ABSTRACTS

Tuesday, December 14, 2010

08:00 - 09:00 **Registration**

09.00 - 10.45 **Session 1: Plenary and Filarial Infection**

Chairs: Bibiana Chazan & Gad Baneth

09.00 - 09.35 *Lisette van Lieshout (Holland).* **Multiplex real-time PCR as a diagnostic tool to study the epidemiological distribution of helminths in low-income countries**

09.35 - 10.05 *Asrat Hailu (Ethiopia).* **Onchocerciasis and lymphatic filariases in Ethiopia**

10.05 - 10.25 *Yuval Gottlieb.* **Wolbachia endosymbiont in filarial nematodes**

10.25 - 10.45 *Eyal Meltzer, Eli Schwartz.* **Acute travel related filarial diseases**

Multiplex real-time PCR as a diagnostic tool to study the epidemiological distribution of helminths in low-income countries

Lisette van Lieshout

Department of Parasitology; Leiden University Medical Centre, the Netherlands

Classically, diagnosis of intestinal helminths and *Schistosoma* species is performed by microscopic examination of a stool and urine sample. Although relatively simple to perform, microscopy has several important disadvantages, especially when used for large-scale population-based surveys in parasite endemic regions. For example *Schistosoma*, hookworm and *Strongyloides* infections are easily missed due to low excretion of eggs or larvae and the high day-to-day variation. The use of specific laboratory techniques such as a Baermann-procedure, glycerine sedimentation or copro-culture may improve the diagnostic yield, but this substantially increases the workload. Collection and examination of consecutive samples will further improve detection rates, but this again is more laborious and often reduces compliance within the study population. As an alternative to microscopy, our group developed and implemented during recent years a number of multiplex real-time PCR assays to detect and quantify helminth-specific DNA in small volume stool or urine sample. These assays were designed to achieve maximal sensitivity in combination with virtually 100% specificity, validated with a range of control samples (n=145). In this presentation the diagnostic potentials of multiplex real-time PCR in epidemiological and clinical research will be illustrated with data from studies performed in Ghana, Kenya, Mozambique and Malawi, focusing on the diagnosis of *Schistosoma*, hookworm and *Strongyloides*. Intensity of infection, normally reflected by the number off eggs or larvae seen in stool or urine, can be quantified by parasite-specific DNA loads. With the use of a high throughput platform, multiplex real-time PCR can be used to map the distribution of several helminth species simultaneously and to monitor intervention programmes such as mass drug treatment. Although reagents costs of PCR are higher as compared to microscopy, the use of a single (ethanol preserved) faecal sample simplifies operation and complex organization of labour-intensive field studies, in particular in remote rural areas. Moreover, real-time PCR technology is becoming rapidly available in centrally located research centres within parasite endemic regions, omitting the need to transport samples outside the country.

Onchocerciasis and lymphatic filariases in Ethiopia

Asrat Hailu Mekuria, PhD

Faculty of Medicine, Addis Ababa University, Addis Ababa, Ethiopia; E-mail: a_hailu@hotmail.com

Onchocerciasis and lymphatic filariasis (LF) are common filarial diseases that cause serious damage to skin and the lymphatic system often leading to physical dysfunction, disability and social stigma. These diseases are widespread in Ethiopia, especially in the western regions of the country. Onchocerciasis in Ethiopia is transmitted by *Simulium damnosum complex* and *Simulium woodi ethiopiense.* Based on the results of Rapid Epidemiological Mapping of Onchocerciasis (REMO), onchocerciasis is prevalent in 6 administrative regions; 4 of which are either meso- or hyperendemic. These areas extend from Takaze valley in the northwest to the Omo valley in southwest, with varying levels of endemicity. Data on prevalence of onchocerciasis, intensity of infection, and age/sex related distribution of the infection are available for selected endemic localities. Presently, 3 million people are infected and 10 million are at risk. The main symptoms of the disease in Ethiopia are dermal manifestations, characterized by intense itching and thickening of the skin. Hanging groin and depigmentation of the skin are also common especially in areas of long-standing endemicity. Ocular onchocerciasis is not uncommon, while blinding onchocerciasis is rare or absent. Onchocercal skin disease is associated with significant economic losses and school absenteeism. Currently, it is estimated that more than 10 million Ethiopians are at risk of onchocerciasis and three million are infected.. Community Directed Treatment with Ivermectin (CDTI) has been in place since 2000, and was rolled out to many of the endemic areas. Attempts to monitor the impact of MDA are ongoing. *Wuchereria bancrofti*, is the species that causes LF in Ethiopia. The disease is transmitted by anopheline mosquitoes: *Anopheles gambiae* complex and *Anopheles fenestus*. Studies carried out in the seventies and nineties have implicitly restricted the geographical limits of LF to the lowlands of southwestern Ethiopia, especially around Gambella Region. A wider geographical distribution of LF was suggested by ecological indicators, including distribution of mosquitoes. Elephantiasis of the feet, mostly considered to be of non-filarial origin (podoconiosis) is a common disease among poor rural communities of Ethiopia, whose geographical overlap with LF has not been determined. An ongoing epidemiological study using the immunechoromatographic test (ICT) has revealed a wider geographical distribution in western region, mostly overlapping with onchocerciasis. So far, 33 of 112 Districts covered by the surveys were confirmed to be endemic and eligible for the contemplated elimination program. The surveys also demonstrated high geographical clustering and variation in prevalence of antigenaemia, ranging from less than 3% to more than 50% in endemic localities. A tentative distribution map has been drawn using the utilities of GIS. Sentinel-site based morbidity and prevalence studies are planned, to facilitate the effective implementation of the elimination program.

Wolbachia endosymbiont in filarial nematodes

Yuval Gottlieb

Koret School of Veterinary Medicine, The Hebrew University of Jerusalem. The Robert H. Smith Faculty of Agricalture, Food, and Environment, Rehovot.

Endosymbiotic bacteria of the genus *Wolbachia* are probably the most prevalent bacteria within arthropods causing diverse phenotypic effects to their hosts. This alpha-proteobacteria also infects many filarial nematodes, and is essential for the worm development, viability and fertility. Filarial nematodes are the cause of human and other mammal filariasis, in which the most pathogenic diseases, lymphatic filariasis and onchocerciasis, comprise a major cause of global morbidity. In addition to its obligatory nature in filarial nematodes, *Wolbachia* also contributes to inflammatory disease pathogenesis. The nematode dependency on its endosymbiont is used for anti-bacterial based therapy which is effective but not practical. Therefore, other strategies based on comparative genomics, bioinformatics and experimental analysis are being developed, in order to specifically target molecules that interfere with this mutualistic interaction.

Acute travel related filarial diseases

Eyal Meltzer, Eli Schwartz

Sheba Medical Ctr., Tel Hashomer

Filarial infections are uncommon in travelers. Although filarial diseases are endemic in many regions, there is an increased risk with travel to Africa. We present two cases of filarial infection in Israeli travelers, returning from a protracted stay in Africa. The first case presented as an acute lymphedema of the upper extremity. The second presented as recurrent migratory edematous lesions. In both patients significant blood eosinophilia existed. In both cases the infection was not parasitologically patent, and the diagnosis relied on serology. Diagnostic delays occurred in both cases – a common occurrence in travel related filariasis. A review of the current literature will be presented. Increased awareness of the clinical manifestations of early filarial infection and an algorithmic approach to blood eosinophila in the returning traveler may decrease diagnostic delays in future cases.

11.15 – 13.00 Session 2: Geohelminthes

Chairs: Galia Rahav & Daniel Gold

11.15 – 11.40 *Avner Reshef.* **Does chronic helminthic infection confer protection against allergic disease?**

11.40 – 12.05 *Zvi Bentwitch.* **Eradication of neglected tropical diseases in Ethiopia - An Israeli initiative**

12.05 – 12.25 *Haim Maayan.* ***Strongyloides stercoralis*** **- Hyperinfection in Israelis emigrating from endemic areas**

12.25 – 12.40 *Esther Marva, Tzippi Cohen, Liza Grinberg, Tamar Grossman.* **Serological evidence for the presence of toxocariasis in Israel**

12.40 – 13.00 *Tamar Grossman, Tzippi Cohen, Liza Grinberg, Esther Marva.* **Diagnostic methods in Israel: current state and future plans**

Does chronic helminthic infection confer protection against allergic disease?

Avner Reshef

Allergy, Immunology and Angioedema Center, Sheba Medical Center, Tel Hashomer

There is an epidemic rise in immunologic and atopic diseases (i.e. asthma, allergy, autoimmune diseases) in Westernized societies. Atopic state is defined by a cluster of few allergic diseases in the same person, i.e., rhinitis, asthma, food allergy and atopic dermatitis. It is a hyperactive immune response, involving environmental factors (allergens), production of allergen-specific IgE antibodies, Th2 cytokines (IL-4, IL-5, IL13), mast cells, basophiles and eosinophiles. Helminth parasitic infections manipulate the Th2 arm of the immune system, to induce an asymptomatic, chronic, tolerant, infectious state in the host. Such mechanisms prevent immune recognition and expulsion of larvae and adult forms of the parasite and insure its survival. Immune mechanisms common to chronic helminth infection and atopy co-exist in rural populations infested by parasites. Studies which employed active interventions, like controlled de-worming of large populations in Brazil, Venezuela, Vietnam and Gabon, demonstrate a tendency toward increased prevalence of allergic sensitivity as well as clinical asthma and eczema. This conforms the 'Hygiene hypothesis'' which proposes that reduced exposure to microbes, parasites and viruses by a change of life-style, healthier conditions, antibiotics, vaccines etc, may give rise to a biased immune response manifested by increased allergy, inflammation and autoimmune diseases. Although previous epidemiologic and cross-sectional studies, as well as systematic review of the literature and meta-analysis, gave conflicting results, recent studies provide a strong case for a regulatory role of chronic helminth infections, in down-regulating sensitization and preventing an active allergic immune response. This presentation will discuss the epidemiologic evidence and the immune mechanisms involved in chronic parasitic infections, and point at possible future therapeutic avenues. Using modern technologies, it may be possible to employ molecules expressed during chronic helminth infection to induce a tolerant state in the allergic host.

