# LEISHMANIASIS IN ISRAEL, JORDAN AND THE PALESTINIAN AUTHORITY

**Sheba Medical Center-Tel-Hashomer**

**October 23, 2003**

# PROGRAM AND ABSTRACTS

**ORGANIZED BY:**

**ISRAEL SOCIETY FOR PARASITOLOGY**
**PROTOZOOLOGY AND TROPICAL DISEASES**

**PARTICIPATING ORGANIZATIONS**

**Israeli Society of Parasitology, Protozoology & Tropical Diseases**
**Israel Society of Dermatology & Venereology**
**Israel Society of Infectious Diseases**

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**Israeli Defense Forces, Medical Corp**
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**UNDER THE AUSPICES OF:**

**THE KUVIN CENTER FOR THE STUDY OF INFECTIOUS AND TROPICAL DISEASES, DEPARTMENT OF PARASITOLOGY, HEBREW UNIVERSITY-HADASSAH MEDICAL SCHOOL, JERUSALEM**

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## CONTRIBUTORS

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**TEVA, ISRAEL**

# SCIENTIFIC PROGRAM

**09.00-10.00 Registration and welcome coffee**

**10:00-10:15 Opening remarks: Eli Schwartz, President, Israel Society for Parasitology, Protozoology and Tropical Diseases**

**10.15-11.55 Epidemiology**

**Chair: Daniel Vardi (Ben-Gurion University, Beer-Sheva)**
**Dani Cohen (Tel-Aviv University)**

**10.15-10.35 Anis, E., A. Leventhal, Y. Elkana, A. Wilamowski and H. Pener.** Epidemiology of leishmaniasis in Israel

**10.35-10.55 Rimlawi, A.** Epidemiology of leishmaniasis in the Palestinian Authority

**10.55-11.15 Bilbissi, A.** Epidemiology of leishmaniasis in Jordan

**11.15-11.35 Grotto, I., M. Huerta and R. Balicer.** Epidemiology of leishmaniasis in the Israeli Defense Forces

**11.35-11.55 Dabas, M. and Isaam Imaash.** Epidemiology of leishmaniasis in Jordan Army

**12.00-13.00 Emerging pathogens**

**Chair: Amos Yinnon (Shaarei Zedek Hospital, Jerusalem**

**Alex Zvulunov (Joseftal Hospital, Eilat)**

**12.00-12.20 Warburg, A.** Transmission of *Leishmania tropica*

**12.20-12.40 Vinitsky, O., H. Habiballa, A. Or, S. Zarka, Z. Dror, D. Amar and U. Shalom.** *Leishmania tropica* - The experience of Ministry of Health and Environment in Northern Israel

**12.40-13.00 Baneth, G.** Canine visceral leishmaniasis in Israel: 1994-2003

**13.00-14.00 Lunch**

**14.00-15.30 Clinical presentation and treatment**

**Chair: Shlomo Maayan (Hadassah Hospital, Jerusalem), Yossi El-On (Ben-Gurion University, Beer-Sheva)**

**14.00-14.15 Shani Adir, A, D. Rozenman, E. Schwartz, M. Ramon, S. Kamil, L. Zalman, C. Jaffe and M. Efrat.** *Leishmania*

*tropica* in Israel - a clinical overview of a newly identified focus in Tiberias

**14.15-14.30 Efrat, M.** Human visceral leishmaniasis in Israel

**14.30-14.45 Rahav, G.** Leishmaniasis in immune suppressed patients

**14.45-15.00 Schwartz, E., N. Sahar, A. Scope and H. Trau.** *Leishmania braziliensis* and mucosal involvement in returning travelers

**15.00-15.15 Enk, D.** Treatment of cutaneous leishmaniasis

**15.15-15.30 Golenser, J., T. Ehrenfreund and A. Domb.** New treatment options in research with special emphasis on Amphotericin B-arabinogalactan conjugate

**15.30-15:45 Coffee break**

**15.45-16.50 Diagnosis & Control**
**Chair: Uri Shalom (Ministry of Environment),**
**Lionel Schnur (Kuvin Center, Jerusalem)**

**15.45-16.00 Bensoussan, B., A. Nasereddin, F. Jones and C. L. Jaffe.** Species specific diagnosis of leishmaniasis, its about time

**16.00-16.15 Klement, E, R. Kayouf, M. Yavzori, N. Orr, J. El-On, M. Efrat and D. Cohen.** Evaluation of the serologic response to *Leishmania major* exoantigen in symptomatic and asymptomatic *Leishmania major* infections

