ANNUAL MEETING OF THE

ISRAEL SOCIETY FOR PARASITOLOGY

PROTOZOOLOGY AND

TROPICAL DISEASES

KFAR HAMAKABIA, JANUARY 9, 2003

Guest Lecturer: Dr. Stephen L. Hoffman, MD, DTMH

Sanaria LCC, USA

Past President, American Society of Tropical Medicine and Hygiene

SCIENTIFIC PROGRAM

09.00-09.30
Welcome Coffee and Late Registration

Session 1: General Parasitology (09:30-11:30)

Chair: Prof. Charles Greenblatt and Dr. Joseph Hamburger, **HU**

Number before the time indicates the abstract number

1. 09.30-09.45
Molecular identification of prepatent schistosome infection in field-collected snails
Hoffman, O[1], Kariuki, HC[2], Muchiri, EM[2], Abbasi, I[1] and Hamburger J[1], **HU & MoH, Kenya**

2. 09.45-10.00
Complement-inhibitory effect of Schistosome-derived paramyosin
J. S. Deng, Z. Fishelson & D. Gold, **TAU**

3. 10.00-10.15
Infection with a new variant of *Babesia* in domestic cats associated with icterus and anaemia
Gad Baneth**,** M.J. Kenny, S. Tasker, Y. Anug, V. Shkap, A. Levi & S.E. Shaw, **HU, Kimron, Pathovet Lab. Vet. Med., Bristol, UK**

4. 10.15-10.30
Excess hemoglobin digestion and the osmotic stability of *Plasmodium falciparum*-infected red blood cells
Virgilio L. Lew, Teresa Tiffert, Miriam Krugliak & Hagai Ginsburg**, HU, Physiological Laboratory, University of Cambridge**

5. 10.30-10.45
Iron chelators as drugs against malaria may pose a potential risk
Jacob Golenser & Abraham Domb, **HU**

6. 10.45-11.00
Early events in cutaneous leishmaniasis: The role of sand fly saliva
Alon Warburg, **HU**

11.00-11.15
7. Vectorial capacity of ticks for West Nile virus
Kosta Y. Mumcuoglu, Mertyn Malkinson, Caroline Banet & Uri Shalom, **HU, Kimron, MoE, Jerusalem**

8. 11.15-11.30

Surveillance of West Nile virus in mosquitoes during the years 2001 and 2002 in Israel
Uri Shalom, Laor Orshan, Hanna Bin, Heather Schnur, Anat Kaufman and Hedva Pener **MoE & MoH, Jerusalem and Tel Hashomer**

11.30-11.45 Coffee break

Session 2: Parasite Genome Wide Analyses (11.45-13.30)

Chair: Prof. Dan Zilberstein, **Technion** and Dr. Varda Shkap, Kimron

9. 11.45—12.25
Guest speaker: Stephen L. Hoffman**, USA**
The potential impact of *Plasmodium*, human and *Anopheles* genomics on the control of malaria

10. 12.25-12.50
Using genome wide approach to study Leishmania development
Dan Zilberstein**, Technion**

11. 12.50-13.10
Diagnosis of local and imported Leishmaniasis by PCR: the new gold standard?
Abedelmajeed Nasereddin, Gabriele Schoenian, Gad Baneth, Dalit Strauss-Ayali, Eli Schwartz, Moshe Ephros, Lionel Schnur & Charles L. Jaffe, **HU, TAU, Technion, Humboldt Univ., Berlin**

12. 13.10-13.30
The *Entamoeba histolytica* genome project
Serge Ankri, **Technion**

13.30-14.30
Lunch

SESSION 3: Clinical Parasitology (14.30-16.40)

Chair: Dr. Eli Schwartz, **TAU** and Dr. Michael Giladi, **TAU**

13. 14.30-15.00
Guest speaker: Stephen L. Hoffman**, USA**
Malarone- The new anti malaria drug: How close to the ideal for malaria prophylaxis and treatment?