Eradication of neglected tropical diseases in Ethiopia - An Israeli initiative

Zvi Bentwich

Center for Tropical Diseases and AIDS, Faculty of Health Sciences, Ben Gurion University, Beer Sheba

Background: Neglected Tropical Diseases (NTDs) and particularly helminth infections have a profound effect on the immune system. We have previously suggested that it therefore has a significant effect on the pathogenesis of the major epidemics –AIDS, Tuberculosis and Malaria, in Africa. We have performed several studies in Ethiopia and in Israel that have lent support to this idea. A growing awareness of NTDs has become evident in the world more recently, and active efforts to eradicate them are being carried out in developing countries. Our center joined these efforts and has initiated a number of such projects in Ethiopia .

Methods: Three pilot intervention projects for eradication of soil transmitted helminthes (STH) and schistosomiasis, were initiated in the Rift Valley, and in Addis Ababa, reaching a population of 30,000 people, in the spring of 2008, and a larger intervention project, in the city of Mekele, planned to reach a population of 250,000, in October 2008. In all these projects a comprehensive approach combining health education, community participation, improved water sanitation and hygiene, have been developed and implemented, together with mass drug administration (MDA), two to three times a year. The efficacy of the intervention has been evaluated by pre and post intervention surveys in which the prevalence of the various STH and Schis was determined, as well as by questionnaires, to evaluate knowledge attitudes and practice (KAP) of the population .

Results: Eight months post the last intervention, the prevalence of STH declined from a mean of 20 % to below 5% and that of schistosomiasis, in locations where it was above 80%-to below 20%. Infection burden determined by Stool's Eggs per Gram (EPG) also showed a sharp decline to minimal levels. KAP questionnaires results also showed a clear improvement though comparison of pre- and post- determinations was not available at all sites. Reaction of the communities to the intervention were very positive and resulted in demanding upscaling and spread of these initiative to neighboring communities .

Conclusions: 1) Eradication of STH and schistosomiasis is possible using a comprehensive approach which combines health education, involvement and commitment of the community and mass drug administration. 2) Changes in attitude and practice is possible and is critical for success of such efforts. 3) The long term efficacy of such initiatives has to be critically determined in order to reach high levels of success. 4) Long term intervention on a national level should be made in order to cover the whole country. 5) The impact of deworming on various parameters of immunity and immune mediated diseases should be studied in this setting.

Strongyloides stercoralis - Hyperinfection in Israelis emigrating from endemic areas

Haim Maayan

Department of Medicine E Chaim Sheba Medical Center, Tel Hashomer

Background. *Strongyloides stercoralis* infection is endemic in some parts of the world where Israelis emigrate from. The hyperinfection syndrome is common in immunocompromised patients especially in those treated with steroids. The disease is fatal when it is unrecognized early on.
Methods. Two patients were admitted to our ward one with a fulminant fatal disease and the other with a severe disease. The clinical and laboratory data is shown.
Results. The two patients were diagnosed to have *Strongyloides stercoralis* infection. Both were treated with corticosteroids for a few months. Both had eosinopenia while on steroids. One had slight eosinophilia prior to initiation of steroids. Diarrhea was manifested in both patients. Diagnosis was done in the first patient by BAL and later on by intestinal biopsy and in the second patient by colonoscopy and biopsy.
Prophylactic therapy for those prone to this fatal syndrome and endeavors to diagnose its existence prior to starting steroid therapy will be discussed
Conclusions. *Strongyloides stercoralis* hyperinfection syndrome is a fatal disease in patients harboring this helminth years prior to the fatal syndrome. We must be aware of this syndrome in patients from endemic areas and should prevent this severe disease.

Serological evidence for the presence of toxocariasis in Israel

Esther Marva, Tzippi Cohen, Liza Grinberg, Tamar Grossman.

Ministry of Health, Central Laboratories, Reference Parasitology Laboratory. (Email: Esther.marva@eliav.health.gov.il)

Background: Toxocaraiasis is a disease caused by the ascarid nematodes *Toxocara canis* or *Toxocara cati*. The definitive host of Toxocara is domestic dogs and cats, in which they live as adults. In a human host, infection can occur by ingesting viable embryonated eggs from contaminated sources. Infective larvae hatch after ingestion of eggs, and wander throughout the body for months or up to several years, migrating through the liver, lungs, and central nervous system. There are two main syndromes: Visceral larva migrans (VLM) and ocular larva migrans (OLM) restricted to the eye and the optic nerve. Far more common is non-classic toxocariasis, which may manifest with only some of the clinical features found in visceral larva migrans, especially wheezing, pulmonary infiltrates, and eosinophilia. In this presentation the current state of toxocariasis in Israel is introduced, based on serological tests to sera received in the Reference Parasitology Laboratory from patients suspected to have toxocariasis.
Methods: Serum samples were tested by enzyme immunoassay EIA – IVD commercial kit using *T. canis* excretory-secretory (TES) antigens from infective-stage larvae. Total immunoglobulin antibodies were measured.
Results: Between January 2004 and September 2010, 450 serum samples were examined. 44 human samples were found to be positive for Toxocara, among which, 21 were with high eosinophilia. 31 were males and only 9 were females. Most of the positive cases were children under the age 15; 5 were immigrants from Ethiopia, 2 were immigrants from Russia, 1 was a foreign worker, 7 were from Arab rural villages, 1 case was from a psychiatric hospital and 1 from a girl with pica syndrome. **Conclusions:** Recognition of toxocariasis as a common parasitic disease in Israel has to be further investigated and to be taken into consideration with patients suffering from toxocariasis symptoms such as wheezing, pulmonary infiltrates, and eosinophilia.

Diagnostic methods in Israel: current state and future plans

Tamar Grossman, Tzippi Cohen, Liza Grinberg, **Esther Marva**

Ministry of Health, Central Laboratories, Reference Parasitology Laboratory (Email: Tamar.grossman@eliav.health.gov.il)

The Israeli Parasitology Reference lab provides help in diagnosis of parasites to peripheral labs, validation of findings and first line diagnosis when needed. Infection with parasites is detected by means of finding evidence for the presence of parasites in clinical samples and/or serological testing for the presence of specific antibodies. Microscopy by trained personnel is considered the gold standard for parasite identification, as stated by the CDC reference laboratory. In addition to microscopy, our lab employs kits that target parasite antigen for the detection of *Entamoeba histolytica*, *Giardia lamblia* and *Cryptosporidium spp.* Recent publications have emphasized the benefits of newly developed RT-PCR methods. During the past two years, identification of plasmodium is performed mainly by using a RT-PCR method, in addition to microscopy of blood samples. The results will be discussed. Our answer influenced the primary lab diagnosis in about 20% of the cases. In some of the *P.ovale* positive samples further evaluation by sequencing was needed due to the existence of mutations in the probe attaching region. In addition, RT-PCR methods for the detection of *Strongyloides stercoralis*, *E. histolytica*, *G. lamblia* and *Cryptosporidium spp.* in stool samples are being implemented in the lab. Eight different serology tests are available currently, including newly introduced tests against *Trypanosoma cruzi*, *Tenia solium* and *S. stercoralis*. Overall our lab is in the stage of implementing new methods and favors an integrated approach for identifying parasite infection.

14.00 – 15.30	**Session 3: Food-borne helminthic diseases** **Chairs: Iris Ostfeld & Esther Marva**
14.00 – 14.20	*Shulamit Loewenthal, Shifra Ken-Dror, Orly Sagi.* **Laboratory diagnosis of helminthic infestations in the Clalit Health Services**
14.20 – 14.40	*Alex Marcovics.* **Prevalence and epidemiology of cysticercosis and trichinellosis in Israel**
14.40 – 15.00	*Dikla Revivo.* **Taeniasis among hospitalized patients in the western Galilee region.**
15.00 – 15.20	*Eyal Leshem, Iris Kliers, Rebekah Karplus, Mati Bakon, Moshe Gomori, Tal Zucker, Israel Potasman, Eli Schwartz.* **Neurocystocercosis in Israel**
15.20- 15.30	**Discussion**

Laboratory diagnosis of helminthic infestations in the Clalit Health Services

Shulamit Loewenthal[1], Shifra Ken-Dror[2] and Orly Sagi[3]

[1]Central Laboratories, Tel Aviv, [2]Nesher Laboratories, Haifa, [3]Soroka Hospital, Beer Sheva

Infestation by helminthes such as *Schistosoma spp.*, hook worms, *Strongyloides stercoralis* was always considered as an imported medical condition, whereas those by *Entrobius vermicularis, Taenia spp* and *Ascaris lumbicoides* having rather a minor medical significance. The present findings, gathered in our laboratories between the years 2007-2010 and after reviewing each case showed that they are in accordance with the above mentioned suppositions.