**16.15-16.35 Schlein, Y., R. L. Jacobson and G. C. Müller.** The use of *Bougainvillea* against sand flies

**16.35- 16.50 Orshan, L., U. Shalom, A. Wilamowski and H. Pener.** Approaches to sandfly control

**16.50-17.00 Closing remarks**

# ABSTRACTS

## Ordered alphabetically according to the first author

### Epidemiology of leishmaniasis in Israel

**Anis, Emilia[1], Alex Leventhal[2], Yehudit Elkana[3], Amos Wilamowski[3] and Hedva Pener[4]**

[1]Department of Infectious Diseases, [2]Department of Public Health Services, [3]Department of Epidemiology, and [4]Laboratory of Entomology, Ministry of Health

Cutaneous leishmaniasis (CL) is a zoonotic disease, endemic and notifiable in Israel. The vectors are sandflies of the genus *Phlebotomus* and the hosts are mainly field rodents. The infective agents are Leishmania parasites. *Ph. papatasi* is the recognized vector of *L. major*, while *Ph. sergenti* is considered to be the vector of *L. tropica*.
Only a few human cases of Kala Azar are reported in Israel every year – mainly among non-Jewish children aged 5-14 years. The reservoir is stray dogs and the vector is the sandfly. The annual number of reported CL cases during the period 1961-2002 varied between less than 10 to over 250, with rates varying between 0.13 to over 7 per 100,000. Two peaks, between 1967-1969 and 1980-1982 were observed. These peaks reflect environmental changes caused by the introduction of non-immune people (mainly Jews) into the area of endemic foci, enhanced urbanization by expansion of settlements bordering this area, agricultural/industrial projects and most probably the effect of Global Warming. In recent years, most reported cases were from Tiberias and were caused by *L. tropica*. Recently, an increasing trend in the prevalence of the disease has been reported also by the Palestinian Authority and countries in the Mediterranean basin, reflecting common changes in modern demographic and environmental conditions. These factors include population growth and movements, as well as ecological changes. Cooperation of the Ministries of Health and Environment of the countries of the whole Middle East region in combating the vectors and the reservoirs in animal hosts must be encouraged.

### Canine visceral leishmaniasis in Israel: 1994-2003

**Baneth, Gad**

School of Veterinary Medicine, Hebrew University

Canine visceral leishamniasis (VL) has been reported from most of the countries in the Mediterranean basin. The domestic dog is considered the major reservoir for human VL caused by *Leishmania infantum*. In 1994, a dog from the village of Nataf, 11 km. west of Jerusalem was diagnosed with VL. It was the first animal to be diagnosed with VL in central Israel for at least 40 years. Since then, canine VL appears to have spread considerably and 153 dogs from 46 different locations have been diagnosed with VL between 1994-2003. Of these dogs, 40 (26%) were from northern Israel. Canine VL is currently prevalent from the Kiryat Gat area in south-

central Israel to the Lebanese border in the north. The location of human VL patients appears to parallel the presence of the canine disease. However, the number of clinical human VL patients is considerably lower than the number of sick dogs. For every human VL patient diagnosed during 1994-2003 in Israel, approximately 15 dogs have been detected with this infection. In addition, there are probably many infected dogs that are not noticed or reported. Serosurveys in jackals and foxes have indicated that *Leishmania* infection is also present in populations of these wild canine species in Israel. Thus, these wild canids may play a role in the epidemiology of VL in Israel. Canine VL is primarily found in rural settings. Of the 153 infected dogs, only 15 (10%) were originally from an urban environment. Of these, 8 dogs originated from the new city of Modiin-Macabim-Reut. Additional cases included dogs from large municipalities such as Tel-Aviv, Jerusalem and Rishon Lezion, who according to their owners never left these cities. This trend of urbanization of VL is of concern, because VL has been reported to cause urban epidemics in people in other regions of the world. A recent study that genetically compared *L. infantum* isolates from Israel showed different DNA banding patterns in dog isolates originating from distant geographic regions and a similarity in banding among local isolates. Most isolates from certain regions in central Israel clustered together and differed from northern isolates. This suggested that the emergence of VL in central Israel might have been caused by the settlement of previously sparsely inhabited areas. The insurgence of humans and their dogs into natural habitats where sylvatic cycles of infection existed might be responsible for the emergence of VL, rather than spread of the infection from the endemic north southward.