14. 15.00-15.20
Unique clinical aspects of Schistosoma infection in travelers
Israel Potasman, Neora Pick, Gila Shazberg, Eli Schwartz, **Bnei Zion Hospital, Haifa**

15.20-15.40

15. Experience with New World cutaneous leishmaniasis in Israeli travelers

Alon Scope, Henry Trau, Gerlind Anders, Yitzhak Konfino, Aviv Barzilay, Eli Schwartz, **Sheba Medical Ctr. Tel-Hashomer, TAU**

15.40-16.00
16. Changing epidemiology of visceral leishmaniasis in Israel
I. Adini, Moshe Efros, J. Chen and C.L. Jaffe, **HU, Technion**

17. 16.00-16.20
Morbidity among Israeli travelers to tropical countries
Michael L. Elkan and Lihi Winner**, Soroka Hospital, Beer-Sheva**

18. 16.20-16.40
Vaccinations for travelers abroad: An update
Shmuel Rishpon**, MoH, Haifa.**

16.40-16.45
Closure remarks
Eli Schwartz, chairman
Israel Society of Parasitology, Protozoology and Tropical Diseases

16.45-17.15
General Assembly of the Society

Note: Due to a technical problem the presentation of Drs. Irene Pankova-Kholmyansky, Zeev Zaslavsky and Eliezer Flescher was not included in the program. Please see abstract no. 19.

ABSTRACTS

1. Molecular identification of prepatent schistosome infection in field-collected snails

Hoffman, O[1], Kariuki, HC[2], Muchiri, EM[2], Abbasi, I[1] and Hamburger J[1].

[1]Helminthology Unit, Hebrew University, Jerusalem, Israel ; [2]Division of Vector Borne Diseases, Ministry of Health, Nairobi, Kenya.

The full value of monitoring prepatent infection has not been assessed because of operational limitations in the tests available for parasite detection in snails. Recently, we identified the DraI repeat sequence of *Schistosoma haematobium* and found it to be group-specific. We have adapted the DraI-based PCR assay for identifying prepatent infections in schistosome-infected snails from *S. haematobium* transmission sites in the south coast of Kenya where animal schistosomes are rare. The host snail in the study area, *Bulinus nasutus*, was identified by morphometric analysis, PCR and PCR-RFLP of COI. Laboratory infected *B. nasutus* from our study area yielded only 12% cercarial shedders and shedding rate in field collected snails was accordingly low- <2%. By contrast to the low rate of cercarial shedding the rate of PCR positive field-collected *B. nasutus* was up to 50%, suggesting a high degree of contamination of the water by *S. haematobium* eggs. A possible correlation with water contact intensity is being investigated. Further, the PCR assay enabled the identification of a substantial proportion (0-72%) of non- host-snails to be PCR positive for schistosome infection, and this was confirmed by exposure of lab-bred non-host snails (*Lanistes*, *Melanoides*, *Bulinus forskalii*) to *S. haematobium* miracidia. The possible role of non-host snails in diverting miracidia from penetrating host snails is therefore suggested. Lastly, infection of laboratory-bred *Bulinus* host snails, followed by crushing and PCR tests, demonstrated that the PCR signals progressively intensify with the advancement of schistosomal development within the snail. This is in line with previous findings on the relation between the intensity of PCR signals and schistosomal DNA quantity when tandemly repeated sequences are amplified. PCR may thus be useful for determining the effect of environmental conditions on miracidial penetration and later development within snails.

