antibiotic identical to paromomycin. An injectable formulation of 500 mg of AM sulfate has been on the market in several countries for over 30 years for the treatment of bacterial and parasitic infections. The drug has anti-leishmanial activity *in vitro* and *in vivo* and acts synergistically with antimonials. Prior studies on AM+Sb found the combination highly efficacious and well-tolerated. Minimal comparative data are available thus far on single-agent AM treatment. The objective of this Phase II randomized open label controlled trial was to assess the efficacy and tolerability of single agent aminosidine (AM) at three daily doses (12, 16 and 20 mg/kg) for 21 days vs standard sodium stibogluconate (Sb) for 30 days. Patients were hospitalised for treatment and received a 180 day follow-up. Entry criteria: both sexes aged 6-50 years with symptoms and signs suggestive for visceral leishmaniasis (fever, loss of appetite, enlarged spleen) were eligible for the study if *Leishmania* amastigotes were demonstrated on Giemsa stained aspirates of spleen or bone marrow. Of the 120 patients enrolled (30 per treatment arm), 119 completed the treatment and 180 day follow-up. A final cure at the end of follow-up was achieved in 23 (76.7%), 28 (93.3%) and 29 (96.7%) of the patients treated with AM 12, 16, and 20mg/kg/day, respectively, vs. 19 (63.3%) cures in the Sb treatment group. At 16 and 20mg/kg/day, AM was significantly more active than Sb in both clinical and laboratory measures of efficacy. No significant clinical or laboratory toxicity occurred in any treatment group. A 21 day course of aminosidine dosed 16 or 20mg/kg/day should be considered as first line therapy for the treatment of VL in Bihar, India.

353 THERAPY OF MURINE CUTANEOUS LEISHMANIASIS CAUSED BY *LEISHMANIA AMAZONENSIS* WITH THE NOVEL DRUG KY62. Al-Abdely HM*, Graybill JR, Melby PC. The University of Texas Health Science Center and Audie Murphy VA Hospital, San Antonio, TX.

Current drug therapy for leishmaniasis is associated with significant toxicity and a long duration of parenteral therapy with antimonial salts or pentamidine. Recent animal and human data indicate very good activity of amphotericin B (AMB, a polyene antifungal) against variety of leishmania species. KY62 is a water soluble polyene antifungal which is better tolerated by mice than AMB. We compared the eff icacy of KY62 to AMB in a murine (BALB/c) model of cutaneous leishmaniasis caused by *Leishmania amazonensis* (LA). Minimal protozocidal concentrations (*in vitro*) were 0.5 mcg/mi for both KY62 and AMB. Six groups of BALB/c mice (10 mice each) were inoculated in the ear and tail with $5x10^6$ LA promastigotes. Therapy with KY62 at 30 mg/kg, 15 mg/kg, 5mg/kg and 1 mg/kg and AMB at 5 mglkg by daily intraperitoneal injection was started at day 3 post infection and continued for a total of 7 days. Control mice received only the drug vehicle. Measurement of ear and tail lesions was performed weekly for 4 weeks. At the end of 4 weeks tail lesions were 0.1 1 mm, 0.1 4mm, 0.30mm , 0.29mm, 0.28mm and 0.31 mm for KY-30mg/kg, KY-1 5mg/kg, KY-5 mg/kg, KY-1 mg/kg, AMB, and controls respectively (P values 0.0005, 0.002, 0.8, 0.7 and 0.5, respectively, treated groups compared to control). Ear lesions were 2.20mm, 2.80mm, 2.82mm, 2.64mm, 2.40mm and 2.60mm for the same treatment groups and controls (P>0. 1 for all). This study indicates good efficacy of short course therapy with KY62 against LA infection. Further studies to define the optimal treatment regimen with KY62 are in progress.

354 LACK OF EFFICACY OF TOPICAL PAROMOMYCIN/MBCL IN THE TREATMENT OF AMERICAN CUTANEO US LEISHMANIASIS. Soto J, Fuya P, Herrera R, and Berman J*. Universidad Militar Nueva Granada and CIMPAT-Universidad de los Andes, Bogota, Colombia; and Walter Reed Army Institute of Research, Washington, DC.

We determined the efficacy of the combination of the topical formulation Leshcutan (15% paromomycin sulfate/12% methylbenzethonium chloride) plus a short, 7 day course of parenteral meglumine antimonate for Colombian cutaneous leishmaniasis in a phase III study. A previous phase II study showed this combination to be 90% effective. Patients were randomly assigned in unequal allocation (2:1:1:1) to the experimental group "Leshcutan plus 7 days meglumine", one negative control group "placebo topical plus 7 days meglumine", a second negative control group "Leshcutan plus 3 days meglumine", and the positive control group "20 days meglumine." Cure was defined as complete reepitheliazation of all lesions without relapse by 9-12 months of follow up. Cure rates were: Leshcutan plus 7 days meglumine--34/59 (58%); placebo topical plus 7 days meglumine--16/30 (53%); Leshcutan plus 3 days meglumine--6/30 (20%); meglumine 20 days--26/31 (84%). 70% of speciated organisms were *L. panamensis*. In contrast to the previous phase II study, this phase III study showed that 10 days of Leshcutan therapy does not augment the response of predominately *L. panamensis* cutaneous leishmaniasis to a short course of meglumine. Clinical results with other topical antileishmanial formulations will also be summarized and reviewed.

Tibayrenc, Michel

355 *LEISHMANIA TROPICA*:EMERGING OR RESURGING PARASITE IN NORTH MOROCCO. Guessous-Idrissi N*, Riyad M, Banuls AL, Bichichi M, and Tibayrec M. Unité d'Etudes et de Recherche sur les Leshmanioses, Faculté de Médecine et Centre Hospitalier Ibn Rochd, Casablanca, Morroco; and Centre d'Etudes sur le Polymorphisme des Microorganisms, UMR CNRS/ORSTOM, Montpelier, France.