Prevalence and epidemiology of cysticercosis and trichinellosis in Israel

Alex Marcovics

Department of Parasitology, Kimron Veterinary Institute, P. O. B. 12, Beit Dagan, 50250 Israel

Human behavior, culture, religion and eating habits strongly influence the prevalence and epidemiology of most parasitic diseases, especially the foodborne zoonoses. *Cysticercus cellulose* was never diagnosed in Israel due to prohibition of consumption of pork by the Jewish and Muslim religions, as well as restricted and industrial methods of domestic pork raising. The prevalence of *Cysticercus bovis* is also very low and sporadic. Based on the reports of the Veterinary Services, the annual incidence ranges between 0.1% – 0.4%. Higher rates of infection were recorded in imported beef cattle for fattening or direct slaughter from Cyprus and Australia (1.3% and up to 4.2%, respectively). Only 2 outbreaks of *Cysticercus bovis* were recorded in the last 3 decades and in both cases the source of infection was a feedlot worker or a worker employed on a construction in close proximity to the feedlot. The first record of *Trichinella* infection in Israel was reported in humans in 1971, in an outbreak that occurred in Elaboun, a Christian village near Nazareth where 39 people were severely affected. The second case was reported in 1991 where three members of one family became severely ill. In both cases, the source of infection was a wild boar from the Golan Heights and the Carmel mountains. During the following decade, over 70 hunters or foreign workers were infected in 7 unrelated events. Four outbreaks of trichinellosis were reported in 2002 alone. A total of 123 Thai workers were affected in these 4 outbreaks, of which 68 were hospitalized, some of them for a long period. Since the first positive diagnosis of *Trichinella* in a wild boar in 1992, up to one thousand wild boars are annually examined for the presence of *Trichinella* infection. The annual incidence of the infection in the last 10 years ranged from 1.06% in 2007 to 4.98% in 2005, with an average rate of 2.26%. In addition, samples of diaphragms from 425 red foxes and 631 golden jackals were examined for *Trichinella* larvae during the years 2002 - 2009. The samples were collected from animals submitted for rabies diagnosis to the Kimron Veterinary Institute. *Trichinella* larvae were found in 131 (20.8%) jackals but only in 12 (2.8%) foxes. *Trichinella* infected animals were detected only in the northern parts of Israel and Jerusalem mountains with similar, high infection rates. The infection rates in the Golan Heights, Carmel and Jerusalem mountains were 36.7%, 27.3% and 27.5%, respectively. A lower rate of infection was diagnosed from the Galilee (12.5%) and only recently the infection was diagnosed in 3 jackals from Mitzpe Ramon. On the other hand, all 177 foxes and 50 jackals from the central area, as well as 118 foxes and 111 jackals from southern Israel (excluding the above mentioned 3 positive), were found negative for infection. These data of high prevalence of *Trichinella* infection in wild carnivores in the northern and mountain areas of Israel confirm the findings of high prevalence of trichinosis in wild boars on the Golan Heights (9.2%) and Western Galilee (8%) and the absence of *Trichinella* infection in wild boars from the central coastal plain and southern Israel.

Taeniasis among hospitalized patients in the western Galilee region

Dikla Revivo

Clinical Microbiology Laboratory, Western Galilee Hospital, Nahariya

Background: Taenia species are common Cestode parasites of humans worldwide, causing infections ranging from minimal symptomatology to invasive tissue damages. Taeniasis is not a reportable disease and little is known about infestations by these worms in Israel. In this study, infestations caused by Taenia among patient in the Western Galilee region, is reported.
Methods: Retrospective electronic chart review of patients hospitalized at the Western Galilee Hospital and given a diagnosis of Taenia infestations between the years 2007-2009.
Results: 11 patients infested with Taenia species were found. Their mean age was 37.5 years (age range: 12-67 years). All patients were non-Jewish and resided in villages of the Western Galilee area; four patients resided in the same village. Patients were admitted to the hospital with medical conditions non-related to Taenia infections. Laboratory results were non-specific and no eosinophilia was present. *Taenia saginata* was diagnosed in 9 out of 11 patients by proglottids passed in stool. Invasive tissue infections were not evident. Six patients were treated with praziquantel and no adverse events were recorded.
Conclusions: This retrospective series of patients infected with Taenia is the largest reported in Israel. All patients were admitted due to non Taenia-related causes while invasive infestations by this parasite in patient were not evident. Traditional, regional, undercooked meat dishes may account for the observation that infestations occurred mainly in the non-Jewish population.

Neurocysticercosis in Israel

Eyal Leshem, Iris Kliers, Rebekah Karplus, Mati Bakon, Moshe Gomori, Tal Zucker, Israel Potasman, Eli Schwartz

The Chaim Sheba Medical Center; Assaf Harofeh Medical Center; Hadassah-Hebrew University Medical Center; Bnai Zion Medical Center

Background: Neurocysticercosis is the most common cause of adult onset seizures in developing countries. In recent years with the rise in the number of immigrants to developed countries and travelers to endemic areas, neurocysticercosis is increasingly diagnosed in non-endemic countries.
Aims of the study: We describe the clinical and epidemiologic characteristics of patients diagnosed with neurocysticercosis in Israel
Methods: A retrospective national survey of patients diagnosed with neurocysticercosis during 1994-2009. Clinical and epidemiologic data were recorded. Case definition consisted of roentgenologic, serologic and pathologic features.
Results: In all, 17 cases of neurocysticercosis were diagnosed in Israel during the study period. Nine (53%) cases were diagnosed in travelers to endemic areas, and six (35%) in immigrants from endemic areas. Two cases were native Israelis who had never traveled to an endemic area. Most immigrants suffered from multiple brain lesions. Two immigrants underwent brain biopsy.
Conclusions: This is the first report of the clinical and epidemiologic characteristics of patients diagnosed with neurocysticercosis in Israel. Neurocysticercosis must be included in the differential diagnosis of seizures, headache or neurologic deficit with single or multiple brain lesions especially in immigrants from endemic countries. Invasive procedures may be obviated by appropriate clinical diagnosis, imaging and serology.

Wednesday, December 15, 2010

09:00 -10:30 **Plenary lectures**

Chairs: Alon Warburg & Eli Schwartz

09:00 -09:30 *Rick Hodes (USA/Ethiopia).* **Medical care for the indigent in Ethiopia, far more than primary care**

09:30 -10:00 *Asrat Hailu (Ethiopia).* **Leishmaniases in Ethiopia**

10:00 -10:30 *Gaby Zollner (USA).* **Comparative host-seeking behavior of biting flies and efficacy of personal preventive measures**

10:30 - 11:15 **General assembly**

Honoring Dan Shapira and Zalman Greenberg

Zalman Greenberg. **Israel Jacob Kligler – The story of a little big man"**

Medical care for the indigent in Ethiopia, far more than primary care

Rick Hodes (USA/Ethiopia)

Abstract not available

Leishmaniases in Ethiopia

Asrat Hailu Mekuria, PhD

Faculty of Medicine, Addis Ababa University, Addis Ababa, Ethiopia; E-mail: a_hailu@hotmail.com

Leishmaniases in Ethiopia are a consequence of parasitic infections by *L. donovani* and *L. aethiopica*, causing visceral or cutaneous diseases respectively. Visceral leishmaniasis (VL) causes significant morbidity or mortality in affected communities, while cutaneous leishmaniasis (CL) results in mutilating lesions of mucosal tissue or the skin. In endemic settings, the two diseases rarely overlap in their geographical distribution, as VL is limited in lowlands and CL in the highlands. Estimates on the burden of these diseases in Ethiopia show that over 4,000 cases of VL; and 7,000 cases of CL occur each year. Ongoing epidemiological assessments are expected to provide more accurate figures. In Ethiopia, two disease ecologies of VL are identified making the northern and southern ecotypes; which are characterized by varied set of sand fly vectors, molecular parasitological, and epidemiological patterns. These ecotypes exhibit distinct disease phenotypes, and patterns of response to treatment with anti-leishmanial agents. The southern ecotype is associated with the termite mounds, which harbor *Phlebotomus martini* (and the sibling species *P. ciliae*) as confirmed sand fly vectors. The northern ecotype is associated with the widespread Acacia-Balanites woodlands and black cotton soil, in which the presumed sand fly vector, *P. orientalis*, breeds. In endemic areas, asymptomatic infections of *L. donovani* and herd immunity are widespread. In the north Ethiopian VL endemic foci, the disease is more prevalent among migrant daily laborers who are exposed to sand fly bites in agricultural fields and the surrounding forests. Thus far, no animal reservoirs of VL have been found. Under hospital settings of northern Ethiopia, the prevalence of HIV in VL patients can vary from 15% to over 50%, while it is below 1% in southern Ethiopia. The clinical management of HIV co-infection remains to be a challenge. Ongoing clinical trials are expected to offer opportunities for better management VL during HIV co-infection, and to avail treatment options in general. CL due to *L. aethiopica*, is a well known zoonosis associated with two sets of sand fly vectors, *Phlebotomus longipes* and *P. pedifer*; and two species of hyraxes: *Procavia capensis* and *Heterohyrax brucei*. The disease is widespread throughout the highlands of Ethiopia, including Addis Ababa. Even though Ethiopian CL is mostly self-healing, variations in the disease phenotype that affect deeper mucosal tissues (mucosal cutaneous leishmaniasis, MCL) and those leading to metastasizing nodular lesions (diffuse cutaneous leishmaniasis, DCL) are difficult to treat. In some treatment centers, up to 30% of patients are of MCL or DCL type, even though these variants are rare in the general patient population. Both VL and CL, being neglected tropical parasitic diseases, remain to be public health threats. Control efforts are limited by unavailability of tools.

Comparative host-seeking behavior of biting flies and efficacy of personal preventive measures

Gabriela Zollner, Ph.D.

Division of Entomology, Walter Reed Army Institute of Research, Silver Spring, MD, USA

Mosquitoes, sand flies, ticks and other biting arthropods are important vectors of disease pathogens (e.g. *Plasmodium* spp., *Leishmania* spp., dengue fever virus and tick-borne viruses), which are transmitted by an infectious bite. Arthropod vector species use a complicated array of sensory stimuli to locate a human host to obtain a blood meal, including visual, auditory, mechanical, environmental and host chemical cues. This presentation focuses on the host-seeking behavior of mosquitoes, sand flies and other biting flies as they search for a blood meal. This behavior can be divided into activation, oriented flight to the host, alighting on the host, probing, ingestion (blood feeding), withdrawal and take-off. Consideration will be given to the array of skin bite reactions and the efficacy of insect repellents and other personal protective measures to prevent bites from different vector species, including infected versus uninfected flies.

Israel Jacob Kligler – The story of a little big man

Zalman Greenberg

Public Health Laboratory, Ministry of Health, Jerusalem

In "The Southern Jewish Weekly" of 31st October 1947, in one of the comic strips, the following was written: "The man who was almost single-handedly responsible for the elimination of malaria in the Holy Land, has since his death in 1944 been called "The Jewish martyr of science". Those words referred to Israel Jacob Kligler who, since then, has been almost totally forgotten. Kligler was born in Poland in 1889. At the age of 10, he immigrated to the USA with his parents and received his Ph.D. from Columbia University in 1915. Kligler made Aliyah to Palestine in 1920 as a member of one of the American Zionist Medical Units (AZMU). During the following years, until his sudden death at the age of 55, he became the most prominent medical researcher in Palestine and, undoubtedly, the most fertile writer of scientific articles. In 1921 Kligler was the laboratory manager of Hadassah Hospital, from 1922 to 1925 he was the director of the Malaria Research Unit and from 1926 to 1944, Kligler was the first professor of the Hebrew University and the head of the Bacteriology and Hygiene Department which he founded. Kligler carried out research in many fields: bacteriology (culture media, typhus, typhoid…), virology (yellow fever, rabies, fowl-pox…), parasitology (worms, Trypanosoma…), public health, nutrition, and more. His greatest achievement was in malaria eradication. Kligler should be remembered as a giant in the field of public health in Palestine, to whom so many people owe so much.