2. Complement-inhibitory effect of Schistosome-derived paramyosin

J. S. Deng, Z. Fishelson, D. Gold

Sackler School of Medicine, Tel Aviv University, Ramat Aviv, Tel Aviv 69978

In the past, we have reported that paramyosin of *Schistosoma mansoni* is a CD59-like protein found on the surface of intact schistosomula and adult worms, which bound to purified C8 and C9 of the human complement cascade. Further studies disclosed that paramyosin inhibited Zn2+-induced C9 polymerization in vitro and poly-C9 deposition on rabbit erythrocytes, thereby inhibiting the hemolysis of rabbit and antibody-sensitized sheep erythrocytes by human complement. Similar to polyclonal anti-CD59 antibody, polyclonal anti-paramyosin enhanced in vitro killing of

schistosomula by human complement in a dose-dependent manner. Analysis of paramyosin binding to C9 digested by thrombin or trypsin indicates that paramyosin binds to a C9 site located between Gly245 and Arg391. By competitive binding between human CD59 and recombinant paramyosin to denaturated C9 on cellulose acetate membrane, it was shown that human CD59 inhibited the binding of paramyosin to C9 in a dose-dependent manner, suggesting that the binding site of paramyosin within C9 is identical to the binding site of CD59 or close to it, i. e., between Cys359 and Cys384. Using an anti-CD59 monoclonal antibody which can specifically block the binding site of CD59 to C9, we found that it also directly blocked the binding epitope of paramyosin to C9, indicating that both epitopes are either identical or very similar. We intend now to find the amino acid sequence of the functional epitope of paramyosin, and synthesize a peptide serving as a vaccine molecule against infection by *Schistosoma mansoni* in an animal model.

3. Infection with a new variant of *Babesia* in domestic cats associated with icterus and anaemia

G Baneth[1], MJ Kenny[2], S Tasker[2], Y Anug[3], V Shkap[4], A Levi[5], SE Shaw[2].

[1]School of Veterinary Medicine, Hebrew University. [2]Acarus Unit, School of Veterinary Medicine, University of Bristol. [3] Pathovet Laboratory, Kfar Bilu, Israel. [4]Kimron Veterinary Institute, Beit Degan, Israel. [5]Mevasseret Veterinary Clinic, Israel.

Babesiosis is a tick-borne infection caused by apicomplexan piroplasms described from many species of domestic and wild animals. Naturally occurring babesiosis in domestic cats has been reported mostly from South Africa where the infection is caused by *Babesia felis*, a small *Babesia* that induces anemia and icterus. Sporadic cases of *Babesia* spp. infection in domestic cats have been reported from several countries including France, Germany, Thailand and Zimbabwe.
Large Babesia piroplasms were detected on blood smears from two domestic cats living in the same household in central Israel. Both had a history of exposure to ticks. One cat was admitted with complaints of acute lethargy and anorexia, fever (40°C), anaemia, icterus, and a parasitaemia of 2%. The cat recovered clinically following an intramuscular injection of 2.5 mg/kg imidocarb dipropionate and 10 mg/kg/day of doxycycline orally for 21 days. It tested positive for feline immunodeficiency virus (FIV) antibodies and for *'Candidatus Mycoplasma haemominutum'* (basonym *Haemobartonella felis*) by real-time PCR. The second cat presented with haematuria, was not anaemic, was negative for FIV, and had a low parasitaemia (< 1%). PCR of blood using Babesia specific primers for the 18S rRNA gene were positive for the 2 cats. Sequencing of a 623 basepair segment of the 18S rRNA gene from one cat showed 99.4% identity with Babesia canis. Sequencing of a portion of the internal transcribed spacer region (ITS) which allows sub-speciation of *B. canis*, showed only 70% identity with *B.canis rossi,* and a lower identity with other *B. canis* sub-species. Genetic characterization of the feline *Babesia* isolates is ongoing.
In conclusion, these represent the first cases of feline babesiosis reported in Israel. The infection in the FIV positive cat was associated with fever, anaemia and icterus.

Genetic characterization of one isolate indicates that it might be closely related to *B. canis*.

