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SESSION: RELAPSING FEVER

13. The epidemiology of tick-borne relapsing fever in Israel

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Tick-borne relapsing fever (TBRF), commonly called in Israel 'Cave Fever' is characterized by recurring episodes of fever and nonspecific symptoms. The illness is caused by infection with *Borrelia* species that have the genetic ability to vary their surface antigens extensively, leading to repeated stimulation of the immune system by each new antigen and a febrile response in the patient. The TBRF *Borrelia* is transmitted to humans by exposure to the bite of an infected *Ornithodoros* tick. Relapsing fever is a reportable disease in Israel, both in the civilian and the military population. The demographic, clinical and geographic information from civilian and military reports during the years 1971 through 2003 was evaluated. A total of 600 cases were reported during these years, 277 (46%) of them in civilians, and 323 (54%) in military personnel. In civilians, the incidence has declined from an average of 0.35-cases/100,000 population/year in the years 1975-1985 to an average of 0.11-cases/100,000 population/year in the years 1986-2002 ($p<0.001$). The incidence of TBRF in the military during the years 1983-2002 has been relatively constant, and there has even been a slight increase in the incidence of TBRF during the last decade, with an average of 5.9-cases/100,000 population/year in the years 1983-1991, compared with 6.5-cases/100,000 population/year in the years 1992-2002. Altogether, exposure in caves was reported in only 64% of cases. TBRF continues to be endemic in Israel, and still poses a significant hazard for soldiers and travelers, even without history of caves exposure. Although there has been a significant reduction in the incidence of TBRF in civilians, the incidence in soldiers has not declined and probably reflects more accurately the existence of the pathogen in Israel. Insufficient information is available on the habits of the *Ornithodoros tholozani* tick and its reservoirs, which is essential in order to further reduce the incidence of TBRF. In addition accurate mapping the locations infested by the *Ornithodoros* ticks is needed.

14. Post exposure prophylaxis with doxycycline for the prevention of relapsing fever

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Tick borne relapsing fever (TBRF) is an acute febrile disease characterized by a pattern of remission and relapse and caused by spirochetes of the genus Borrelia. Evidence is lacking on the safety and effectiveness of post exposure prophylactic treatment for TBRF. In this double blind, placebo controlled trial healthy volunteers with tick bites and close contacts with no bite signs were randomly assigned to receive doxycycline (200 mg for first day and 100mg/d for 4 days) or placebo. Blood smears were examined for Borrelia at inclusion and during fever rise. Serology for Lyme disease cross-reactivity and PCR for Borrelia GlpQ gene were examined. Cases of TBRF were defined as subjects having fever and a positive smear. 582 subjects in 17 cohorts at risk of exposure to Borrelia were screened, 125 were eligible for recruitment, 81 (13.9%) with tick-bite signs and 44 (7.6%) contacts. 93 (73.8%) volunteered, 51 with bite signs and 42 contacts. Volunteers were treated approximately 2 days after they were bitten. There were no significant adverse effects to treatment. Ten smear-proven cases of TBRF were identified and all belonged to the placebo group conferring a 100% efficacy of treatment. All positive cases had identifiable tick-bite marks. PCR was negative during incubation period but positive for all sick individuals during fever rise. Prophylactic treatment with doxycycline is safe and efficacious in preventing TBRF after suspected exposure in a high-risk environment. PCR for Borrelia GlpQ may help the diagnosis of acute disease but not to detection of exposure.