**Species specific diagnosis of leishmaniasis, its about time**

**Bensoussan, B.,[1] A. Nasereddin,[1] F. Jones[2] and Charles L. Jaffe[1]**

[1]Department of Parasitology, Kuvin Centre for the Study of Tropical and Infectious Diseases, Hebrew University-Hadassah Medical School and [2]Department of Dermatology, Hadassah University Hospital, Jerusalem 91120, Israel

Cutaneous and visceral leishmaniasis caused by *L. major*, *L. tropica* and *L. infantum* are endemic to Israel and the surrounding region. In addition, returning tourists may present lesions containing *Leishmania* that can cause mucocutaneous disease. Ideally diagnostic techniques where multiple species exist should be sensitive, specific, quick, and identify each species directly in clinical samples without parasite culturing. Many PCR assays fulfill these criteria, and their routine implementation will allow rapid and effective treatment to be administered. The sensitivity of two PCR approaches which amplify part of the ssu rRNA gene and the ribosomal internal transcribed spacer (ITS), respectively, was determined using human and dog blood seeded with *Leishmania* promastigotes. The ssu-rRNA-PCR was more sensitive than the ITS1-PCR, however species identification is only possible using the latter approach. Digestion of the ITS1 amplicon with *Cfo*I or *Hae*III distinguished all medically relevant *Leishmania*. The reliability of the ITS1- and the spliced leader mini-exon (ME)-PCR, both able to characterize leishmanial species, were compared with diagnosis by parasite culturing and microscopic examination. Samples from 34 patients clinically suspected of cutaneous leishmaniasis (CL) were examined by all four methods. Parasites were observed microscopically in only 52.9% (18/34) cases,

compared to 29.4% (10/34) by parasite culturing. ME-PCR was positive with 35.3% (12/34) samples, while the ITS1-PCR was positive in 25/34 (73.5%) samples. The ITS1-PCR detected parasite DNA in 22/23 (95.6%) samples found positive by at least 1/3 of the other diagnostic methods, in addition 3 patients were only found positive by ITS1-PCR. Parasite species, *L. major, L. tropica* or *L. braziliensis,* were characterized in 18/25 positive samples collected between 2000-2003 and 14/15 positive samples from 2003. This method has been used to diagnose >162 local and imported suspected cases of leishmaniasis in Israel, the Palestinian Authority and Germany. It can also amplify and identified parasites at the species level from archived non-stained and Giemsa stained microscope slides. The ITS1-PCR should increase the sensitivity and reliability of diagnosis and identification, supplementing existing serological methods in epidemiological and clinical studies.

**Human visceral leishmaniasis in Israel**

**Efrat, Moshe**

Department of Pediatrics, Carmel Medical Center and the Technion-Israel Faculty of Medicine, Haifa

Human visceral leishmaniasis (HVL) in Israel is usually caused by *L. donovani* complex parasites (*L. infantum)*, and rarely by *L. tropica*. In Israel it remains predominantly a disease of young children though increasing numbers of adults have been diagnosed, some with HIV co-infection, some with their leishmaniasis acquired elsewhere. Clinically patent disease is lethal if untreated, but it seems that in Israel, there is a vast population of asymptomatic, exposed individuals, much larger relative to the number of symptomatic HVL cases than reported elsewhere. HVL was reported most frequently during the 1960's (>50 cases), primarily in children, mostly in the Arab population. The reported incidence has markedly declined since. HVL was reported nearly exclusively form northern Israel until the 1990's, when HVL began to be reported from central Israel, in all segments of the population. The new focus in central Israel can probably be explained by the new presence of humans residing in previously unpopulated areas endemic for canid VL. Two studies of asymptomatic HVL in northern Israel have shown that over time, *L. infantum* seroprevalence in this area remains high despite the virtual disappearance of clinical HVL. Asymptomatic HVL was identified using an enzyme-linked immunosorbent assay. In 1989, one village was studied and was found to have 10% seropositivity without clinical disease during the preceding decade. During 1994-6, in a study of over 20 villages, positive sera were more prevalent in endemic (2.97%) compared to non-endemic (1.01%) regions ($p=0.021$). Veterinary studies have documented the persistence of canid VL in these areas as well. Parasite exposure is higher than expected despite the small number of clinical HVL cases, suggesting factors other than infection per se influence clinical outcome. The evolving epidemiology of both symptomatic and asymptomatic HVL in Israel must continue to be studied carefully in the future. Classical diagnostic methods (smear and culture) have been augmented by serology and more recently PCR. The clinical presentation of HVL is usually classical with fever, hepatosplenomegaly, pancytopenia and hypergammaglobulinemia. In 2 young adults, the diagnosis was made by splenectomy (for presumptive hematological malignancy).