4. Excess hemoglobin digestion and the osmotic stability of *Plasmodium falciparum*-infected red blood cells

Virgilio L. Lew*, Teresa Tiffert*, Miriam Krugliak** and Hagai Ginsburg**

*Physiological Laboratory, University of Cambridge, Downing Street, Cambridge CB2 3EG, United Kingdom, and **Department of Biological Chemistry, Institute of Life Sciences, The Hebrew University of Jerusalem, Jerusalem 91904, Israel

During their asexual reproduction cycle (~ 48 h) in human red cells *Plasmodium falciparum* parasites consume most of the host cell hemoglobin, far more than they require for protein biosynthesis. They also induce a large increase in the permeability of the host cell plasma membrane to allow for an increased traffic of nutrients and waste products. Why do the parasites digest hemoglobin in such excess? And how can infected red cells retain their integrity for the duration of the asexual cycle when comparably permeabilized uninfected cells hemolyse earlier? To address these questions we encoded the multiplicity of factors known to influence host cell volume in a mathematical model of the homeostasis of a parasitized red cell. The predicted volume changes were subjected to thorough experimental tests by monitoring the stage-related changes in the osmotic fragility of infected red cell populations. The results supported the model predictions of biphasic volume changes comprising transient shrinkage of infected cells with young trophozoites followed by continuous volume increase to about 10 % below the critical hemolytic volume of ~ 150 fL by the end of the asexual cycle. Analysis of these results and of additional model predictions demonstrated that the osmotic stability of infected red cells can be preserved only by a large reduction in impermeant solute concentration within the host cell compartment. Thus, excess hemoglobin consumption represents an essential evolutionary strategy to prevent the premature hemolysis of the highly permeabilized infected red cell.

5. Iron chelators as drugs against malaria pose a potential risk

Jacob Golenser[1] and Abraham Domb[2]

[1]Departments of Parasitology and [2]Medicinal Chemistry, The Hebrew University, Jerusalem Israel

Plasmodial asexual stages differ from most mammalian cells which acquire iron from circulating carriers: they use an “internal labile pool” as the source of iron. Therefore, deprivation of iron by a chelator depends mainly on its penetration into the parasitized erythrocyte. The main parasite target is assumed to be the iron dependent enzyme ribonucleotide reductase. A second possibility is that iron chelators act by dissociating haemozoin-iron that release toxic iron moieties which, in turn, induce the production

of reactive oxygen species (ROS). The parasites are more sensitive to oxidant stress than the host cells. Iron chelation is also considered for malaria treatment because of the possible effect on cerebral malaria which is caused by oxidant stress in an ischemia-like mechanism. A similar concept is related to production of toxic parasite products which are accumulated by phagocytosis of infected cells. This process hampers vital macrophage activation.
Some iron chelators which may reduce parasite load pose a potential risk for individual patients. For example, chelators may redistribute toxic metals to various organs. This may explain the dispute over the role of deferprone which in some patients was beneficial for treatment of iron overload, but in others did not reduce iron overload and increased hepatic fibrosis. Following in vitro success, DFO was suggested for both malaria and tumor therapy. It had a transient beneficial effect on malaria and enhanced the development of Kaposi's sarcoma in a human trial, possibly by affecting immune functions.
At the molecular level, the interrelationship among calcium, glutathione and ferritin may affect the extent of damage caused by ROS. Interference by an iron chelator may affect the level of these molecules in such a way as to tip the balance towards severe malaria. Iron chelators may inhibit deoxyribonucleotide production which is needed for DNA repair, and decrease the expression of cyclins and hypoxia inducible factors. The chelation may lead to G(1)/s arrest, appoptosis and senescence. However, it is assumed that mammals can tolerate the deleterious effects of this therapy for a short period during which the treatment is lethal to plasmodia.
Iron chelators have a tremendous effect on immune functions which in turn alter the outcome of malaria. We have demonstrated a correlation between the in vivo anti-plasmodial effects (in a mouse model) and their effects on immune responses. Only those iron chelators that decreased IL-10, increased γ-interferon and TNF-α levels and did not markedly reduce lymphocyte proliferation and free radical production, were protective.
In conclusion, chelation therapy should be carefully examined on the basis of direct and indirect effects on the parasite and on the patient. In addition, metal selectivity is important because of the risk of depletion of the patients' stores of essential metals.