11:45 - 13:00 **Parallel sessions**

11:45 - 13:00 **Session 4: Travel Medicine**

Chairs: Shlomo Maayan & Michal Chowers

11:45 - 12:00 *Bianca Streltsin, Shmuel Stienlauf, Eli Schwartz.* **Pre-existing medical conditions in Israeli travelers to developing countries: the experience of the Travel Clinic, Sheba Medical Center**

12:00 - 12:15 *Irit Goldstein, Moshe Efrat, Shmuel Rishpon.* **Factors influencing intent to comply and compliance with malaria prevention recommendations in two travel clinics**

12:15 - 12:30 *Pamela Rendy-Wagner (Austria).* **The new Hepatitis B (PreS/S) vaccine**

12:30 - 12:45 *Eyal Leshem, Hana Bin, Uri Shalom, Maayan Perkin, Eli Schwartz.* **Autochtonous dengue: USA, France, Croatia. Is Israel the next?**

12:45 - 13:00 *Shomron Ben-Horin, Yoram Bujanover, Moshe Nadler, Alon Lang, Shuli Goldstein, Uri Kopylov, Lior Katz, Adi Lahat, Eli Schwartz, Benjamin Avidan.* **The traveling Inflammatory Bowel Disease (IBD) patient – a case-controlled study of travel-associated health risks**

Pre-existing medical conditions in Israeli travelers to developing countries: the experience of the Travel Clinic, Sheba Medical Center

Bianca Streltsin, Shmuel Stienlauf & Eli Schwartz

Sheba Medical Center, Tel-Hashomer, Israel

Background: Each year, about 170,000 Israelis travel to developing countries. The stereotypical Israeli traveler is a young person, during their post-army service, who is traveling to a remote area for a prolonged stay. Recently this stereotype has been reexamined.
Aims: Describe the demographic and travel characteristics of this cohort. Describe medical problems and potential contraindications of medications and vaccines.
Methods: A retrospective evaluation of The Sheba's Travel Clinic files between 2005 and 2007.
Results: From 2005 to 2007, there were 20,274 travelers who attended the pre-travel clinic. Complete demographic details were available for 19,626 travelers (97%, while 4841 travelers (25%) reported chronic medical problems. The mean age of healthy travelers was 29.3 (±12.2) compared with a mean age of travelers with pre-existing medical conditions, which was 45.2 years (± 18.1). Their length of stay was 65±124 days in travelers with pre-existing medical conditions compared to 109±162 days in healthy travelers. The most common medical conditions among the group with chronic conditions were Endocrine/Metabolic (29%), Cardiovascular (20%) and Pulmonary diseases (12%). 3% of these travelers were immune compromised (oncology patients, post-transplant patients). The most common destinations among the travelers were S. E Asia (52% of healthy travelers, 47% of travelers with medical problems), Latin America (30% of healthy travelers, 40% of travelers with medical problems) and Africa (9% of healthy travelers and 10% of travelers with medical problems).
Conclusions: The population of travelers to developing countries represented in our travel clinic is diverse, including those with a significant number of preexisting medical conditions. The principal medical problems are endocrine (DM and thyroid disease) and cardiovascular conditions. This group of travelers tends to be older but their destinations are similar to the healthy travelers. Those with chronic conditions are potentially a challenge to medical providers in preparing these individuals for travel, for example, high altitude exposure might be a danger for travelers with cardiovascular and/or pulmonary conditions. The group of severely immune compromised travelers might be traveling to a region where there is a risk of getting yellow fever and vaccine may be contraindicated. They also can be at higher risk for other infectious diseases. This study is only the first step in investigating the population of travelers with preexisting medical conditions to developing countries. Further prospective studies regarding the outcome of their trips are needed.

Factors influencing intent to comply and compliance with malaria prevention recommendations in two travel clinics

Irit Goldstein[1], Moshe Efrat[1,2,3], Shmuel Rishpon[4]

[1]Clalit HMO Travel Clinic, Haifa, Israel; [2]Department of Pediatrics, Carmel Medical Center, Haifa, Israel; [3]Faculty of Medicine, Technion- Israel Institute of Technology, Haifa, Israel; [4]School of Public Health, Faculty of Social Welfare and Health Sciences, Haifa University, Israel

Background. Malaria, endemic to many tropical and subtropical regions, infects ~300 million people annually with a mortality rate of nearly 2 million. About 30,000 of those infected are travelers. In the absence of vaccine, malaria prevention is based on education, mosquito bite avoidance and prophylactic antimalarial drugs. Previous studies have shown poor compliance of travelers with these recommendations. This study investigated intent to comply as well as actual compliance with malaria prevention recommendations given at two travel clinics in Haifa, Israel, and the factors influencing these behaviors.

Methods. Between December 1st, 2007 and May 31st, 2008, during 45 random recruitment days, 307 Israelis planning travel to malaria-endemic destinations for up to six months attended two travel clinics in Haifa, one managed by the Clalit HMO, and the other by Haifa's District Health Office. Participation was offered to all 307 who attended the two clinics and who stated that their trip was planned for up to 6 months. Data were collected via structured questionnaires, including demographic variables, purpose of the trip, destinations, duration, prior knowledge about malaria, recommended preventive behaviors and treatment, pre-trip intent to comply, and actual compliance with recommendations.

Results. Of the 307approached, 98 (31.9%) completed both questionnaires, one administered prior to departure, and the second about a month after return. Of the 307, 122 (39.7%) completed the first questionnaire, and of these 98 (80.4%) completed the second questionnaire. Among the 98 participants who completed both questionnaires, 38.8% declared (pre-travel) their intent to comply while 38.6% indicated (post-travel) that they actually complied. Univariate analysis found higher intent-to-comply and compliance rates among older participants, short-term travelers, and travelers to Africa. Compliance rates were higher among participants in organized tours than among independent/adventure travelers. Logistic regression analysis showed that trip duration was the only significant variable: both low intent-to-comply as well as low compliance rates were associated with trips of longer than 4 weeks duration.

Conclusions. Compliance with prophylactic treatment recommendations among Israeli long-term travelers is poor (38.6%). Because trip duration in endemic areas increases the risk of malaria, travel clinics must focus on long-term travelers to malaria-endemic areas by offering in-depth, personal guidance in order to increase compliance with prophylactic treatment regimens and hopefully to reduce malaria-related morbidity and mortality.

The PreS/S hepatitis B vaccine

Pamela Rendi-Wagner, MD, DTM&H, MSc

Department of Epidemiology & Preventive Medicine, School of Public Health, Sackler Faculty of Medicine, Tel Aviv University

Hepatitis B is an important and frequent cause of acute and chronic infection of the liver. More than a third of the world's population has been infected with hepatitis B virus (HBV), and the World Health Organization (WHO) estimates that it results in 1–2 million deaths every year. Non and poor response to the conventional hepatitis B vaccines remains a continuing problem in terms of providing protection against infection. In chronic dialysis population yeast-derived hepatitis B vaccination regimens result in a disappointing 50 to 75% rate of development of anti-HBs. There is considerable evidence that the pre-S1 and pre- S2 domains of the surface antigen of HBV have an important immunogenic role in augmenting protective surface antibody (anti-HBs) responses; Sci-B-Vac™ is a recombinant, hepatitis B vaccine derived from a mammalian cell line, containing hepatitis B surface antigen (HBsAg) as well as preS1 and preS2 antigens. Comparative immunogenicity studies in mice, rabbits and humans have repeatedly confirmed the excellent immunogenicity and safety of this third-generation HBV vaccine. Conventional recombinant hepatitis B vaccines (second-generation HBV vaccines) contain the S-component of the HBs antigen particle but lack the Pre-S1 and Pre-S2 domains which have been shown to play an important immunogenic role in stimulating cellular immune responses, circumventing genetic non-responsiveness, augmenting hepatitis B surface antibody response, and eliciting antibodies that are effective in clearing viruses and preventing hepatocyte attachment and entry. Moreover, the third-generation PreS1/PreS2 vaccine is significantly more immunogenic and induces a higher seroprotection rate at 100 and 10 IU/l levels than conventional vaccine in documented non-responders and low responders to conventional yeast-derived vaccines.

Autochthonous dengue: USA, France, Croatia. Is Israel next?

Eyal Leshem[1], Hanna Bin[2], Uri Shalom[3], Maayan Perkin[3], Eli Schwartz[1]

[1]The Center for Geographic Medicine & Tropical Diseases and Internal Medicine C, Chaim Sheba Medical Center, Tel Hashomer, Israel;[2]National Center for Zoonotic Viruses Central Virology Laboratory, Ministry of Health, Tel Hashomer, Israel; [3]Division of Pest Surveillance & Control, Ministry of Environmental Protection, Israel

Background: *Aedes albopictus* has invaded Israel since 2002. A recent national survey revealed wide distribution of *A. albopictus* in Israel. *A. albopictus* is known to be a vector of several arboviruses including dengue and chikungunya. Dengue is increasingly reported in Israeli travelers. Herein we report the possible importation of dengue virus by travelers to *A. albopictus* endemic areas in Israel.
Methods: All cases of serologically proven acute dengue and chikungunya registered during the last 3 years at the National Center for Zoonotic Viruses were included. Data regarding the current location of patients was plotted on a map describing the currently known distribution of *A. albopictus* in Israel. We evaluated the number of dengue and chikungunya patients in *A. albopictus* endemic regions.
Results: During the last 3 years, 41 dengue patients and 15 chikungunya patients were diagnosed at the National Center for Zoonotic Viruses. 27/41(66%) of dengue patients and 12/15 (80%) of the chikungunya patients live in *A. albopictus* endemic areas.
Conclusions: The establishment of *A. albopictus* in Israel provides suitable conditions for autochthonous transmission of both dengue and chikungunya. Although it was traditionally regarded a secondary vector for dengue virus, *A. albopictus* is well capable of spreading the disease. Recently reported cases of autochthonous dengue from both France and Croatia were presumed to be related to newly spread *A. albopictus*. Moreover, an outbreak of chikungunya occurred in the Italian province of Ravenna during the summer of 2007, with over 200 people infected. *A. albopictus* spread in Hawaii was regarded the cause of a dengue outbreak in 2001. In Florida dengue acquisition was recently documented in Key West where *A. aegypti* is established. We report the importation of dengue and chikungunya by travelers to *A. albopictus* endemic areas in Israel. The reported number of serologically proven cases underestimates the true burden of the disease in Israeli travelers as underdiagnosis and underreporting are common. Both dengue and chikungunya should be considered in the differential diagnosis of acute febrile illnesses even when the patients do not report recent travel to tropical areas. Enhanced surveillance may be needed to prevent epidemic spread of the disease.