In non-immune-compromised HVL there was no mortality. Treatment, until recently, was with sodium stibogluconate (Pentostam), and when given for 28 days without "rests" in a dose or 20 mg/kg/day, cure was achieved with minimal to no toxicity. Recently liposomal amphotericin B (Ambisome) has been used with similar success.

## Treatment of cutaneous leishmaniasis

**Enk, David**

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Treatment of cutaneous leishmaniasis (CL) is directed toward eradication of amastigotes and reduction of the size of the lesions to promote healing with minimal scaring and to prevent metastatic spread. Choosing among the numerous treatment options is bewildering: The different leishmania species display variable sensitivities to therapeutic measures, and most therapeutic modalities are anecdotal and have not been compared in randomized controlled trials. Furthermore, the clinician often finds himself in a situation where he has to choose between treatment options where dose and duration have been determined under different geographical settings in terms of leishmania species and clinical syndromes. In addition, decisions regarding adequate treatment are complicated by the self-healing nature of CL. When confronting CL patients, 3 important considerations must be taken into account: Is therapeutic intervention required at all? Should the therapeutic regime be local or systemic? Which therapeutic modality is optimal considering the strain of leishmania involved, the immune status of the host, the toxicity profile the drug, as well as practical issues such as availability, costs, and patient compliance. *Local/Intralesional modalities* include: cryotherapy, thermotherapy, electrotherapy, surgery, paromomycin, pentavalent antimony, and antifungals. *Parenteral systemic therapy* includes pentavalent antimony, pentamidine, paramomycin, liposomal amphoteracin B, and Interferon-γ. *Oral systemic therapy* includes allopurinol, antifungals, and dapsone. Selected aspects of these modalities will be discussed with special emphasis on evidence-based proof of efficacy. Finally, the experience with 2 new experimental modalities, photodynamic therapy and the topical immunomodulator, imiquimod, will be mentioned.

## New treatment options in research with special emphasis on Amphotericin B-arabinogalactan conjugate

**Golenser, J.,[1] T. Ehrenfreund[2] and A. Domb[2]**

[1]Department of Parasitology, and [2]Dept. of Medicinal Chemistry, Hebrew University-Hadassah Medical School, Jerusalem

The current treatment of leishmanial infections is inadequate, due to limited availability of effective drug formulations, the many problems associated with their toxicity and the emergence of *Leishmania* resistant to the marketed first line drugs. Presently, pentavalent antimonials such as sodium stibogluconate (Pentostam®) and meglumine

antimoniate (Glucantime®) are used as the first line of treatment. Amphotericin B (AmB), a polyene antibiotic, is a standard drug for the treatment of fungal infections and is currently recommended as an alternative antileishmanial compound. A liposomal AmB formulation (Ambisome®) is too expensive for use in the endemic regions. The only new available drug that had been introduced recently is an alkyl phospholipid, miltefosine which has minor side effects but is teratogenic and has already induced resistance. Consequently, new antileishmanial drugs are being examined. Likewise, drugs interfering with ergosterol metabolism (e.g. inhibitors of isoprenoid biosynthesis) and with transfer of fatty acids and biphosphonates which display inhibition of parasitic farnesyl pyrophosphote synthase. Other target enzymes are DNA polymerase, topisomerase, cysteine proteinase and glycerol-3 phosphate dehydrogenase. Diospyrin (bisnaphtoquinoid) exerts oxidant stress. Approaches that are based on modulation of immune responses have a therapeutic value if Th1 type response is activated (e.g. immunostimulatory oligodeoxynucleotide). Modification of existing drugs for oral absorption and targeting to infected organs, and combinations of drugs in order to avoid induction of resistance are considered.