6. Early events in cutaneous leishmaniasis: The role of sand fly saliva

Alon Warburg

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

The immunology of murine CL caused by *Leishmania major* serves as a model for the study of T-Helper (Th) lymphocyte differentiation. By a fortunate coincidence, its vector's saliva and in particular the role it plays in promoting pathogenesis, were also the focus of some studies. As a result, today we can provide more complete information on early events in leishmaniasis than any other vector-borne disease. Sand flies transmit 100-1000 parasites, a dose that results in immunity when delivered in vitro. However, injected with saliva, even small doses result in lesions that grow faster and reach a larger size than when parasites are injected on their own. In this talk I shall present a summary of the experimental data showing that sand fly saliva

suppresses and subverts the murine immune system thereby, exacerbating the proliferation of Leishmania parasites.

7. Vectorial capacity of ticks for West Nile virus

Kosta Y. Mumcuoglu[1], Mertyn Malkinson[2], Caroline Banet-Noach[2] and Uri Shalom[3]

[1]Department of Parasitology, Hebrew University-Hadassah Medical School, Jerusalem, [2]Department of Virology, Kimron Veterinary Institute, Bet-Dagan and [3]Division of Pest Surveillance and Control, Ministry of the Environment, Jerusalem

In an attempt to discover whether there are vectors other than mosquitoes for West Nile Virus (WNV), ectoparasites were collected from wild and domestic birds, their nests and from poultry houses. Ectoparasites were most abundant in nests and consequently this study is based on their examination. Free-living stages were also collected from vegetation by flagging. Most of the samples were collected in areas were WNV had been detected in mosquitoes in the years 2000 – 2001. Samples were collected from 38 localities in Israel. Bird nests (36 pigeon, 19 sparrows, 210 cattle egret and 7 others), 42 chickens, 20 pigeons and bedding material of geese (7), chickens (43) and penguins (4) were examined. In six localities the areas around human habitations were examined by flagging. One remarkable finding was the presence of a soft tick, *Argas arboreus*, which has not been described before in Israel. Laboratory experiments in Egypt showed that WNV could persist and multiply in its body, and then be transmitted to sentinel chicks. Seven colonies of the cattle egret were localized and 20–50 nests were examined from each colony. All the colonies were infested with this tick and up to 4,040 specimens were isolated from a single colony. Approximately 10,500 ticks were collected. Out of 37 cattle egret chicks examined, 37.8% had serum neutralizing antibodies to WNV.These findings indicate that in localities where WNV is endemic, there are also large numbers of argasid ticks, which could act as vectors and transfer the virus from one bird generation to another and eventually to humans. It is possible that these ticks play an active role in the maintenance of the WNV in Israel, especially in areas and at times where the mosquito populations are low.

8. Surveillance of West Nile virus in mosquitoes during the years 2001 and 2002 in Israel

Uri Shalom[1], Laor Orshan[1], Hanna Bin[2], Heather Schnur[3], Anat Kaufman[4], and Hedva Pener[3]

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A national survey to check adult mosquitoes infected with West Nile virus (WNV) was conducted throughout Israel during 2001 and 2002, following the 2000 West Nile fever outbreak in this country. Mosquitoes were collected with CDC miniature light traps, sorted by species and sex and pooled in groups of 10-50 females each.

In 2001 and 2002 (until November) more than 61,000 specimens, in over 1,450 pools comprising 16 different species, were tested for the presence of WNV by RT-PCR. The dominant species caught and tested were *Culex pipiens* (52% of the total pools) and *Cx. perexiguus* (29%). Each of the other species came to less than 10% of the total pools. A further 9 species were trapped in small numbers but not pooled or tested.

The WNV was detected in *Cx. perexiguus*, *Cx. pipiens*, *Cx. antennatus*, *Cx poicilipes* and *Aedes caspius*. Almost 10% of all *Cx. perexiguus* pools tested positive (42 out of 435 pools) while less than 2% of all *Cx. pipiens* pools tested positive (11 of 777 pools). All the positive pools were found from May to November, with a peak in July-September.