The traveling Inflammatory Bowel Disease (IBD) patient – a case-controlled study of travel-associated health risks

Shomron Ben-Horin[1], Yoram Bujanover[1], Moshe Nadler[1], Alon Lang[1], Shuli Goldstein, Uri Kopylov[1], Lior Katz[1], Adi Lahat[1], Eli Schwartz[2], Benjamin Avidan[1]

[1]Gastroenterology Department and [2]The Center for Geographic Medicine, Sheba Medical Center Tel Hashomer, Tel-Aviv University, Israel (Email: sben-horin@013.net.il)

Background: Despite the increasing prevalence of international travelling, there are no data regarding the hazards of travelling in IBD patients. We aimed to assess travel-related illness in IBD**.**

Methods: This was a case-controlled retrospective study comparing the incidence and characteristics of travel-related illness among IBD patients versus a control population during 5-year period. Data were retrieved by structured questionnaires, personal interviews and chart review**.**

Results: The analysis comprised of 1061 trips by 429 individuals (221 controls, 208 IBD), with a median age of 33±14 (206 females). Immunomodulators and/or biologic medications were taken by IBD patients during 211/496 (43%) of trips. An illness episode occurred in 72/496 (14.5%) of trips by IBD patients compared to 54/565 (9.6%) trips by controls (Odds ratio 1.6, 95% CI 1.1-2.3, P=0.01). Travel-related illness mostly consisted of abdominal symptoms in both patients and controls. When destination countries were classified according to the U.N. human development index, IBD patients tended to refrain from travelling to developing countries: 189/496 trips of IBD patients were to developing countries versus 331/565 travels in controls (OR 0.43, 95%CI 0.34-0.55, P<0.001). However, the rate of illness during travelling to developing countries was similar among IBD and controls (35/189 vs. 47/331 of trips, OR 1.37, 95%CI 0.85-2.2, P=0.19). Immunomodulators were taken by IBD patients in 36% of their 211 trips to developing counties and illness occurred in 18/77 (23%) of these trips, which was a significantly greater rate than among the control population (OR 1.8, 95%CI 1-3.4, P=0.05). Unexpectedly, the increased rate of illness among IBD patients taking immunomodulators compared to control population was more pronounced when only trips to developed countries were analyzed (OR 5.5, 95%CI 2.2-13.5, P<0.001). The majority of travel-disease episodes in both groups were mild and self-limited and only two episodes, both in IBD patients, required a short-term hospitalization.

Conclusions: There is a greater rate of illness during travelling in IBD patients compared to controls. However, the pattern of illness indicates that this increased risk likely stems from flares of IBD rather than susceptibility to infections. Moreover, the absolute increase in risk is small and the majority of these episodes are mild and self-limited.

11:45 - 13:00 **Parallel sessions**

11:45 - 13:00 **Session 5: General Parasitology**

Chairs: Joseph El-On & Kosta Y. Mumcuoglu

11:45 – 12.10 **Plenary lecture:** *Hagai Ginsburg.* **Refreshed approaches to the therapy of malaria – the case of natural medicine**

12:10 – 12:30 *Jacob Golenser, Yechezkel Barenholz, Judith Waknine-Grinberg, James McQuillan, Nicholas Hunt, Richard Haynes.* **Artemisone is effective against murine cerebral malaria (CM), and is synergistic with chloroquine**

12:30 – 12:45 *Adi Moncaz, Wassenseged Lemma, Teshome Gebre-ichael, Alon Warburg.* **Identification and characterization of sandflies breeding sites in NW Ethiopia and Israel**

12:45 – 13:00 *Amos Wilamowski and Heather Schnur.* **Cases of myiasis in man and domestic animals**

Refreshed approaches to the therapy of malaria – the case of natural medicine

Hagai Ginsburg

Dept. Biological Chemistry, Institute of Life Sciences, The Hebrew University of Jerusalem, Jerusalem, Israel

Although the completion of genome project of the most virulent malaria parasite *Plasmodium falciparum* in 2002 evoked great hopes for the identification of new targets for novel drugs, but these were hitherto not fulfilled. This disappointment and the successful use of natural compounds emerging from traditional medicine for the chemotherapy of malaria (quinine, artemisnin) have recently invigorated a search for new antimalarials in natural sources. Hundred thousands compounds were screened and some promising leads were identified. However, the great advantage of traditional medicine is a result of demonstrable synergism between the constituents of the crude extract. The origin and the modes of action of this synergism will be discussed. In consequence, it is suggested that greater emphasis should be given to traditional medicine and some considerations for its controlled implementation will be mentioned.

Artemisone is effective against murine cerebral malaria (CM), and is synergistic with chloroquine

Golenser, Jacob[1,3], Yechezkel Barenholz[2], Judith Waknine-Grinberg[1,2], James McQuillan[3], Nicholas Hunt[3], and Richard Haynes[4]

[1]Departments of Microbiology and Molecular Genetics, The Kuvin Centre for the Study of Infectious and Tropical Diseases, Jerusalem, Israel; [2]Biochemistry, The Hebrew University of Jerusalem-Hadassah Medical School, Jerusalem, Israel; [3]Department of Pathology and Bosch Institute, The University of Sydney, Sydney, NSW, Australia; [4]Department of Chemistry, Institute of Molecular Technology for Drug Discovery an, The Hong Kong University of Science and Technology, Hong Kong.

Artemisinins have become essential components of malaria treatment due to their unique mechanism of action, rapid effect on plasmodia, and high efficacy in vivo. Administration of artemisinins in combination with other anti-plasmodials is the first-line treatment for uncomplicated (anemic) falciparum malaria. However, their efficiency in cases of CM remains to be determined. We examined artemisinin derivatives for treatment of experimental CM, induced by *Plasmodium berghei* ANKA in ICR (Swiss, outbreed) or C57BL/6 (inbreed) mice and demonstrated that artemisone is more effective than dihydroartemisinin and artesunate, two drugs used in antimalarial artemisinin-based combination therapies. Artemisone could prevent death even when administered at relatively late stage of cerebral pathogenesis. These findings are important, as human malaria is diagnosed only after clinical symptoms are apparent, and especially so if the rapid process of CM has been initiated. No parasite resistance to artemisone was detected, even in cases of treatment with a low dose which eliminated the parasites to a non-detectable level but was followed by a recrudescence (which could be treated by a higher dose). Co-administration of artemisone with chloroquine was more effective than mono-therapy with either drug, and led to complete cure. Artemiside was even more effective than artemisone, but this substance has yet to be submitted to preclinical toxicological evaluation. Altogether, our results support the use of artemisone for therapy of cerebral malaria.

Identification and characterization of sandflies breeding sites in NW Ethiopia and Israel

Adi Moncaz[1], Wassenseged Lemma, Teshome Gebre-Michael[2] and Alon Warburg[1]

[1]Kuvin Center for the Study of Tropical and Infectious diseases, the Hebrew University, Hadassah Medical School, Jerusalem, Israel; [2] Aklilu Lemma Institute of Pathobiology, Addis Ababa University, Addis Ababa, Ethiopia

Phlebotomine sand flies are the principal vectors of the leishmaniases, a group of parasitic diseases affecting infected populations exceeding 12 million worldwide. Identification and characterization of the breeding sites of sand flies is essential for the development and implementation of effective source-reduction approaches to their control. A preliminary study has been initiated concurrently in Israel and Ethiopia for the vectors of cutaneous and visceral leishmaniasis respectively. The main efforts in Ethiopia were focused in three sites located in the Northern endemic area bordering Eastern Sudan (Humera, Metema, and Addis Zemen). Four types of suspected larval breeding habitats were examined: Deep cracks in vertisols (black cotton soils), *Balanites aegyptica* and *Acacia seyel* forests, dried riverbeds and termite mounds. Emerging sand flies were captured with traps consisting of a sticky surface suspended off the ground and covered with a fine mesh to prevent any flies from escaping and/or others entering the structure. In some areas, sticky traps were deployed alongside emergence traps, to evaluate general populations of sand flies. Sand flies emergence traps and methods were further examined and developed in Israel. The research in Israel was designed to identify breeding habitats in caves and cracks in the rocky environment surrounding Kfar Adumim in the Judean desert. Caves, small animals borrows and artificial support walls made of large boulders were isolated with fine mesh, and sticky traps were deployed inside and out outside the mesh.. Sand flies were collected, mounted and their species were determined. Freshly emerging adult males were identified based on un-rotated terminalia and counted separately. The predominant species captured in Ethiopia *Sergentomyia* spp. that are not considered vectors of human leishmaniasis. However, *Phlebotomus orientalis*, the proven vectors of Kala Azar in Ethiopia were captured emerging from cracks in the soil of dry riverbeds. Exceptional results were found in Addis Zemen, where over 160 *P.orientalis* males were captured on a single sticky trap. In Kfar Adumim, Israel the isolation of caves and support walls with fine mesh resulted in a decline in the numbers of sand flies within these habitats indicating that the majority were resting populations and not freshly emerging flies. However, newly emerged flies were found albeit in and outside the caves. This indicates that flies do breed in and around caves in the rocky slopes below the village. These findings are consistent with earlier assumptions on potential breeding habitats in both study sites. Further in depth studies are planned for the coming seasons.