Anne-Laure

In Morocco, *Leishmania tropica* was known until 1995 as the etiologic agent of few human and dog cutaneous leishmaniasis (CL) in Central South Morocco. In 1994, and for the first time, we reported one case of canine visceral leishmaniasis due to *L. tropica* MON-102 from the northern area of Morocco, and in 1995, an emerging focus of human CL also due to *L. tropica* MON-102 in a neighboring northern city was identified. The RAPD comparative analysis of some northern and southern *L. tropica* stocks from humans and dogs showed polymorphic profiles using 11 primers. Two main groups could be individualized and amongst them one seems associated with the most virulent stocks, while no marker of geographical origin could be identified. these preliminary data suggest a new hypothesis about the history of *L. tropica* in North Morocco.

356 DYNAMICS OF THE TRANSMISSION OF VISCERAL LEISHMANIASIS IN TUNISIA : FROM THE FIELD TO THE MODELS. Ben Salah A *, Smaoui H, Diwani F, Anderson RM, Dellagi K, and Ben Ismaïl R. Laboratoire d'Epidémiologie et Ecologie Parasitaire, Institut Pasteur de Tunis, Tunisia; Ecole Nationale des Ingénieurs de Tunis, Tunisia; Department of Zoology, Oxford University, UK; and Laboratoire d'Immunologie, Institut Pasteur de Tunis, Tunisia.

A deterministic mathematical model allowed the simulation of the dynamics of the transmission of visceral leishmaniasis (VL) among the vector, the dog reservoir and the human host. Structure and parameters of the model were drawn from extensive epidemiological surveys in the field : i) A prospective study of a cohort of 917 dogs followed for three years in the focus of visceral leishmaniasis in northern Tunisia since 1994, ii) Leishmanin skin testing of 9000 people living in different epidemiological situations (general populations of endemic areas for canine infection with and without human cases, contacts of human VL cases) and iii) Epidemiological investigation of 187 cases of human visceral leishmaniasis that occured between 1990 and 1995 in Kairouan, iv) Entomological surveys for the density of sandflies in the classic focus of visceral leishmaniasis in northern Tunisia. Sensitivity of the model to the different parameters of transmission showed that contact rates between hosts and parasites are the key factors influencing the prevalence of the infection. This result is in agreement with epidemiological findings which indicate that full-blown Kala-azar is associated with an early intense contact between humans and parasites, witnessed by the leishmanin skin reactivity among human VL contacts in the governorate of Kairouan. An age structured version of the model revealed a good agreement between the expected and observed prevalences at the equilibrium. These findings clearly support the relevance of mathematical modelling for the understanding of the dynamics of leishmaniasis when they are based on deep epidemiological knowledge.

Anne-Laure

357 MOLECULAR EPIDEMIOLOGY OF PERUVIAN AND BOLIVIAN LEISHMANIASES. Banuls AL*, Dujardin JC, Guerrini F, Arevalo J, Solano MA, Bermudez H, De Doncker S, Jacquet D, Le Ray D, and Tibayrenc M. Michel CEPM, centre ORSTOM Montpellier, France; Laboratory of Protozoology, Prince Leopold Institute of Tropical Medicine, Antwerpen, Belgium; Laboratory for Trypanosomatidae Biochemistry, Instituto de Medicina Tropical Alexander Von Humbolt, Lima, Peru; and Centro, Universitario de Medicina, Universidad Mayor de San Simon, Cochabamba, Bolivia.

In this study, we analyzed by Multilocus Enzyme Electrophoresis (16 loci) and Random Primer Amplified Polymorphic DNA (10 primers) a Peruvian and Bolivian sample of 188 Leishmania natural isolates. Two main lines of results were reached: (1) certain species were recorded for the first time in given countries: *Leishmania lainsoni* in Bolivia and *L. guyanensis* in the Peruvian AndeanValleys. (2) drastically different species can coexist in the same focus, and even,in the same host. These results emphasize the need for a sharp molecular identification of *Leishmania* species, the more so since that different species tend to be associated with distinct clinical forms. Both MLEE and RAPD provide markers specific of: (i) given species; (ii) given geographical areas; (iii) possibly given clinical forms, although this last result definitely has to be confirmed on larger samples.

358 IMPACT OF DOG CONTROL ON CANINE AND HUMAN VISCERAL LEISHMANIASIS IN JACOBINA, BAHIA, BRAZIL. Ashford DA*, David JR, Freire M, Sherlock I, Eulalio MC, Sampaio DP, and Badaro R. Department of Tropical Public Health, Harvard School of Public Health, Boston, MA; Universidade Federal da Bahia, Salvador, Brazil; and Fundacao Osvaldo Cruz-Bahia, Salvador, Brazil.

To assess the effect of removing *Leishmania*-infected dogs on the incidence of visceral leishmaniasis, a controlled intervention study was performed in northeast Brazil. In the intervention area, the attempted elimination of seropositive dogs resulted in an initial significant decline in the annual incidence of seroconversion among dogs from 36 to 6 percent over the first 2 years. In the following 2 years, the incidence of seroconversion among dogs in the intervention area increased to 11 and 14%respectively. In a control area in which dogs were surveyed but seropositive dogs were not removed, the cumulative incidence did not vary significantly from year to year, ranging from 16 to 27%. In the intervention area, the prevalence of visceral leishmaniasis among dogs declined from 36% before the intervention to 10% and remained stable. Also, when the number of human cases before and after the

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