Findings differed between 2001 and 2002. In 2002, three times as many mosquitoes were trapped, classified and tested as in 2001. This could be attributed partly to technical factors (improved collection techniques) and partly to the increase in winter rainfalls and the late spring rainfalls in 2001/2002. Only two species tested positive in 2001, (*Cx. pipiens* and *Cx. perexiguus*) while in 2002, all five of the above mentioned mosquito species tested positive. The infection rate of WNV in *Cx. pipiens* and *Cx. perexiguus* was similar in both years.

These results show that WNV is still prevalent in Israel with high infection rates in *Cx. perexiguus*. Surveillance over a period of several years is necessary to establish changes in patterns of infection rates of WNV in mosquitoes throughout this endemic country.

10. Using genome wide approach to study *Leishmania* development

Dan Zilberstein, Department of Biology, Technion, Haifa

Leishmania genome sequencing is near completion. Currently, 30 Mb of completed and unfinished sequences and 7 Mb of Genome Survey Sequences (GSS) have been submitted to the sequence database. Thus, it is likely that the complete 35 Mb genome sequence will be available by June 2003. Annotations of the *L. majorF* genomic sequence revealed more than 5000 protein-coding genes, of which only 30% are similar to known genes. Several laboratories have developed and are probing *Leishmania* DNA microarrays. Subsequent to *Leishmania* genome sequencing, several laboratories have initiated analysis of its proteome, using 2 dimensional gel electrophoresis and/or isotope-coded affinity tagging (ICAT) technology. The results of both *Leishmania* genome and proteome sequences have been published in the genome network web site. Using a host-free system for *L. donovani* promastigotes to amastigotes differentiation, we have analyzed changes in mRNA abundance and in the level of cellular proteins, using microarray for gene expression and 2 dimensional gel electrophoresis and ICAT-MS for proteins. The results revealed that 1.18% of cellular proteins are up-regulated in amastigotes and 0.9% that are down-regulated

during this process. Our studies revealed transient changes during the initial steps of promastigote to amastigote differentiation.

11. Diagnosis of local and imported leishmaniasis by PCR: the new Gold Standard?

Abedelmajeed Nasereddin[1], Gabriele Schönian[2], Gad Baneth[3], Dalit Strauss-Ayal[3], Eli Schwartz[4], Moshe Ephros[5], Lionel Schur[1], and Charles L. Jaffe[1]

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[2]Institute of Microbiology and Hygiene, Humboldt University, Charité, Berlin, Germany
[3]Koret School of Veterinary Medicine, Hebrew University of Jerusalem, Israel
[4]Sheba Medical Center, Tel-Hashomer, and the Sackler School of Medicine, Tel Aviv University, Tel Aviv
[5]Department of Pediatrics, Carmel Medical Institute of Technology, Haifa, Center, Faculty of Medicine, Technion-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 and identify each species directly in the clinical samples without parasite culturing. 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 was not possible by the former approach. When a nested ITS1-PCR was used its sensitivity equaled the ssu-rDNA-PCR. Furthermore, digestion of ITS1 amplicon with the restriction enzymes *Cfo*I or *Hae*III distinguished all medically relevant *Leishmania*. ITS1-PCR was used to diagnose 162 local and imported suspected cases of leishmaniasis in Israel, the Palestinian Authority and Germany. 113 cases were positive by PCR and species identification was possible in 110 samples. *Leishmania* DNA was also amplified and identified at the species level from archived non-stained and Giemsa stained microscope slides. Recent molecular techniques should increase the sensitivity and reliability of diagnosis and identification, supplementing existing serological methods in epidemiological and clinical studies.