Cases of myiasis in man and domestic animals

Amos Wilamowski, Heather Schnur
Entomology Laboratory, Ministry of Health, Jerusalem.

Myiasis is the infestation of tissues of living vertebrates by dipteran fly larvae. Only a few human cases have been reported in Israel, among them, some imported cases. Species of Calliphoridae lay their eggs on organic animal material, including wounds. The larvae penetrate living tissues, feed and develop, leaving the tissues to pupate on the ground. Larvae of *Lucilia* sp. were removed from the ear of a woman, and *Calliphora* sp. from the leg wound of another woman. A first stage Calliphorid larva was identified from near the ear of a baby. The identification of larvae removed from wounds is problematic if they are very small or damaged during removal. Sarcophagidae females are larviparous. Two 5-6 day-old larvae of *Wohlfartia magnifica* were removed from the gum of a soldier suffering from mouth pains. It is assumed that the larvae were deposited in the mouth while the soldier was sleeping outdoors. During the last years, several cases of myiasis were found in hospital patients, some of which were on respirators. The larvae developed in the mouth or nasal cavities, and were discovered while moving out through the tubes in order to pupate. *Sarcophaga* sp. larvae were found in 3 cases of respirator patients and in the wounds of 3 others. *Sarcophaga* species can only be identified by the genitalia of the male adults. Stage III *Lucilia sericata* (Calliphoridae) larvae were also identified from 2 respirator patients. Several cases of *Oestrus ovis* (Oestridae) in human eyes were recorded. This species deposits larvae in the nasal membranes of cattle and sheep. Larvae deposited in human eyes are accidental, and cannot develop to stage II. A few backpackers returning from South America were infested with *Dermatobia hominis* (Oestridae). The parasitizing method of this species is very special – the female traps a blood-sucking fly or mosquito, and attaches her eggs to its abdomen. The carrier then attaches to a host at which time the eggs hatch and penetrate its skin, causing a furuncle as it grows. The backpacker may feel the growing larva moving in his skin. A larva of *Cordylobia anthropophaga* (Calliphoridae), known from Africa, was found in a boil-like lesion on the back of a geologist working in Congo. Myiasis has been reported in Israel from domestic animals, especially sheep and goats. In a 2005 survey from Jerusalem and its surroundings, 51 dogs, 1 cat, 3 goats, 2 camels and 1 horse were found infested with *W. magnifica*; 1 dog was infested with *Chrysomya albiceps* and *Lucilia sericata* (Calliphoridae); 2 cats and a sheep were infested with *L. sericata* and 2 goats were infested with *Przhevalskiana silenus* (Oestridae). 90% of the animals in this survey were infested with *W. magnifica*. The larviparous females deposit only near the host wounds, including very small wounds such as tick bites, or on the mucous membranes. Five of the infested dogs also had dog ticks. *W. magnifica* is common all over Israel. It deposits 120-170 larvae per batch. The larvae may cause severe tissue damage and may be fatal without suitable treatment. In some cases, several different larval stages occurred, indicating multiple depositions. In some dogs, there was more than one infestation focus. Most of the infested dogs spent much time outside. Most infestations were on areas not covered with thick fur, mainly the head and neck, genitalia and anal region and also on the paws and tail. The species *C. albiceps*, which was found on one dog together with *L. sericata*, is known to cause secondary myiasis in tissues already infested with the primary species. Myiasis in cats is rare, probably because of grooming. The species *P. silenus* has been reported as a pest in goat herds in Western Galilee.

14:00 - 16:00 **Parallel Sessions**

14:00 - 16:00 **Session 6: Tropical Medicine**

Chairs: Allon Moses & Itamar Grotto

14:00 - 14:30 *Lisette van Lieshout (Holland).* **Multiplex real-time PCR for routine diagnosis of parasitic infection in travellers and immigrants- the Leiden experiences**

14:30 - 14:50 *Silvio Pitlik.* **A single dose therapy for parasitic diseases**

14:50 - 15:10 *Eli Schwartz, Eyal Meltzer, Zahava Heyman, Hanna Bin.* **Capillary leakage in travelers with Dengue Fever**

15:10 - 15:25 *Shiri Tenenboim, Moshe Shabtay, Gad Baneth, Eli Schwartz.* **An unusual breast mass: A case report**

15:25 - 15:40 *Eran Kopel, Eli Schwartz, Danielle Goldmann, Ziva Amitai, Rivka Sheffer, Emilia Anis.* **Vivax malaria outbreak in Eritrean refugees in Israel, 2010**

15:40 - 15:55 *Zohar Mor, Galia Pinsker, Emilia Anis, Efrat Hadad, Alex Leventhal.* **Tuberculosis and HIV among migrant workers in Israel**

15:55 –16:00 **Discussion**

Multiplex real-time PCR for routine diagnosis of parasitic infections in travelers and immigrants - the Leiden experiences

Lisette van Lieshout

Department of Parasitology & Clinical Microbiology Laboratory; Department of Medical Microbiology; Leiden University Medical Centre, The Netherlands

The first parasite-DNA detection PCR to be introduced at the routine clinical diagnostic laboratory of our hospital in 2004 was a multiplex real-time assay for the differentiation of Entamoeba histolytica and E. dispar. Since then, step-by-step PCR detection of 15 different parasite targets have been implemented in our clinical setting and some of these multiplex real-time PCR assays even completely replaced more classical diagnostic procedures such as microscopy and copro-antigen detection. In the beginning we mainly focused on the detection of diarrhoea causing protozoa in travelers, children and immunocompromised individuals, followed by the introduction of Leishmania and Toxoplasma detecting PCRs. Lately we introduced PCRs for specific detection of Schistosoma and Strongyloides DNA in traveler and immigrants and started with testing all malaria requested blood samples with a multiplex real-time PCR for the detection of the four main human Plasmodium species. This presentation will summarize our experiences with DNA detecting assays as a routine diagnostic tool, focusing on these most recently introduced assays. Findings will be illustrated with a few case reports.

One and only one: Single-dose treatments in infectious diseases

Silvio Pitlik MD

Department of Medicine C. Beilinson Hospital, Rabin Medical Center, Petah Tikva, Israel 49100

On December 11, 1908 Paul Ehrlich delivered his Nobel laureate lecture. The last paragraph of his speech reads: "For with the help of this substance it is really possible in every animal species and with every kind of trypanosome infection to achieve *a complete cure* with *one* injection, a result which corresponds to what I call *therapia sterilisans magna*". His legacy in the field of infectious diseases can be summarized into two important messages: first, the frequently quoted concept of a *magi*c *bullet*, i.e. a drug that is delivered to a specific target or receptor and hits the microorganism and not the host; and second, the original idea of using *therapia sterilisans magna*, meaning the administration of one and only one- single dose of a medication with an exceptionally high potential for cure. The extraordinary vision of the German Nobel Prize recipient has become real in the field of infections. There is a wide evidence based platform to support the use of one and single dose treatments achieving a complete cure or preventing effectively dozens of different infectious diseases.

Capillary leakage in Travelers with Dengue Fever

Eli Schwartz[1, 4], Eyal Meltzer[1, 4], Zahava Heyman[2], Hanna Bin[3]

From the Center for Geographic Medicine and Department of Medicine C[1], The Department of Imaging[2], and The Central Virology Laboratory, Ministry of Health[3] at the Sheba Medical Center, Tel Hashomer, and the Sackler School of Medicine, Tel Aviv University, Tel Aviv Israel[4]

Background: Dengue hemorrhagic fever (DHF) is characterized by the presence of a capillary leak syndrome. Its pathogenesis is presumed to differ from that of "classical" dengue fever (DF), and to be associated with secondary dengue infection.
Methods: Returning travelers diagnosed with DF were evaluated for the presence of a capillary leakage with abdominal sonography. Data was compared between travelers with primary/secondary infection, defined by epidemiological and serological parameters.
Results: 12/35(34.3%) cases had sonographic signs of capillary leakage. Most cases with capillary leakage (85%) had "classical" DF. Capillary leak was diagnosed in 32% of primary dengue cases and in 40% of secondary dengue cases (p=0.69). The two cases diagnosed with DHF both had primary infections.
Conclusions: The high prevalence of capillary leakage among travelers, most of them with primary exposure to dengue, calls into question the importance of secondary infection in causing capillary leakage in dengue infection.

An unusual breast mass: A case report

Shiri Tenenboim[1], Moshe Shabtay[1], Gad Baneth[2], Eli Schwartz[1]

[1]Sheba Medical Center, Tel Hashomer; [2]Koret School of Veterinary Medicine, Hebrew University, Rehovot

A 50 years old woman with a history of breast cysts underwent a routine mammography and breasts ultrasound. The US demonstrated a 1.4 cm mass in the upper quadrant of the left breast, 8 cm from the areola. The mass was scored by the radiologist as BIRADS 3 (most probably benign) and a biopsy was recommended. The latter revealed a surprising result.
Diagnosis: to be discussed

Vivax malaria outbreak in Eritrean refugees in Israel, 2010

Eran Kopel[1], Eli Schwartz[2], Danielle Goldmann[3], Ziva Amitai[1], Rivka Sheffer[1], Emilia Anis[3]

[1]Tel Aviv District Health Office, Ministry of Health, Tel Aviv, Israel; [2]Center for Geographic Medicine and Tropical Diseases, Sheba Medical Center, Tel Hashomer, Ramat Gan, Israel; [3]Division of Epidemiology, Ministry of Health, Jerusalem, Israel

Background. Malaria, once endemic in Israel, was eradicated almost 50 years ago, although its vectors, several malaria-transmitting species of Anopheles mosquitoes, still exist in various parts of the country. Every year between 60 and 100 imported cases of malaria are reported to the Ministry of Health. Most of these cases are travelers returning from endemic countries to Israel and only a few of them are immigrants from Sub-Saharan Africa. As of the beginning of 2010, there has been an outbreak of relapsing *Plasmodium vivax* malaria among Eritrean refugees in Israel.

