema wider than 10 mm could be found this indicating a good response (5 mm is generally accepted as positive reaction) (Restrepo Isaza 1981, Freeman

1983); the positive response to specific antimonial treatment; the collection of smears prepared with material obtained by scraping the undermined active border of the lesion, stained with May-Grünwald Giemsa and examined for amastigotes; two smears were prepared in each of 66 cases. In 44 of these adult patients a biopsy as well as a smear was taken with a wedge-shaped cut radial to the lesion, including material from both the bottom and the border in ulcerated lesions, as described by Ridley (1979). Material has been preserved in 10% formalin.

Other data collected were: sex and age of patient; nutritional status, only children under 5 years of age were considered. They were

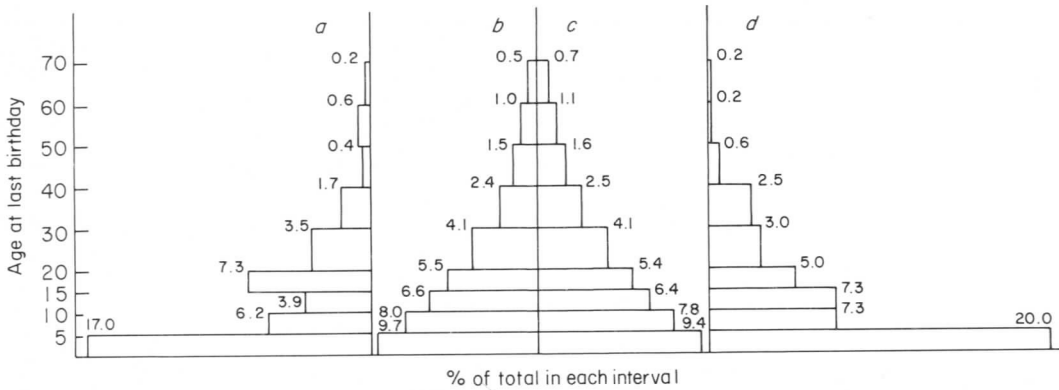


Figure 2. Histograms of distribution according to sex and age (up to 70 years) referred to % of total in each interval. Interval width 5 years. Distribution of general population ($n=2\,733\,000$) is shown for comparison. (a) Males in our sample; (b) males in general population; (c) females in general population; (d) females in our sample.

Table 2. Nutritional status

Nutritional status	Number	%
Normal	31	36.5
1st grade	36	42.3
2nd grade	17	20
3rd grade	1	1.2
Total	85	100

Table 3. Sex

	Parasitological diagnosis	Others	Total
Female	6 (50%)	131 (53%)	137 (52.9%)
Male	6 (50%)	116 (47%)	122 (47.1%)
Total	12	247	259

Table 4. Number of lesions in each patient

Number of lesions	Parasitological diagnosis	Others	Total
1	4 (33.3%)	105 (42.5%)	109 (42%)
2-3	5 (41.6%)	82 (33.1%)	87 (33.6%)
4-5	1 (8.3%)	31 (12.5%)	32 (12.4%)
>5	2 (16.6%)	29 (11.7%)	31 (12%)
Total	12	247	259

Table 5. Maximum diameter of lesions

Diameter (cm)	Parasitological diagnosis	Others	Total
<1	2 (16.6%)	48 (19.4%)	50 (19.3%)
1-2	5 (41.6%)	141 (57%)	146 (56.4%)
3-5	2 (16.6%)	44 (17.8%)	46 (17.8%)
>5	3 (25%)	14 (5.7%)	17 (6.5%)
Total	12	247	259

Table 6. Incidence of lesion-type

Type	Parasitological diagnosis	Others	Total
Dry (crust or nodular)	5 (33.3%)	121 (42.4%)	126 (42%)
Ulcerous	9 (60%)	144 (50.5%)	153 (51%)
Verrucous or cauliflower-like	1 (6.6%)	20 (7%)	21 (7%)
Total	15	285	300

Note: a patient could present more than one type at a time.

