

Leishmaniasis: Como se trata hoy?

Antonio Rondón Lugo

Coordinador comité de Bioética Instituto de Biomedicina

rondonlugo@yahoo.com

www.antoniorondonlugo.com



LEISHMANIASIS

Leishmaniasis Tegumentaria en la América precolombina



Nazca 200 AC – 600 DC



Mochica Siglos I-VIII DC

Lesiones naso-palatinas demostradas por análisis de rayos X de cráneos de momias Incas.

Lesiones destructivas craneana por leishmaniasis en Markat-Tampu durante el Imperio Inca: S XV-XVI, Valle de Bajo Rimac, Peru.

Altamirano AJ, Moreira JS, Marzochi MCA.

Rev Archaeol Etnol Museum Univ São Paulo 2001

Inca Siglo
XV-XVI



Epidemiología

Ocurren dos millones anuales de nuevos casos de leishmaniasis en el mundo (1.5 millones de leishmaniasis cutánea y 500.000 de leishmaniasis visceral) aunque se estima que la cifra pueda llegar hasta 12 millones, ya que de los 88 países donde se presenta, 78 se encuentran en vías de desarrollo y solo en 32 es obligatorio su reporte. La población en riesgo es de 350 millones

Espectro de la Leishmaniasis

- § PARASITOS
- § CONDICIONES INMUNOLOGICAS
- § CONDICIONES AMBIENTALES
- § NUMERO Y LOCALIZACION DE PICADURAS
- § CONDICIONES NUTRICIONALES
- § INFECCION BACTERIANA

Espectro: Clínico-HP-Immunológico

Convit J, Pinaroli ME .

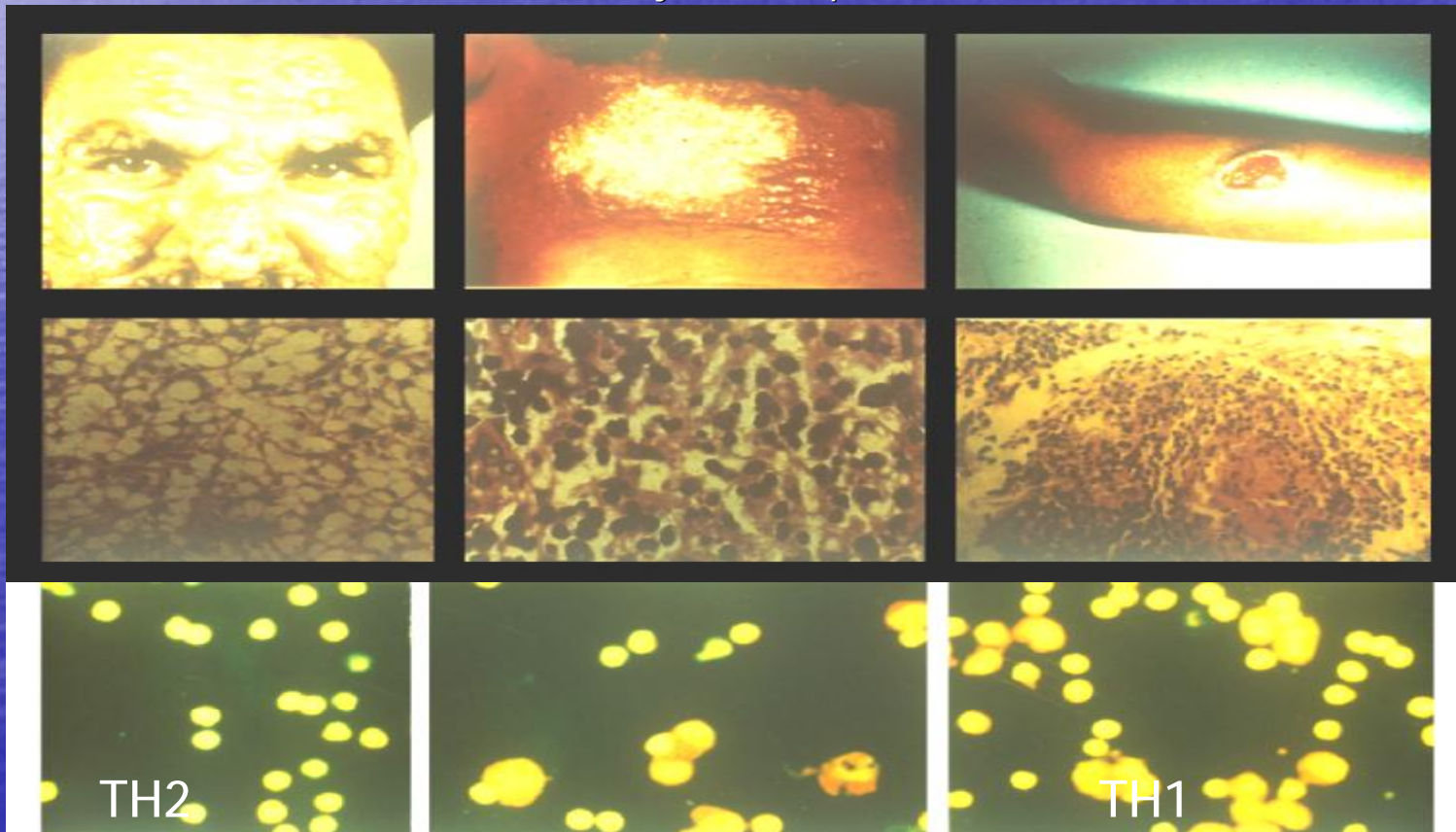
Cutaneous Leishmaniasis : the clinical and immunopathological Spectrum .Ciba Foundation Symposium