Methods. An epidemiological investigation was initiated by the Ministry of Health. The case definition was laboratory-confirmed malaria, excluding returning travelers. Among the investigation measures were species identification by thick and thin smears, with confirmation by real-time reverse-transcriptase PCR. Medical records of these patients were obtained from hospitals. Oral interviews were conducted with 4 of them by a native speaker of Tigrinya.

Results. Since the beginning of 2010, 120 patients with malaria, who met the case definition, have been identified nationwide, 111 were males (92.5%). Median age was 23.1 years (interquartile range [IQR], 21.2-28.1 years). This represents more than a 5-fold increase in the incidence rate of non-traveler malaria; the incidence of malaria among migrants entering Israel from the Egyptian border in 2010 (as at 31 October) was 3.98 per 1000 migrants, compared to 0.77 per 1000 migrants during 2009. Complete medical records were available for 27 patients, who were all Eritrean, and had laboratory-confirmed *P. vivax* malaria. Of these patients, 16 were found to have had a previous attack of malaria, with 7 having had the previous attack in Sudan, while traveling to Israel, and 4 upon arrival to Israel. There are no data for the remaining patients. The median time interval between the attacks was 4 months [IQR, 2-6 months). A possible place of exposure was found to be the region of the Eritrean refugee camps in eastern Sudan.

Conclusions. The observed increase of human reservoir of malaria in the region may potentiate the risk for the re-emergence of locally acquired mosquito-transmitted malaria in Israel and neighboring countries. This warrants tight national surveillance for new cases, proper clinical management as well as follow-up of current cases, and effective control measures of the local Anopheles vectors. In addition, it highlights the need for increased malaria surveillance in the refugee camps of eastern Sudan.

Tuberculosis and HIV among migrant workers in Israel

Zohar Mor[1,2], **Galia Pinsker**[1], **Emilia Anis**[3], **Efrat Hadad**[1], **Alex Leventhal**[4,5]

[1]Ramla District; [2]Dep. of Tuberculosis and AIDS; [3]Dep.of Epidemiology; [4]Dep. of International Relationships; [5]Braun School of Public Health, Hebrew University

Background: The prevalence of tuberculosis and of HIV in Israel, as in other industrialized countries, is relatively low in the general population. Nevertheless, the burden and the incidence of these infections are related to immigration, since migrant workers originate largely from developing countries where these infections may be endemic. Health authorities in industrialized countries have shown concern for the possibility of transmission of tuberculosis or HIV within their countries. The objective of this study is to assess new cases of Tuberculosis and HIV among migrant workers in Israel, in relation to their countries of origin between 2000 and 2009.
Methods: The Israeli national registries of tuberculosis and HIV were reviewed to identify the countries of origin of infected individuals and to assess their risk behaviors in cases of HIV/AIDS.
Results: Out of 4,425 patients diagnosed with tuberculosis during the study period, 586 (13.2%) were migrant workers, with a notable increase toward the end of the decade. While most migrant workers diagnosed with *M. tuberculosis* in the beginning of this decade originated from south-east Asia or from the former Soviet Union, the majority of patients reported towards the end of the decade originated in countries situated in the horn of Africa. Out of 3,463 patients notified with HIV/AIDS during the study period, 584 (16.9%) were migrant workers, with increasing trend reported towards the end of the decade. While the most of the migrant workers infected with HIV/AIDS in the beginning of this decade originated in countries situated in the sub-Saharan region, most patients reported towards the end of the decade originated in the horn of Africa, and the males were all heterosexuals.
Conclusions: The proportion of migrant workers diagnosed with tuberculosis or HIV in Israel has increased during the last decade and the countries of origin have changed, reflecting the flow of labor migration to Israel. This calls for a change of health policy towards the undocumented migrant workers for appropriate screening policies for incoming immigrants. Their demographic, behavioral and social determinants should be addressed in order to treat, control and prevent the spread of tuberculosis or HIV.

14:00 - 16:00 **Parallel Sessions**

14:00 - 16:00 **Session 7: Molecular Parasitology**

Chairs: Joseph Shlomai & Charles Jaffe

14:00 - 14:15 *Mary Dan Goor, Nasereddin Abedelmajeed, Charles L. Jaffe.* **Purification and characterization of a shed CK1 from *Leishmania donovani*: a virulence factor?**

14:15 - 14:30 *Dalit Talmi-Frank, Charles L. Jaffe, Abedelmajeed Nasereddin, Gad Baneth.* ***Leishmania tropica*** **experimental infection in the rat using luciferase transfected parasites**

14:30 - 14:45 *Alexandra Zinoviev, Yael Yoffe, Melissa Leger, Gerhard Wagner, Michal Shapira.* **Leishmania parasites use stage-specific cap-binding complexes that associate with a novel 4E-binding protein**

14:45 - 15:00 *Inbar Avraham, Ron Dzikowski.* **The role of *cis* element and antisense ncRNAs in *var* gene regulation in the malaria parasite *Plasmodium falciparum.***

15:00 - 15:15 *Shiri Eshar, Ariel Sebag, Yael Mandel-Gutfreund, Rotem Karni, Ron Dzikowski.* **Characterization of alternative splicing factors in the malaria parasite *Plasmodium falciparum***

15:15 - 15:30 *Itamar Glazer, Anat Moshayov, Hinanit Koltai.* **Inhibiting the 'Recovery' of the nematode *Heterorhabditis bacteriophora* TTO1 infective juveniles with RNAi**

15:30 - 15:45 *Danny Morick, Boris R. Krasnov, Irina S. Khokhlova, Georgy I. Shenbrot, Michael Y. Kosoy, Shimon Harrus.* **Multiple Bartonella genotypes in fleas collected from rodents in the Negev Desert**

15:45 – 16:00 **Discussion**

Purification and characterization of a shed CK1 from *Leishmania donovani*: a virulence factor?

Mary Dan Goor, Nasereddin Abedelmajeed and Charles L. Jaffe

Department of Microbiology and Molecular Genetics, The Kuvin Center for the Study of Infectious and Tropical Diseases, IMRIC, Hebrew University-Hadassah Medical School, P. O. Box 12272, Jerusalem 91120 Israel.

The serine/threonine protein kinase family, casein kinase I (CK1), plays an important role in eukaryotic signaling pathways, and their substrates include key regulatory protein involved in cell differentiation, proliferation and chromosome segregation. Essential CK1s are attractive targets for anti-leishmanial drug discovery as CK1s are monomeric, constitutively active and usually co-factor independent. There are several high resolution structures of CK1s with ATP or inhibitors to aid rational drug or immunization design. *Leishmania major* CK1 isoform 2 has been implicated as an essential enzyme through studies using immobilized or radiolabelled inhibitors. The same compounds were also shown to be cytotoxic to *Trypanosoma brucei*. In order to further evaluate CK1 as a potential anti-parasitic target, a full length *L. donovani* CK1 gene isoform 4 (CK1.4, orthologous to LmjF27.1780) containing a putative secretion signal peptide and three shorter fragments of the gene were cloned by PCR. The products are predicted to encode 4 polypeptides of 62.3, 51.3, 45 and 35 kDa. All the recombinant CK1 *L. donovani* (rLdCK1) polypeptides were expressed in *E. coli* as His tag proteins and characterized. The 62.3 kDa polypeptide showed protein kinase activity, and was partially purified using affinity chromatography. Deletion mapping showed that the N-terminal signal peptide and C-terminal domains of CK1 are required for protein activity. The full length His-tagged rLdCK1 also was over expressed in *L. donovani* parasites using a *Leishmania* specific expression system (pSSU-LdCK1.4). Western blotting analysis showed that rLdCK1 is expressed by promastigotes and secreted by the parasites. Maximum protein secretion was observed after 10 min. Over expression of rLdCK1 had a significant effect on promastigote growth in culture; mutants growing faster than wild-type parasites ($p=0.0324$). FACS analysis showed a higher percentage of virulent metacyclic promastigotes on day 3 among the mutant population. Finally, macrophages infection using the rLdCK1 mutants was markedly higher compared to wild-type parasites. The results suggest that rLdCK1 plays an important role in parasite survival and virulence, and further studies are needed to validate CK1.4 as a therapeutic target in *Leishmania* parasites.

Leishmania tropica experimental infection in the rat using luciferase transfected parasites

Dalit Talmi-Frank[1], Charles L. Jaffe[2], Abedelmajeed Nasereddin[2], Gad Baneth[1]

[1]School of Veterinary Medicine, Hebrew University, P.O. Box 12, Rehovot 76100; [2]IMRIC, Hebrew University-Hadassah Medical School, Jerusalem

Background: *Leishmania tropica* is an emerging protozoan pathogen of a growing concern to public health in Israel and other countries (Jacobson et al., 2003, Al-Jawabreh et al., 2004, Ready, 2010). *L. tropica* infection is characterized by skin lesions that take an extended period of time to heal, often resulting in disfiguring scars, and it's more refractory to treatment than leishmaniasis caused by *Leishmania major*. Additionally, *L. tropica* has been shown to cause viscerotropic leishmaniasis, described in veterans of Operation Desert Storm. Published data on animal models for *L. tropica* leishmaniasis is lacking, in part because it is difficult to establish infection *in vivo*. In this study we used luciferase-transfected *L. tropica* parasites inoculated into rats in an attempt to learn more about the pathogenesis of this infection.

Methods: Laboratory Spring-Doli (SD) rats were inoculated in the ear pinna or the footpad with 10^7 metacyclic enriched luciferase transfected *L. tropica* promastigotes (LRC-L590). Rats were anesthetized for blood withdrawal and *in vivo* imaging was carried out by the NightOwl® imaging system (Berthold technologies). Rats were euthanatized six weeks post infection and blood, footpads, ears and spleens were sampled for infection by real-time PCR and cultivation of parasites from the different tissues.

Results: Luciferase- transfected *Leishmania* parasites were visible on the day of infection at the inoculation site. The rats were scanned also at 2, 4, and 8 days post infection and 2, 3 and 6 weeks post infection, but no imaging of fluorescent parasites was detectable. Parasites were detected using real-time PCR in the blood as well as the spleen of all infected rats by 6 weeks of infection, and in much lower numbers in the inoculation sites. Different parasite loads were detected in the blood of rats from 2 days to 6 weeks post infection. Moreover, *L. tropica* was isolated and cultured from the spleen of all rats and from the inoculation sites. All rats remained asymptomatic during the study period.