## Epidemiology of leishmaniasis in the Israel Defense Force

**Grotto, Itamar, Michael Huerta and Ran Balicer**

Army Health Branch, Military Corps, Israel Defense Force

Cutaneous Leishmaniasis is endemic in several Israel Defense Force (IDF) training areas. The majority of cases in the recent years have occurred in the Ketziyot region, located in the western area of the Negev desert. Infection is frequent during the months of July-September, with clinical signs appearing in October-January. The annual incidence of the disease over the last 25 years has been 10-60 per 100,000 soldiers. However, two peaks were noted: In 1981-1982 the yearly incidence was 95-120 per 100,000 soldiers, and in 1998, the rate was 104 per 100,000. Since 1999, a continuous reduction in annual incidence has occurred, reaching an all-time low of 10.6 per 100,000 in 2002. These trends in disease incidence are similar to those reported in the civilian population of Israel, but military rates are 25-60 times higher then civilian incidence. The secular trends noted may be explained by the occurrence of large local outbreaks, which take place mainly when units operate in a new training area. Furthermore, fluctuations over time may be due to changes in weather patterns, as the prevalence of the sand fly vector is influenced by the annual amount of rainfall. The disease is of military significance due to residual scarring; the potential for high attack rates among populations at risk; the loss of training days required for diagnosis and treatment; and the high cost of medical treatment. The control of the disease in the IDF includes use of pesticides on and around Orache (*Artiplex hortensis*) plants, screening of office and barrack windows, personal protective insect repellants, covering of exposed body parts and avoidance of sleeping on the ground. Soldiers in units training in endemic areas are briefed on appropriate behavior prior to entering the affected areas. The epidemiologic investigation of all cases assists in mapping disease endemicity and guides treatment of infected areas. Visceral leishmaniasis is very rare among IDF soldiers. Over the last decade only a single case occurred, caused by *Leishmania infantum*. The soldier was infected in the Galil region.

**Evaluation of the serologic response to *Leishmania major* exoantigen in symptomatic and asymptomatic *Leishmania major* infections**

**Klement, E[1], R. Kayouf[1], M. Yavzori[1], N. Orr[1], J. El-On[2], M. Efrat[3] and D. Cohen[4]**

[1]Center for Vaccine Development and Evaluation, Medical Corps, IDF; [2]Department of Microbiology and Immunology, Ben-Gurion university of the Negev; [3]Carmel Hospital, Haifa; [4]Department of epidemiology and preventive medicine, Sackler faculty of medicine, Tel-Aviv University

**Background:** *Leishmania major* is endemic to the Qeziot area of southwestern Israel and causes significant morbidity to soldiers training there. The development of serological methods for the detection of *L. major* infection can enable swift, sensitive and specific diagnosis of cutaneous leishmaniasis (CL) and serve as a tool for seroepidemiological surveys. **Objective:** To determine the validity of a new serological assay in detecting infection with *L. major* and to evaluate it's utility in determining the extent of parasite exposure in the Qeziot region. **Methods:** The study was carried out during the years 1999-2002. The specificity and sensitivity of ELISA in detecting IgG antibodies specific to an *L. major* exoantigen were determined on a sample of 46 subjects with CL due to *L. major,* diagnosed by smear and/or culture, and 74 presumably unexposed Israeli soldiers. Extent of exposure and the symptomatic to asymptomatic infection ratio was determined by testing sera from 52 subjects, collected at the beginning and the end of the *L. major* infection season. These soldiers were interviewed and were examined for presence of CL-suggestive lesions. **Results:** Sensitivity of the ELISA was determined on the basis of several cutoff values; at specificities of 97.5%, 95% and 90%, sensitivities were 59%, 67% and 80%, respectively. Analysis of the ELISA results was carried out by ROC procedure; area under the curve (AUC) in the current study was 0.891 (95% confidence interval 0.825-0.957), signifying the assay's validity. The ELISA gave a positive result for 12 of the 26 samples found negative by culture and smear. Furthermore, sensitivity of the test increased significantly as the number of lesions increased. Five of the 52 soldiers examined seroconverted (>X2). Of these, 4 had history and lesions consistent with CL, resulting in an ELISA supported incidence of 7.7% during the CL season. **Conclusions**: An *L. major* exoantigen - based ELISA is a good diagnostic tool when used in conjunction with traditional diagnostic assays such as culture or smear. Sensitivity of ELISA is directly proportional to the number of lesions. Our findings also support previous observations, which described the Qeziot area as endemic for CL due to *L. major*.