Table 7. Duration of lesion at time of visit

Time (months)	Parasitological diagnosis	Others	Total
<1	2 (16.6%)	47 (19%)	49 (18.9%)
1-2	6 (50%)	81 (32.8%)	87 (33.6%)
3-5	1 (8.3%)	54 (21.8%)	55 (21.2%)
6-12	2 (16.6%)	40 (16.2%)	42 (16.2%)
>12	1 (8.3%)	25 (10.1%)	26 (10%)
Total	12	247	259

classified as normal and undernourished of first, second and third grade following paediatric weight/age graphs used by the Health Ministry of Nicaragua, corresponding to those elaborated by Marcondes in 1969 (De Andrade e Silva & Ferreira Alves Filho 1981). Number of lesions; diameter of lesions in centimetres; type of lesion; localization; duration of lesion at time of visit (as indicated by the patient); presence of regional lymphadenopathy or nodular lymphangitis; presence of antecedent scars probably due to cutaneous leishmaniasis; family history for the

disease; associated tuberculosis only in cases with bacteriologically confirmed diagnosis.

Results

In the 66 cases where a smear was prepared only seven (10.6%) showed presence of amastigotes. Of the 66, a biopsy was taken in 44 and there were 12 cases (27.3%) in which parasites were found on section. Of these 12 only two (16.6%) had shown the presence of amastigotes on the smear.

Cases with confirmed parasitological diagnosis failed to show statistically (χ^2) significant

Table 8. Sites of lesions

Site of the body	Parasitological diagnosis	Others	Total
Face and neck	2 (8.7%)	59 (16.5%)	61 (16%)
Ear	—	7 (2%)	7 (1.8%)
Trunk anterior	1 (4.3%)	8 (2.2%)	9 (2.3%)
Trunk posterior	1 (4.3%)	5 (1.4%)	6 (1.6%)
Genitals and perineum	—	3 (0.8%)	3 (0.8%)
Glutaei	1 (4.3%)	15 (4.2%)	16 (4.2%)
Arm	3 (13%)	40 (11.2%)	43 (11.3%)
Elbow	—	18 (5%)	18 (4.7%)
Forearm	2 (8.7%)	36 (10%)	38 (10%)
Hand	2 (8.7%)	19 (5.3%)	21 (5.5%)
Thigh	3 (13%)	24 (6.7%)	27 (7.2%)
Knee	—	16 (4.5%)	16 (4.2%)
Leg	5 (21.7%)	95 (26.6%)	100 (26.3%)
Foot	3 (13%)	12 (3.4%)	15 (4%)
Total	23	357	380

Note: if multiple lesions on same site, site is counted once.

Table 9. Other characteristics

	Parasitological diagnosis (<i>n</i> = 12)	Others	Total (<i>n</i> = 259)
Regional lymphadenopathy	3 (25%)	74 (29.9%)	77 (29.7%)
Nodular lymphangitis	1 (8.3%)	12 (4.8%)	13 (5%)
Antecedent scar	1 (8.3%)	60 (24.3%)	61 (23.5%)
Family history positive	5 (41.7%)	99 (40%)	104 (40.1%)
Associated tuberculosis	—	2 (0.8%)	2 (0.8%)

differences with all the others and data are reported in tables for comparison.

The Montenegro skin test was positive in all 42 cases in which it was executed.

Out of 259 patients, 122 (47.1%) were males and 137 (52.9%) females. The distribution is shown in Figure 2; the distribution of the general population of the Republic of Nicaragua is shown together for comparison.

Altogether we observed: 236 cases (91%) of exclusively cutaneous localization; 22 cases (8.5%) of mucous localization mostly with lesions of the nasal septum, often perforation, but one case with involvement of the larynx (parasitologically confirmed) and one case of widespread nodular cutaneous lesions (diffuse cutaneous leishmaniasis).

Other collected data are presented in Tables 2-9.

Discussion

No significant difference of incidence can be found between the two sexes, while a progressive decrease in the incidence is observed with increasing age. Compared with data referring to the general population of the Republic of Nicaragua (United Nations 1982) the incidence in age group 0-5 is significantly higher. This observation coincides with the concept of later acquired immunity toward the disease (Heynemann 1971).

The strong positivity (>10 mm) of the Montenegro test in all tested patients, while

supporting the diagnosis, is probably limited in its significance because of the possible endemic characteristic of the disease in this area (Chandler & Read 1965, Saf'Janova 1971).

Our sample is not random and distribution observations are limited by the characteristics of the studied group: patients who sought medical attention.

Referring to the nutritional status of under-five patients we could not find any correspondence between serious malnutrition and incidence of disease. The nutritional characteristics of our sample are comparable with the percentages of malnourished children in the general child population (Nicaragua 1980).

A number of observations let us hypothesize the contemporary presence of both the *L. mexicana* complex and the *L. braziliensis* complex in the area.