12. *Entamoeba histolytica* genome project

Ankri Serge

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Entamoeba histolytica is an early branching human enteric parasite that infects an estimated 500 million people and is a significant cause of morbidity and mortality. The Institute of Genomic Research (TIGR) and the Sanger Center are currently sequencing the 20 MB *E.histolytica genome* by following a whole genome shotgun strategy. Around three years after the initiation of the *Entamoeba histolytica* genome project, an approximately 7-fold sequence coverage assembly of the *Entamoeba histolytica* genome has been achieved. The presence of multiple copies of an episome encoding the ribosomal DNA (rDNA) genes has complicated the sequencing process because ~15% of the resulting sequence corresponds to this episome. To deal with this problem, a library, which is relatively free of rDNA circles, has been derived at the Sanger Centre by linearizing the rDNA circles with a restriction digest by *Ppo*I and then physically removing the linearized DNA from a pulse field gel. Among the interesting findings that have resulted from the initial characterization of the sequences, is the repetitivity of the genome with 40% of the sequence reads assigned to repetitive elements. Introns are found in 15% of genes encoding proteins. This is higher than expected because only a few *E. histolytica* genes with introns have been identified previously. Furthermore, 13% of the 49000 sequences examined contained transfer RNA (tRNA) genes, most of which are located in tandem arrays. The predominate location of the tRNA arrays at the telomeres could account for the variation in sizes of the homologous chromosomes. Another interesting finding has been the identification of a gene family of >100 proteins containing the CXXC motif, which includes the intermediate subunit of the *E. histolytica* Gal/GalNAc lectin. Full annotation of the genome is still not available but a blast search on the *E.histolytica* database is possible at directly from the NCBI blast home page (http://www.ncbi.nlm.nih.gov/BLAST). One direct application of this genome project is the recent production of DNA microarrays and the identification of new virulence determinants of this important human parasite.

14. Unique clinical aspects of Schistosoma infection.

I. Potasman[1], N. Pick[1], G. Shazberg[2], E. Schwartz[3]

[1]Infectious Diseases and Travel Medicine, Bnai Zion Medical Center and Technion, Haifa, [2]Bikur Holim Hospital, Jerusalem, and the [3]Geographical Medicine, Sheba Med. Ctr., Tel Aviv University.

The classical presentation of schistosomiasis is well known. The purpose of this communication is to highlight some unusual features of the disease. Along with the growth of Israeli tourism to exotic destinations, we have seen a few cases of schistosomiasis presenting with hematospermia or prolonged pulmonary involvement. Diagnosis in the first cases was made by sperm examination or prostate biopsy.

Conventional treatment was unsuccessful. The diagnostic and therapeutic implications will be discussed.

15. Experience with New World cutaneous leishmaniasis in Israeli travelers

Alon Scope [1], Henry Trau[1], Gerlind Anders[3], Yitzhak Konfino[1], Aviv Barzilai[1] and Eli Schwartz [2]

[1]Department of Dermatology and [2]The Center for Geographic Medicine, Sheba Medical Center, Tel Aviv University; [3]Kuvin Center for Infectious and Tropical Diseases, Hadassah School of Medicine, The Hebrew University, Jerusalem.

Travel to South and Central America has become increasingly common among young adults. *Leishmania braziliensis*, which is endemic in the Americas, causes unsightly cutaneous lesions and may be complicated by severe mucosal disease. In the years 1998-2002, we treated 15 patients with imported New-world Leishmaniasis, mostly (93%) acquired in the Bolivian Amazon basin. Fourteen patients presented with cutaneous lesions and one patient with mucocutaneous disease of the upper airway. Five patients (33%) had regional lymphadenopathy. Diagnosis of Leishmaniasis was confirmed histologically. PCR was performed in eleven patients and identified *L. braziliensis* infection in ten of them. In the patient with mucosal disease, PCR was negative but culture yielded *L. braziliensis*. Of thirteen patients followed-up for over one year, ten patients (77%) achieved clinical cure after a single course of intravenous Sodium Stibogluconate (SSG) and three patients (23%) needed an additional course. The patient with mucosal disease had nearly complete resolution of lesions after treatment with IV SSG. Treatment was well tolerated clinically and laboratory abnormalities, mainly elevation of liver enzymes (54%), were reversible. In conclusion, our experience demonstrates that PCR is a useful tool in establishing species diagnosis of Leishmaniasis, and that SSG is a safe and overall effective treatment for *L. braziliensis* infection.