Rondón Lugo AJ., Convit J.

Spectrum of American Cutaneous Leishmaniasis". *Dermatology in five Continents* Springer Verlag. Berlin 1988; 789-792

Convit J., Ulrich M., Tapia FJ., Castes M., Rondón Lugo AJ

The Clinical and Immunological Spectrum of American Cutaneous Leishmaniasis". *Trans. Roy. Soc. Trop. Medic.* 1993. 87: 444-8



Convit J, Pinardi ME .

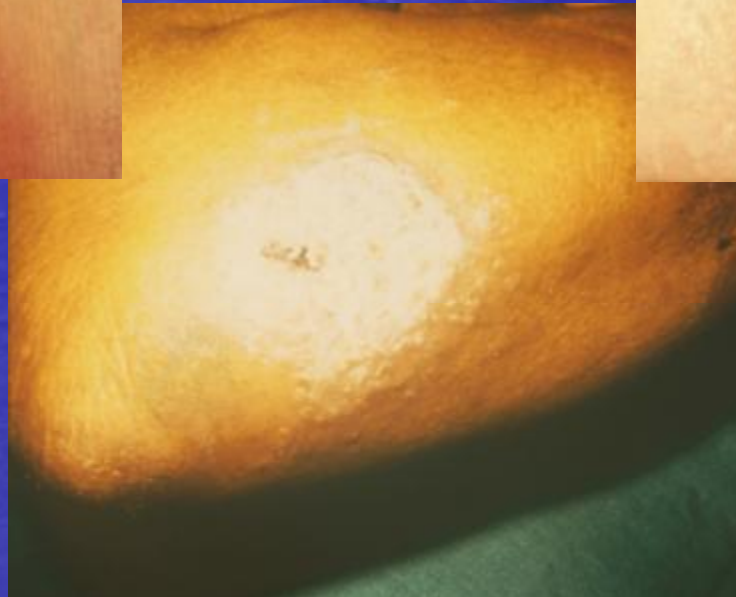
Cutaneous Leishmaniasis :the clinical and immunopathological Spectrum .Ciba Foundation Symposium

Rondón Lugo AJ., Convit J.