**Approaches to sandfly control**

**Orshan, Laor[1], Uri Shalom[1], Amos Wilamowski[2] and Hedva Pener[2]**

[1]Ministry of the Environment; [2]Ministry of Health

Sandflies affect humans by disease transmission and/or nuisance through biting. As a rule, control of holometabolous insect vectors is directed against the larval stages, accompanied by complementary steps taken against the adults. Due to the basic biology of sandflies, control of juvenile stages is practically not feasible; accordingly, the main control methods are directed against the adults. These methods are only

partially successful and in most instances, preventative measures are insufficient for reducing sandfly populations. Limiting the man-sandfly contact is more promising. All control measures against sandfly bites are based on personal protection on one-hand and insecticide applications inside and outside human dwellings on the other. The measures taken for personal protection against sandfly bites are very similar to those taken against mosquito bites. However, because of the difference in the basic biology of the insects, the strategies of insecticide applications are different. The flight range of sandflies is limited and advance is achieved by hopping rather than by continuous flight. Insecticide application on horizontal or vertical surfaces around human dwellings kills sandflies before biting. For effective results residual insecticides and treated surfaces, 1.5-3 meters wide, should be employed. Outdoor spraying with pyrethroids or organophosphates, although licensed, is rather ineffective. Under the harsh environmental condition in the endemic areas, the residual activity of these compounds is not satisfactory. Repeated sprayings at relatively short intervals is necessary for effective results. Consequently, despite the concern of environmental impact, DDT is still permitted for outdoor use in Israel, specifically against sandflies. In order to minimize the sprayed areas, the construction of artificial barriers of impregnated materials around settlements and/or dwellings is advised. New pyrethroids are currently being tested employing this method. Current research is aimed at finding new methods of reducing sandfly populations. Various plants having a lethal effect on sandflies are being considered and tested as potential attractants. Recent publications indicate that *Bougainvillea* plants serve as an effective attractant to sandflies and kill the insect when it feeds on them. Field trials are planned to verify this finding in the endemic areas of the country.

**Leishmaniasis in immunesuppressed patients**

**Rahav, Galia**

Sheba Medical Center, Tel-Hashomer.

Visceral leishmaniasis (VL) is a rare but potentially life threatening opportunistic protozoan infection in immunocompromised patients. The clinical manifestations in these patients are unusual and the diagnosis is difficult. Most cases are related to HIV infection, also transplantation and chemotherapy may also be associated with VL. In regions where coinfection with HIV and Leishmania are common (Spain, southern France, Italy) VL is the third most frequent opportunistic infection among HIV patients; 70% of adult cases of VL are associated with HIV infection and 10% of patients with AIDS present with VL as an opportunistic infection. Primary VL appears at significantly higher CD4 than reactivation VL. VL in HIV patient can be asymptomatic or can be associated with, fever, hepatomegaly, splenomegaly and pancytopenia. Unusual presentations such as extensive GI involvement, absent splenomegaly and involvement of the lungs, pleura, oral mucosa, skin and CNS may also occur. The sensitivity of serological tests in these patients is only 34%. Failures, mortality and relapses are more common in HIV infected patients. More than 90% of transplant cases associated with VL are kidney transplants recipients. The clinical presentation and the natural course of infection in these patients are similar to that in HIV patients. Pentavalent antimonial compounds are the standard recommended therapy. Twenty five percent of HIV patients and VL do not respond because of poor

cellular immune response and relapses occur in up to 80 percent of those who do respond. Lipid-associated amphotericin B compounds are now considered by many to be the treatment of choice for Indian and Mediterranean VL. Long term prophylaxis is recommended following therapy.

## The use of *Bougainvillea* against sand flies

**Schlein, Yosef, Raymond L. Jacobson and Gunter C. Müller**

Department of Parasitology, The Kuvin Center for the Study of Infectious and Tropical Diseases, The Hebrew University- Hadassah Medical School, Jerusalem, Israel

The sand fly *Phlebotomus papatasi* transmits *Leishmania major* in the Old World. In addition to blood the sand flies feed on plants. In a study of this diet we observed that one night feeding on branches of *Solanum jasminoides*, *Ricinus communis* or *Bougainvillea glabra* drastically shortened the life span of the sand flies. Flowering *B. glabra* attracted *P. papatasi* in the field. Nevertheless, in the endemic region of *L. major,* in yards abounding with vector sand flies, the number of *P. papatasi* trapped near hedges of *B. glabra* was eight times less (62: 502 flies trapped) than in the control sites. The results imply that *B. glabra* affords local protection against sand fly bites and decreases the risk of leishmaniasis.