15. Microbiological diagnosis of relapsing fever Borrelia

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Relapsing fever (RF) in Israel is considered to be caused by the spirochete *Borrelia persica* and transmitted to humans by *Ornithodoros tholozani*. Between 1980-2002, 184 cases (i.e. an average of 8 cases per year) were reported to the Ministry of Health. All over the world, 29 species of Borrelia were described. They are the etiologic agents of two distinct diseases: Lyme borreliosis (LB) and RF. These two diseases are very different in many aspects: geographical distribution, vectors, epidemiology, pathogenicity, microbiological diagnosis, etc. Classically, the microbiological diagnosis of RF is based on thick and/or thin blood smears that need to be sampled at the time of fever peak. They are time consuming techniques that require experimented technicians and they also lack sensitivity. Other methods like dark field microscopy or quantitative buffy coat are less used. Contrary to LB strains, most RF strains required animal inoculations procedures. But recently, some species were successfully cultured on modified BSKII medium. Serology is considered of low diagnostic value because of the antigenic variation encountered by the bacterium. DNA extracted from ticks and blood samples were amplified using PCR methods. The advantages of PCR methods are high sensitivity and the ability to identify the exact infective species via sequencing. The *fla, 16s rRNA* and *GlpQ* genes were targeted. By sequencing we have identified the same Borrelia strain from DNA extracts of *Ornithodoros tholozani* ticks

and patient's blood. We found 80% homology between the Israel RF *Borrelia fla* (that is probably *B. persica*) and other RF species *fla* sequences. Taxonomic analysis showed that sequences of the Israel RF Borrelia clustered in a separate group (Middle East RF species) from the American and the African RF species. This is the first report of molecular characterization of the causative agent of relapsing fever in the Middle East.

16. Cave types of Israel and their possible relationship with the spatial distribution of *Ornithodoros tholozani*

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Israel displays a gradient of cave features from the intensive karstification of Lebanon in the north to practically no karst caves in Eilat region at the southern Negev desert. This is attributed mainly to the climatological gradient from alpine-Mediterranean climate in the Lebanon - Hermon mountains in the north, with precipitation >1000 mm/year, to the extremely arid southern Negev, with <50 mm/year. Another factor is the southward decrease in carbonates/clastics ratio of the phanerozoic stratigraphic section. Most caves developed horizontally in limestone. Today these caves are either dry or experience vadose dripwater. Some of them have been isolated from the surface until opened by recent construction activity. Vertical caves experience some water flow and active dissolution during the rainy season. The unique rock salt karst of Mount Sedom exhibits the largest salt caves known in the world. Israel is especially rich in man made caves sustaining abundant fauna. Preliminary observations indicate that the tick *Ornithodoros tholozani* does not appear in : (1) salt caves; (2) vertical caves; (3) wet, muddy caves; (4) Caves which have been isolated from the surface, and opened only recently; (5) caves with no fauna; (6) sea caves. Other factors controlling the tick's spatial distribution need to be investigated.

17. The biology of the relapsing fever tick *Ornithodoros tholozani*

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The "cave" tick, *Ornithodoros tholozani*, belongs to the soft-tick family Argasidae. Biological studies in Israel showed that this tick can be found in caves and archaeological sites in Galilee Mountains, Mount Carmel, Samaria and the Judean

hills, coastal plain, Jordan Valley and the Negev. Rodents, porcupines, badgers, goats, sheep, cattle and humans act as hosts for this parasite. Within limestone caves and archaeological ruins, the ticks are found in shaded or dark corners, in crevices of walls (up to 1 m), in dry manure and under stones. They avoid soil, which is too wet. Mature ticks are concentrated in wall crevices, while nymphs are more frequently found in the soil near walls. In sandstone caves in the coastal plain, ticks are located in the center of caves in the top layer of sand. When a host enters the cave, larvae climb on him within seconds, followed by the younger nymphs and adults. The temperatures in these caves vary from 16–25^{o}C and the RH from 40–60%. Epidemiological studies in Israel of the areas in which humans could have been infested show that these ticks also exist in deserted or inhabited houses (rural houses in villages), bunkers, military tunnels, crevices in rocks and along the slopes of wadis. Accordingly, there is a discrepancy between the places where such ticks were found and areas in which people were infested with ticks and acquired the disease. Therefore, there is a need to examine these potential biotopes of ticks, and the environmental conditions in which they are able to exist. The study of additional biotopes would also have an importance for public health.