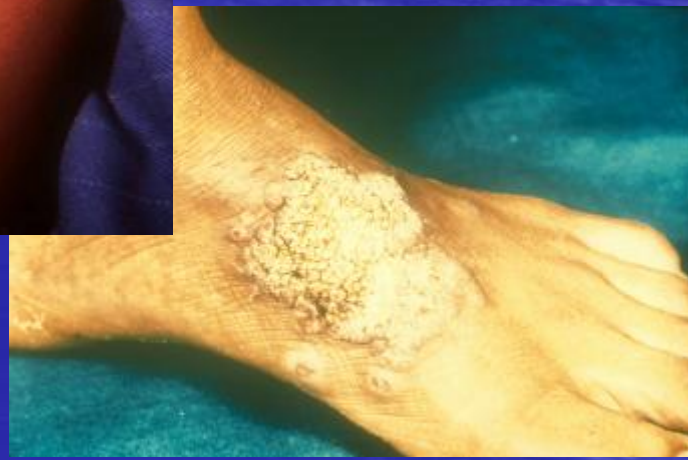
*Spectrum of American Cutaneous Leishmaniasis". Dermatology
in five Continents Springer Verlag. Berlin 1988; 789-792*

Convit J., Ulrich M., Tapia FJ., Castes M., Rondón Lugo AJ

*The Clinical and Immunological Spectrum of American
Cutaneous Leishmaniasis". Trans. Roy. Soc. Trop. Medic. 1993. 87: 444-8*



Halmai O., Arosemena R., Paez E., Weiss E., Rondón Lugo AJ.
"American Cutaneous Leishmaniasis Intermediate Form".
Int. J. of Dermat. 1993, 32:204-5



Reprinted from
TRANSACTIONS OF THE ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE.
Vol. 66. No. 4. pp. 603-610, 1972.

**DIFFUSE CUTANEOUS LEISHMANIASIS: A DISEASE DUE TO AN
IMMUNOLOGICAL DEFECT OF THE HOST**

J. CONVIT, M. E. PINARDI AND A. J. RONDÓN

*Division de Dermatología Sanitaria (M. S. A. S.) and Department of Dermatology, Escuela
de Medicina Vargas, Universidad Central de Venezuela, Caracas*



1948.Convit,Lapenta

MUCO-CUTANEOUS LEISHMANIASIS

NASO-BUCCO-LARYNGEAL LESIONS

NASAL LESIONS



NASO-BUCCAL LESIONS



Moléculas relacionadas con la virulencia de leishmanias

- § Invasive/Evasive determinantes
- § Glycophosphatidil inositos - Glycoprotein - GP63
- § Glycosil phospholipids - Cisteine proteases
- § Lipophosphoglicans - Histones
- § Phosphoglicans – ATphases
- § Proteophosphoglicans

Determinantes Inmunopatológicos

- § Cytoskeletal proteins (kinesins and tubulins)
- § Chaperons (Histones: HSP 60, 70, 83)
- § Ribosomal proteins
- § Nucleosomes
- § Proteosomes

Diagnóstico

- leishmaniasis cutánea –mucosa: se realiza en la mayoría de los casos por la epidemiología, la clínica, demostración del parásito por frotis, cultivo, inoculación y por la histopatología. La PCR es útil también para estudios taxonómicos, los exámenes serológicos son empleados en algunos centros

Tratamiento Local

Controlar la infección bacteriana

Crioterapia : Castro Ron , B. Trujillo , Rosa Francia.

Calor : 1. Mutinga , Mngola East Afr. Med J
1974, 51 : 68-78

2. Rondón Lugo , Convit J Med.Priv
1989,6 : 53-56

Tratamientos

- § Antimoniales
- § Anfotericina B
- § Anfo.. Liposomal
- § Pentamidina
- § Inmunoterapia
- § Miltefosina
- § Ketoconazol
- § Terbinafina
- § Itraconazol
- § Alopurinol
- § Termoterapia
- § Crioterapia
- § Interleuquinas
- § Interferon
- § Laser CO2
- § Imiquimod
- § Rifampicina
- § Trimetropin
- § pentoxifilina

Glucantime

- Dosis 20 /mg /kg dia IM x 20 dias
- Vigilar efectos secundarios:cardiovasculares, renales
- Se pueden repetir 2- 3 series
- **Intralesionales**
- Shaquire 94 % curación L Tropica
- Efectos secundarios : dolor

Anfotericina B

- Dosis de 0.25-1mg-kg- dia . En solución glucosada , lentamente IV dosis total 2gr.
- Efectos colaterales :nefrotoxicidad , anemia ,tromboflebitis.
- Anfotericina liposomal .