16. Asymptomatic visceral leishmaniasis in Northern Israel

Adini, I.,[1] M. Ephros,[2] J. Chen,[1]and C. L. Jaffe[1]

[1]Department of Parasitology, Kuvin Centre for the Study of Infectious and Tropical Diseases, The Hebrew University-Hadassah Medical School, Jerusalem
[2]Department of Pediatrics, Carmel Medical Center, Faculty of Medicine, Technion-Israel Institute of Technology, Haifa

Human visceral leishmaniasis seroprevalence in Northern Israel was compared to a non-endemic region of Israel. Asymptomatic infection with *Leishmania infantum* was identified using an enzyme-linked immunosorbent assay. Positive sera were more prevalent in the endemic (2.97%) compared to the non-endemic (1.01%) region ($p=0.021$). Parasite exposure is higher than expected despite the small number of

clinical cases suggesting that factors other than infection per se influence clinical outcome.

17. Incidence and precipitating factors of morbidity among Israeli travelers abroad

Michael L. Alkan and Lihi Wiener

Soroka Hospital, Beer Sheva

Background: Many Israelis are traveling to third world countries every year. Some of them will suffer from health problems during or after their trip. During the last decade several travelers' clinics have been functioning in Israel, providing advice and vaccinations for travelers.
Goals: To draw a profile of the Israeli traveler, including morbidity and risk factors during travel. To assess the efficacy of the advice given to travelers at one such clinic.
Methods: Retrospective study, contacting travelers after their return, responding to a questionnaire during the years 1996-1997.
Results: The mean age of the travelers was 26.4±9.4 years, the mean duration of stay was 14.7±13.4 weeks. Journey destinations: 59.5% South-East Asia, 30% South America, 10.5% Africa. 73% of the travelers did not have previous experience in traveling to developing countries. Most of them used very basic service during their journey – 83% used mostly public buses as a mean of transportation and 79% used mainly guest-houses for accommodation. 140 travelers (70% of the total population) reported some health impairment during the journey, the mean duration of the diseases was 8±9.1 days. The most frequent problems reported were: GI tract symptoms (43% of the total diseases), fever and respiratory tract symptoms (25%) and injuries (10%). 65 travelers (32.5% of the total population) visited a physician, 8 travelers (4%) were admitted to hospital, 39 (19.5%) consulted a physician after their return. We found a correlation between non-compliance with keeping food hygiene and illness ($p=0.008$). Multiple logistic regression analysis of any single disease showed a correlation with duration of trip ($p=0.002$) and keeping food restrictions ($p=0.04$). Higher compliance with the treatment correlated with: older ages ($p<0.0001$), shorter duration of trip ($p=0.01$) and previous experience in traveling in developing countries ($p=0.0001$).
Conclusions: The Israeli traveler is younger, less experienced, and more daring in his itinerary than other travelers. Morbidity correlates with non compliance with recommendations, especially regarding food safety.

19. Ceramide induces *Plasmodium falciparum* death via a decrease in the parasite glutathione levels

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In mammalian cells, ceramide mediates death by chemotherapeutic drugs and radiation. We have previously reported that ceramide induces the death of *Plasmodium falciparum* (*P. falciparum*). In the present study, we analyzed the mechanism of this malaricidal effect. Ceramide can induce death of cancer cells by decreasing glutathione levels. Ceramide induced dose- and time-dependent depletion of glutathione in *P. falciparum* parasites. N-acetylcysteine, a precursor of glutathione, abolished the cytotoxic effect of ceramide. Thus, ceramide can mediate death of *P. falciparum* parasites, by decreasing their glutathione levels. We evaluated the pharmacological relevance of this mechanism employing two drugs as models. The antimalarial drugs artemisinin and mefloquine induced the death of *P. falciparum* parasites by sphingomyelinase-generated ceramide, and by decreasing parasites glutathione levels. In conclusion, a decrease in glutathione levels mediates ceramide-induced signaling resulting in the death of malarial parasites.