(a) The low percentage of parasitologically confirmed diagnoses in cases where a smear was prepared, together with the low percentage of positive smears compared to the correspondent positive histological sections, a finding common to other studies (Cuba Cuba *et al.* 1981, Sells & Burton 1981, Lainson & Shaw 1979), suggest the aetiological agent belongs to the *L. braziliensis* complex.

(b) The presence of cases with characteristic mucous lesions, in one confirmed case also widely destructive (*L. braziliensis* complex) as well as the presence of lesions generally described as mainly belonging to the *L. mexicana* complex (i.e. Chiclero's ulcer) (Garnham 1971*a, b*, Freeman 1983).

(c) The known geographical distribution of cutaneous and mucocutaneous leishmaniasis in Central America (UNDP/World Bank/WHO 1983, Evans *et al.* 1984, Zeledon *et al.* 1982).

(d) The considerable presence of cases with multiple lesions in our group (58%) (*L. braziliensis* complex is more often considered to produce multiple lesions) (Manson-Bahr 1982).

(e) The interesting variety of features of the observed lesions (Manson-Bahr 1982, Allen 1954, Haghghi & Rezai 1977, Kerdel Vegas 1975). Moreover a notable percentage (26.75%) of cases presenting an antecedent scar, also in one parasitologically confirmed

case, would support the multiple aetiology hypothesis if, as it is said (Heynemann 1971), infection with *Leishmania* confers immunity to a second infection with a homologous strain.

Even if the clinical approach cannot be accepted anymore as a valid one (Peters *et al.* 1983), nothing permits us to exclude the possible validity of such an aetiological hypothesis.

The maximum diameter of examined lesions is in most cases between 1 and 3 cm, an observation anyway probably dependent on duration at the moment of the visit (Chance 1981).

The body distribution of lesions, confirming higher frequency of localization to exposed parts, reflects what is commonly reported in literature (Marsden 1979, Manson-Bahr 1982).

We have not noted any significant association with other diseases.

The high incidence of a positive family history (45.6%) underlines the importance of environmental factors common to the whole family, and extends the significance of the reported data.

The problem of cutaneous leishmaniasis was underestimated in Nicaragua before 1979 (i.e. no cases were declared to WHO) (WHO 1970–1983) and has been taken into account only after the revolutionary war, with the institution of the National Unified Health System which led to a higher presence of health personnel in rural and isolated areas, to a deeper sensitivity of the physician towards the obligatory reporting of infectious diseases, as well as of the administrative staff in elaborating the data and to popular participation in health problems (Halperin & Garfield 1982). This may explain the progressive increase of reported cases of leishmaniasis over the last 4 years. It is possible that we shall observe a further increase in the incidence in the coming years considering on the one hand the establishment of new settlements which follow the opening of important communication ways toward the interior of the country (Saf'Janova 1971), on the other the equally important movement of troops into the natural environment of the disease (Takafuji *et al.* 1980).

More research is called for into the epidemiological and clinical aspects and the species of *Leishmania* involved should be defined.

Acknowledgements

We wish to thank the staff of the Health Centers of Waslala and Rio Blanco, especially the nurses Daniela Gonzo and Myriam Ortiz Alvarado, for their help in collecting data and, for the histological work, Dr Cesare Mariscotti of the Institute of Pathology of the University of Milano.