Pentamidina

- Usada contra tripanosomiasis ,babesia y leishmaniasis .
- Daña el DNA del kinetoplasto de la leishmania
- Dosis 3-4 mg 1- dos veces semanal–
- Efectos colaterales:mareos ,nauseas, vómitos , dolor abdominal ,daño pancreático
- Permanece hasta 24 dias en hígado

Hentzer B Ann Trop Med Para 1977, 71 : 156- 66

Análogos Alkylphosphocholine

- 2 compuestos . Actúan en la proteína kinase C , que está en la membrana de la leishmania. Se absorben en el tracto intestinal.
- **Miltefosina**
- Ha sido comprobado en *L. major* , *L. donovani* , *L. brasiliensis* , *L. mexicana*

Miltefosine

- Miltefosine for New World Cutaneous Leishmaniasis
J. Soto, B. A. Arana, J. Toledo, N. Rizzo, J. C. Vega, A. Diaz, M. Luz, P. Gutierrez, M. Arboleda, J. D. Berman, K. Junge, J. Engel, and H. Sindermann.

Clinical Infectious Diseases
2004;38 (1 May)

- Diffuse cutaneous leishmaniasis responds to miltefosine but then relapses

Zerpa, O.; Ulrich, M.; Blanco, B.; Polegre, M.; Avila, A.; Matos, N.1; Mendoza, I.2; Pratlong, F.3; Ravel, C.3; Convit, J.
British Journal of Dermatology, Volume 156, Number 6, June 2007, pp. 1328-1335(8)

Nuevas terapias

- § Paromomicina tópica y parenteral
- § imiquimod tópico
- § Bifosfonatos como risidranote y pamidronato
- § Plantas como licochalcone A y alcaloide de quinolina

Citoquinas

- Interferon gamma x 28 dias
- Interferon mas antimoniales

Sundar : J infest Dis 1995 , 172 : 167-9

Steven G. Reed

IDRI

Leish-111f + MPL-SE Vaccine

Current Regulatory Strategy

PROPHYLAXIS

- U.S. IND Filed
- Phase 1 Trial (CCLV001-01)
- Dose-Escalation in Healthy Subjects Patients

- 20 ug & Immunogenicity
Immunogenicity

10 ug

THERAPEUTIC

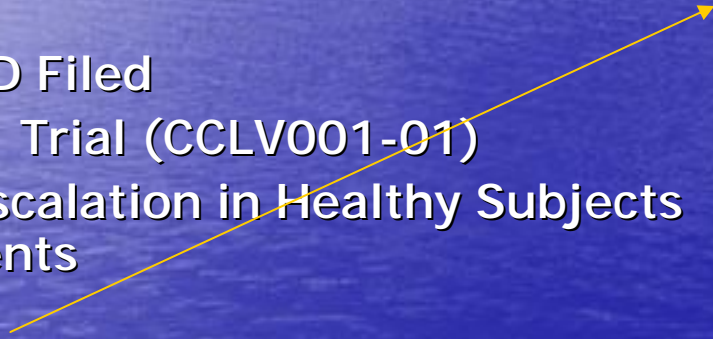
- U.S. IND Filed
- Phase 1 Trial (CCLV001-02)
- Dose Escalation in

with CL or ML

- Safety &

5 ug

10 ug



The Lancet · Saturday 21 February 1987

IMMUNOTHERAPY VERSUS CHEMOTHERAPY IN LOCALISED CUTANEOUS LEISHMANIASIS

JACINTO CONVIT PEDRO L. CASTELLANOS
ANTONIO RONDON MARIA E. PINARDI
MARIAN ULRIICH MARIANELLA CASTES
BARRY BLOOM* LEONARDO GARCIA

*Instituto de Biomedicina (Ministerio de Sanidad y Asistencia Social/Universidad Central de Venezuela), Caracas, Venezuela; and Albert Einstein College of Medicine of Yeshiva University, Bronx, NY 10460, USA**