Conclusions: Infection and persistence of *L. tropica* in the footpad and ear of SD rats was demonstrated despite the absence of overt clinical pathology. Parasite dissemination and maintenance in distant tissues provides evidence that rats are susceptible to *L. tropica* and might serve as reservoirs of infection. The presence of parasites in the peripheral blood of experimentally infected rats makes them potentially available for transmission during the blood meal of sand fly vectors. Although rats may be used as an animal model for the *L. tropica* leishmaniasis, *in vivo* imaging in the rat using the NightOwl® system was not found to be sufficiently sensitive.

Acknowledgments: This study was supported by grant no. SCHO 448/8-1 from the Deutsche Forschungsgemeinschaft and the Israel Science Foundation (ISF) grant no. 135/08

Leishmania parasites use stage-specific cap-binding complexes that associate with a novel 4E-binding protein

Alexandra Zinoviev[1], Yael Yoffe[1], Melissa Leger[2], Gerhard Wagner[2], Michal Shapira[1]

[1]Department of Life Sciences, Ben Gurion University of the Negev, Beer Sheva, Israel, [2]Department of Biological Chemistry and Molecular Pharmacology, Harvard Medical School, Boston, USA

External conditions such as temperature and pH switches trigger the development program of *Leishmania*, and it remains unclear how the translation machinery adapts to function in such a broad range of conditions. All trypanosomatids have an unusual cap-4 structure on their mRNAs, affecting cap-dependent translation. There are four highly diverged eIF4E paralogues in *Leishmania*, none of which can genetically complement the yeast eIF4E. LeishIF4E-4 is the probable initiation factor in promastigotes; it binds cap-4 and m^7GTP with similar efficiencies and it complexes with the eIF4F subunits LeishIF4G-3 and LeishIF4A-1, as well as with LeishPABP-1 and subunits of eIF2 and eIF3. However, the LeishIF4E-4 complex disintegrates in mammalian-like temperatures and in axenic amastigotes. Among the four paralogues, only LeishIF4E-1 maintains its ability to form protein complexes during heat shock. However, these do not include any MIF4G protein at any temperature. Despite the absence of an eIF4G homologue, the LeishIF4E-1 complex contains a multitude of initiation factors, suggesting its involvement with translation initiation. Finally a novel 4E-binding protein (Leish4E-BP, 80kDa) was identified, which specifically binds LeishIF4E-1 in promastigotes and not in amastigotes. LeishIF4E-1 could serve as an amastigote specific initiation factor, which is mostly inactive in promastigotes. Alternatively, if translation in amastigotes is cap-indpendent, LeishIF4E-1 could serve as a translation repressor, which is regulated by Leish4E-BP.

The role of *cis* element and antisense ncRNAs in *var* gene regulation in the malaria parasite *Plasmodium falciparum.*

Inbar Avraham & Ron Dzikowski

Department of Microbiology & Molecular Genetics, IMRIC**.** The Kuvin Center for the Study of Infectious and Tropical Diseases. The Hebrew University of Jerusalem - Hadassah Medical School. Israel

The virulance of human malaria parsite *Plasmodium falciparum* is achieved by antigenic switches in the expression of hypervariable surface proteins, encoded by a multi-copy gene family called *var*. Each individual parasite expresses only a single *var* gene at a time. All *var* genes share a similar structure: *var* promoter upstream of a open reading frame and two exons seperated by a well conserved intron. Within the intron there is a bidirectional promoter that gives rise to both sense and antisence sterile transcripts. Strict pairing between the *var* promoter and the intron is required for both silencing and counting of individual *var* gene by the mechanism that regulate mutually exclusive expression. We hypothesized that the antisense ncRNAs might be involved in the choice for activation. We measured the level of transcription of these ncRNAs in active and silenced genes. We found that the antisense sterile transcripts of the intron promoter are associated with active *var* gene. In addition we were interested to determine the cis regulatory elements that are required for proper regulation of *var* genes. We used an artificial *var* gene on a plasmid with reporter genes and selectable marker. Interestingly, by modifications of *cis* regulatory elements we were able to interfere with mechanisms that controls silencing and mutually exclusive expression. We identified DNA element that is found at the last 102bp of the *var* promoter. This DNA element is found as well in the intron and in the 3' UTR used to terminate the reporter gene in the un-regulated episome. This sequence seems to be required for promoter-promoter interaction between the *var* and intron promoters. We also demonstrated that the strict pairing between the *var* promoter and the intron is significant for the timing of transcription for both the *var* promoter and the bidirectional activity of the intron.

Characterization of alternative splicing factors in the malaria parasite *Plasmodium falciparum*

Shiri Eshar[1], Ariel Sebag[2], Yael Mandel-Gutfreund[3], Rotem Karni[2], Ron Dzikowski[1]

[1]Department of Microbiology and Molecular Genetics, IMRIC, The Kuvin Center for the Study of Infectious and Tropical Diseases, The Hebrew University of Jerusalem - Hadassah Medical School; [2]Department of Biochemistry and Molecular Biology, IMRIC, The Hebrew University of Jerusalem - Hadassah Medical School; [3]Department of Biology, Israel Institute of Technology-Technion, Haifa

Plasmodium falciparum is the causative agent of the deadliest form of human malaria. This parasite has a complex life cycle, during which it undergoes significant morphological and cellular changes in order to adapt to different hosts and changing environments. However, the *P. falciparum* genome is relatively small and comprised of ~5,600 genes, similar to the number of genes in bacteria and yeast. This low number of genes is in paradox with the complexity of the parasite's biology. Many eukaryotic organisms use alternative splicing (AS) in order to expand their protein repertoire. Thus far, ~100 genes were reported to undergo AS in *P. falciparum*, however, the extent, the biological importance and the mechanism of AS in this pathogen was not investigated. We hypothesize that AS may play an important role in gene expression of *P. falciparum*. SR proteins and hnRNPs are known as master regulator of AS in different eukaryotes. We identified SR proteins and hnRNPA1 putative candidates in *P. falciparum* genome and we are currently in the process of characterizing their function as AS factors and their biological importance in the parasite biology.

Inhibiting the 'Recovery' of the nematode *Heterorhabditis bacteriophora* TTO1 infective juveniles with RNAi

Itamar Glazer[1], Anat Moshayov[1]and Hinanit Koltai[2]

[1]Department of Entomology, Nematology Div. [2]Department of Ornamental Horticulture, ARO, Agricultural Research Organization, The Volcani Center, P.O. Box 6, Bet Dagan 50250, Israel. Email: glazerit@agri.gov.il

Among insect parasitic Steinernematid and Heterorhabditid nematodes, 'Recovery' is defined as the process in which the infective juvenile resumes development, following invasion into the hemocoel of the insect host, to the reproductive stage. Characterizing the molecular basis of the recovery process in *H. bacteriophora*, was done by identifying genes that are putatively involved. For this purpose, a large scale bioassay for recovery was established and two subtractions libraries of recovered IJs subtracted by arrested IJs were constructed. Six hundreds expressed sequence tags (ESTs) were sequenced and annotated resulting in 300 useful ESTs that were compared to *C. elegans* Wormbase and categorized into functional categories according to gene ontology. Of these, twenty three genes were chosen for further analysis. These genes were examined for their expression in the recovery process by quantitative (q) RT-PCR. The results of the RT-qPCR supported the results obtained from the subtraction libraries. Further analysis of these genes was done by RNAi-based functional analysis in *H. bacteriophora*. Eight genes displayed significant reduction in recovery as compared to control treatment as well as low expression and measured by RT-qPCR. The possible role of selected genes will be presented.

Multiple *Bartonella* genotypes in fleas collected from rodents in the Negev Desert

Danny Morick,[1] Boris R. Krasnov,[2] Irina S. Khokhlova,[3] Georgy I. Shenbrot,[2] Michael Y. Kosoy,[4] Shimon Harrus[1]

[1]Koret School of Veterinary Medicine, The Hebrew University of Jerusalem, Rehovot, Israel, [2]Mitrani Department of Desert Ecology, Institute for Dryland Environmental Research, Jacob Blaustein Institutes for Desert Research, Ben-Gurion University of the Negev, Sede-Boqer Campus, Midreshet Ben-Gurion, Israel, [3]Wyler Department of Dryland Agriculture, French Associates Institute for Agriculture and Biotechnology of Drylands, Jacob Blaustein Institutes for Desert Research, Ben-Gurion University of the Negev, Sede-Boqer Campus, Midreshet Ben-Gurion, Israel, [4]Bacterial Diseases Branch, Division of Vector-Borne Infectious Diseases, Centers for Disease Control and Prevention, Fort Collins, Colorado

Fleas collected from rodents in the Negev Desert in southern Israel were molecularly screened for *Bartonella* species. A total of 1,148 fleas, collected from 122 rodents belonging to six species, were pooled in 245 pools based on flea species, sex, and rodent host species. Two *Bartonella* gene fragments, corresponding to RNA polymerase B (*rpoB*) and citrate synthase (*gltA*), were targeted, and 94 and 74 flea pools were found positive by PCR, respectively. The *Bartonella* 16S-23S internal transcribed spacer (ITS) region was also targeted, and 66 flea pools were found to be positive by PCR. Sixteen different *Bartonella gltA* genotypes were detected in 94 positive flea pools collected from 5 different rodent species, indicating that fleas collected from each rodent species can harbor several *Bartonella* genotypes. Male and female fleas were found to be highly similar in their capacities to carry *Bartonella* organisms. Based on *gltA* analysis, identified *Bartonella* genotypes were highly similar or identical to strains previously detected in rodent species from different parts of the world. A *gltA* fragment 100% similar to *Bartonella henselae* was detected in one flea pool. Another 2 flea pools contained *gltA* fragments that were closely related to *B. henselae* (98% similarity). The high sequence similarities to the zoonotic pathogen *B. henselae* warrant further investigation.