References

- Allen A. C. (1954) Eruptions caused by protozoa, arthropods and helminths. In *The Skin* C. V. Mosby, St Louis, pp. 496–498.
- Chance M. L. (1981) Leishmaniasis. *British Medical Journal* **283**, 1245–1247.
- Chandler A. C. & Read C. P. (1965) *Introduction to Parasitology* 10th edn, John Wiley & Sons, New York, pp. 119–129.
- Cuba Cuba C. A., Marsden P. D., Barreto A. C., Rocha R., Sampaio R. R. & Patzlf L. (1981) Parasitologic and immunologic diagnosis of American (mucocutaneous) leishmaniasis. *Bulletin of the Panamerican Health Organization* **15**, 249–259.
- De Andrade e Silva P. S. & Ferreira Alves Filho V. (1981) Crescimento e desenvolvimento e seus problemas. In *Pediatria: Diagnostico e Tratamento* 2nd edn, (ed. J. Murahovschi), Sarvier, Sao Paulo, pp. 95–96.
- Evans D. A., Lanham S. M., Baldwin C. I. & Peters W. (1984) The isolation and isoenzyme characterization of *Leishmania braziliensis* subsp. from patients with cutaneous leishmaniasis acquired in Belize. *Transactions of the Royal Society of Tropical Medicine and Hygiene* **78**, 35–42.
- Freeman M. K. (1983) American cutaneous leishmaniasis. *Journal of the Royal Army Medical Corps* **129**, 167–173.
- Garnham P. C. C. (1971a) American leishmaniasis. *Bulletin of the World Health Organization* **44**, 521–527.
- Garnham P. C. C. (1971b) The genus *Leishmania*. *Bulletin of the World Health Organization* **44**, 477–489.
- Haghighi P. & Rezai H. R. (1977) Leishmaniasis: a review of selected topics. *Pathology Annals* **12**, 63–89.
- Halperin D. C. & Garfield R. (1982) Developments in health care in Nicaragua. *New England Journal of Medicine* **307**, 388–392.
- Heynemann D. (1971) Immunology of leishmaniasis. *Bulletin of the World Health Organization* **44**, 499–514.
- Kerdel Vegas F. (1975) American leishmaniasis. In *Clinical Tropical Dermatology* (ed. O. Canizares), Blackwell Scientific Publications, Oxford, pp. 191–197.
- Lainson R. & Shaw J. J. (1979) The role of animals in the epidemiology of South American leishmaniasis. In *Biology of Kinetoplastida* (eds W. H. R. Lumsden & D. A. Evans) Academic Press, London, p. 27.
- Manson-Bahr P. E. C. (1982) Cutaneous leishmaniasis of the New World. In *Manson's Tropical Diseases* 18th edn, Baillière Tindall, London, pp. 109–113.
- Marsden P. D. (1979) Current concepts in parasitology: leishmaniasis. *New England Journal of Medicine* **300**, 350–352.
- Müller W. (1954) Ärztliche Arbeit an der Miskito Küste (Nicaragua). *Zeitschrift für Tropenmedizin und Parasitologie* **2**, 255–269.
- Nicaragua (1980) *Aportes para el analisis historico de la educaci3n y la participaci3n popular en salud* Ministerio de Salud de Nicaragua, Managua, p. 16.
- Peters W., Evans D. A. & Lanham S. M. (1983) Importance of parasite identification in cases of leishmaniasis. *Journal of the Royal Society of Medicine* **76**, 540–542.
- Restrepo Isaza M. (1981) La reacci3n de Montenegro en la epidemiolog3a de la leishmaniasis suramericana. *Bolet3n de la Oficina Sanitaria Panamericana* **89**, 130–138.
- Ridley D. S. (1979) The pathogenesis of cutaneous leishmaniasis. *Transactions of the Royal Society of Tropical Medicine and Hygiene* **73**, 150–160.
- Saf-Janova V. M. (1971) Leishmaniasis control. *Bulletin of the World Health Organization* **44**, 561–566.
- Sells P. G. & Burton M. (1981) Identification of *Leishmania* amastigotes and their antigens in formalin fixed tissue by immunoperoxidase staining. *Transactions of the Royal Society of Tropical Medicine and Hygiene* **75**, 451–467.
- Takafuji E. T., Hendricks L. D., Daubek J. L., McNeil K. M., Scagliola H. M. & Diggs C. L. (1980) Cutaneous leishmaniasis associated with jungle training. *American Journal of Tropical Medicine and Hygiene* **29**, 516–520.
- UNDP/World Bank/WHO (1983) *Special Programme for Research and Training in Tropical Diseases* TDR/PR-6/83.7—LEISH.
- United Nations (1982) *Demographic Indicators of Countries: Estimates and Projections as Assessed in 1980* UN, New York, pp. 214–215.
- Urcuyo F. G. & Zaias N. (1982) Oral ketoconazole in the treatment of leishmaniasis. *International Journal of Dermatology* **21**, 414–416.
- WHO (1970–1983) *World Health Statistics Annuals* Geneva.
- WHO (1980) *Sixth Report on the World Health Situation, Part Two* Geneva, pp. 99–102.
- Woke P. A. (1947) Arthropods of sanitary importance in the Republic of Nicaragua, C.A. *American Journal of Tropical Medicine* **27**, 357–375.
- Zeled3n R., Macaya G., Ponce C., Chaves F., Murillo J. & Bonilla J. A. (1982) Cutaneous leishmaniasis in Honduras Central America. *Transactions of the Royal Society of Tropical Medicine and Hygiene* **76**, 276.