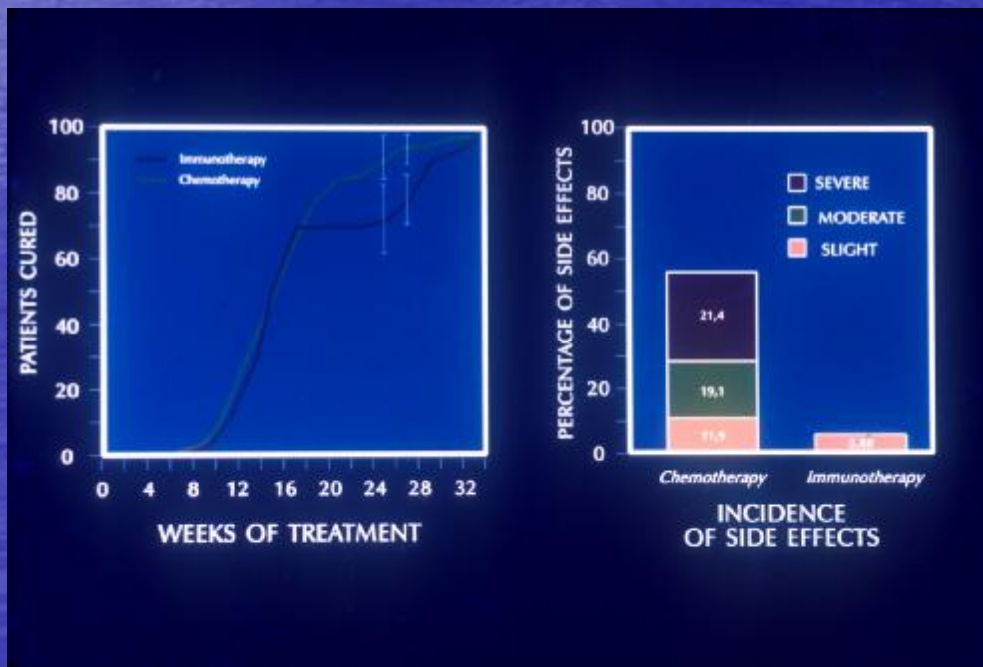
THE JOURNAL OF INFECTIOUS DISEASES · VOL. 150, NO. 1 · JULY 1989
© 1989 by The University of Chicago. All rights reserved. 0022-1899/89/0001-0018\$01.00

Immunotherapy of Localized, Intermediate, and Diffuse Forms of American Cutaneous Leishmaniasis

Jacinto Convit, Pedro L. Castellanos, Marian Ulrich, Marianella Castés, Antonio Rondón, María E. Pinardi, Noris Rodríguez, Barry R. Bloom, Santina Formica, Lourdes Valecillos, and Antonio Britaña

From the Instituto de Biomedicina, Caracas, Venezuela, and Albert Einstein College of Medicine, Bronx, New York

The clinical efficacy of immunotherapy for localized American cutaneous leishmaniasis with a combination of heat-killed *Leishmania mexicana amazonensis* promastigotes and viable BCG (bacille Calmette Guérin) has been compared with meglumine antimoniate chemotherapy and with BCG alone in a controlled clinical study in 217 patients. The results in the first two groups were comparable, with >90% clinical cures with an average time of 16–18 w required for healing. The cure rate was considerably lower (42%) and more prolonged in the group receiving BCG alone. Secondary effects were observed in <5% of the patients receiving combined immunotherapy or BCG alone. In contrast, 49% of the patients receiving chemotherapy showed side effects. High therapeutic efficacy was also observed using combined immunotherapy in patients with intermediate and diffuse cutaneous leishmaniasis who were previously unresponsive to chemotherapy. Cure or clinical improvement was seen in all 11 patients with intermediate forms of the disease, and marked clinical improvement was observed in 9 of 10 patients with diffuse disease. The results on the efficacy of the combined vaccine in immunotherapy for American cutaneous leishmaniasis provide a strong rationale for studying its effectiveness in prophylactic trials.



Vacuna Ideal

- § Induce respuesta efectiva tipo I , con apropiados antígenos celulares
- § Segura
- § Reproducible ,transferible y reproducible
- § Induzca inmunidad por largo tiempo
- § Proteja contra mas de una especie de leishmania .
- § Costo razonable

Gracias



**Muito
Obrigado**

dermatol@cantv.net
www.antoniorondonlugo.com
rondonlugo@yahoo.com