## *Leishmania braziliensis* and mucosal involvement in returning travelers

**Schwartz, Eli, Nadav Sahar, Alon Scope and Henry Trau**

The Center for Travel and Tropical Medicine and the Department of Dermatology, Sheba Medical Center, Tel-Hashomer

Travel to South and Central America has become increasingly common among young Israeli adults. *Leishmania braziliensis*, which is endemic in the Americas, causes unsightly cutaneous lesions and may be complicated by severe mucosal disease. In recent years, New World cutaneous leishmaniasis including mucosal involvement has been seen at a higher incidence among returning Israeli travelers. This study describes a nationwide survey of travelers returning from the Americas with leishmaniasis . In the period of 1993–2003, 63 cases were identified, of which 80% were males. The mean age was 24 years (range 23–39). In almost all cases, the disease was contracted in the Amazon region of Bolivia. During the last 3 years, the polymerase chain reaction (PCR) has been used for species specific diagnosis. In all cases of Bolivian infection *L. braziliensis* was shown to be the causative agent. The clinical picture of the disease, beside the cutaneous involvement, showed regional lymphadenopathy in 42 % of patients. In this group, three patients (5%), none of whom had received systemic treatment for the cutaneous disease, were found to have mucosal involvement of the upper airway. Treatment by 20mg/kg sodium stibogluconate was administered intravenously for 21 days for the cutaneous lesions. There was a 25%

relapse rate after a single course. The treatment was well tolerated clinically. Laboratory findings, mainly elevation of liver and pancreatic enzymes (58%), were reversible. We concluded that PCR is a useful tool for establishing the species diagnosis of leishmaniasis and that systemic treatment is needed. Sodium stibogluconate (Pentosatam) is a safe and overall effective treatment for *Leishmania braziliensis* infection. We recommend that mucosal examination should be part of the follow-up for *L. braziliensis* infections in travelers, and mucosal leishmaniasis should be part of the differential diagnosis of mucosal lesions in all patients with a history of travel to South America.

## *Leishmania tropica* in Israel - a clinical overview of a newly identified focus in Tiberias

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**Background:** Most reported cutaneous leishmaniasis (CL) in Israel is apparently caused by *L. major*. Recently a new focus of leishmaniasis caused by *L. tropica* has been described in Tiberias and the surrounding area. **Objective:** To evaluate clinical and laboratory parameters at diagnosis, response to treatment, and outcome of patients with CL from the Tiberias area, during the past year, most of whom apparently had *L. tropica*. **Methods:** Clinical records were reviewed and telephone surveys were performed. Patients were re-examined when necessary. **Results:** Between September 2002 and August 2003, 43 patients with confirmed CL were treated in 4 institutions: Haemek, Rambam, Carmel and Chaim Sheba Medical Centers. Mean age was 32 years (range: 1- 63); 84% of patients live in Tiberias and surrounding area; mean number of lesions was 2.8 (range 1-10). Lesions were commonly located on the face (65%) and upper limbs (62%). 91% of patients younger than 14 years of age had facial lesions. All patients included in the study had positive direct smears. PCR analysis was performed in 21 patients and was positive in 20/21 cases for *L. tropica*. 42/43 (97%) of patients were treated with various regimens. Topical paromomycin was used in 36 patients (83.7%), with complete response reported in 12 patients (33%). Of the patients treated with intralesional sodium stibogluconate (n=9, 20.9%) a complete response was reported in 6 (66%) while in those treated with intravenous sodium stibogluconate (n=5, 11.6%) a 60% cure rate was achieved. 50% of patients studied received multiple therapeutic regimens due to failure or incomplete response to treatment. Additional clinical data, both retrospective and prospective are being collected so as to better clinically describe this focus of CL due to *L. tropica*. Factors to consider when choosing treatment for patients with *L. tropica* and problems with current therapeutic modalities are discussed.

# *Leishmania tropica* – the experience of the Ministries of Health and Environment in Northern Israel

**Vinitsky, Olga, Hamza Habiballa , Amnon Or, Salman Zarka, Zahava Dror, Dafna Amar and Uri Shalom**

Increased incidence of Leishmaniasis in some areas of the region has been recorded by the Northern District of the Ministries of Health and Environment since January 2000 and up to date 71 cases of Cutaneous Leishmaniasis were identified. The main cluster of cases (78%) was found in the Kinneret Sub-district, and most of them in the town of Tiberias