REVIEW 10.1111/j.1469-0691.2009.02767.x

Relapsing fever borreliosis in Eurasia—forgotten, but certainly not gone!

M. V. Assous[1,2] and A. Wilamowski[3]

1) Laboratory of Microbiology and Immunology, Shaare Zedek Medical Center, 2) Department of Clinical Microbiology, Hadassah Medical School, Kiryat Ein Kerem and 3) Entomology Laboratory, Ministry of Health, Jerusalem, Israel

Abstract

Tick-borne relapsing fever (TBRF) has been reported in Eurasia and attributed mainly to *Borrelia persica*, although other entities have also been described. *Ornithodoros tholozani* is the most important tick vector, found in India and Kashmir, the southern countries of the former USSR, Iran, Iraq, Syria, Jordan, Turkey, Israel, Egypt, and Cyprus. It inhabits caves, ruins, and burrows of rodents and small mammals. In the northern countries, *O. tholozani* also lives in houses and cowsheds. In Israel, 30–60% of caves were found to be infested. PCR studies of *Borrelia* infection of *O. tholozani* ticks collected in caves showed very variable rates, ranging from less than 2% to 40%. The number of human cases reported varies among countries, from eight cases per year in Israel to 72 cases per year in Iran. The incubation period is 5–9 days. The fever attacks last from several hours to 4 days, and are accompanied by chills, headache, nausea and vomiting, sweating, abdominal pain, arthralgia, and cough; complications are rare. Other described *Borrelia* species are *Borrelia caucasica*, *Borrelia latyschewii*, *Borrelia microtii*, and *Borrelia baltazardi*. The classic taxonomy based on the co-speciation concept is very complex and very confusing. For this reason, 16S rRNA and *flaB* genes were used for taxonomic clarification. Sequencing of Israeli TBRF *flaB* genes, from human and tick samples, has demonstrated a third cluster corresponding to the Eurasia strains, in addition to both New World and Old World clusters. Thin and thick blood smears remain the most frequently used methods for laboratory diagnosis, with a sensitivity of 80%. PCR-based diagnosis is the most sensitive method, and has the advantage of allowing species identification.

Keywords: *Borrelia persica*, Eurasia, Middle East, *Ornithodoros tholozani*, review, tick-borne relapsing fever

Clin Microbiol Infect 2009; **15:** 407–414

Corresponding author and reprint requests: M. V. Assous, Laboratory of Microbiology and Immunology, Shaare Zedek Medical Center, P.O.B. 3235, 91031 Jerusalem, Israel
E-mail: mvassous@gmail.com

Introduction

In Eurasia, tick-borne relapsing fever (TBRF) was first described by Dschunkowsky [1] in the Ardabil region of Iran, and for this reason it was called *Borrelia persica* [2]. However, in the same area, as early as 1882, Tholozan published the first clinical description of a case of TBRF, which he called 'fièvre récurrente asiatique', and which was transmitted to humans by an *Ornithodoros* tick [3]. In the following decades, cases of relapsing fever (RF) were reported all over the Middle East region and were attributed mainly to *B. persica*, but other bacteria were also described [4–10]. Despite this, little was known about the bacterium itself or its natural reservoirs. In the years 2002–2008, several studies were published in Israel that involved gathering data about the vector, the disease, and the bacterium, demonstrating that this long-standing disease is still present [11–15].

The Vectors and The Reservoir

Ornithodoros tholozani

The distribution area of *O. tholozani* overlaps the distribution area of clinical RF cases caused by *B. persica*. The tick is widely distributed throughout India and Kashmir, the southern countries of the former USSR (Kazakstan, Kyrgizia, Tajikistan, Turkmenistan, and Uzbekistan), Iran, Iraq, Syria, Jordan, Turkey, Israel, and Egypt [16]. Goubau [17] also reported this tick in Cyprus, and noted the possibility that RF might exist in Afghanistan, Pakistan, and Libya.

The biology of *O. tholozani* was studied in Israel by Lidror [18] and Avivi *et al.* [19,20]. It inhabits areas such as caves, ancient ruins, and archaeological sites, where it digs itself into the soil up to a depth of 1 m, or hides in wall crevices where suitable microclimatic conditions exist, i.e. very high humidity of 70–80%, relatively low temperature (17–25°C),

and dim light. In the northern countries of its distribution area—Iran, Kashmir, Afghanistan, and the southern countries of the former USSR—*O. tholozani* also lives in houses and cowsheds, where suitable conditions are found [21,22].

O. tholozani feeds on any warm-blooded host that comes into its habitat range. It can detect and attach to its host within as little as 10–20 min [5,23]. According to Goubau [17], the ticks are capable of locating their host from a distance of almost 30 m. The tick sucks blood from the host for 20–30 min, and then returns to its hiding place. Consequently, the population level and length of the life cycle are dependent upon the presence of a host for blood meals. If hosts are plentiful, the whole life cycle lasts between 7 and 12 months. With only sporadic host availability, ticks at all stages can survive for 5–10 years or more without feeding [24].

In contrast to other ticks, *Ornithodoros* does not migrate from its original habitat. In rare cases, ticks may be transferred to another biotope by the host while the tick is attached for feeding. In Israel, it was found that between 30% and 60% of caves were infested with *O. tholozani*, but infestation levels decrease in hotter and dryer areas, with no infestation in desert environments in southern Israel [20].

O. tholozani ticks collected using CO_2 traps (Fig. 1) have been investigated using PCR to determine their infection rates [15]. The number of ticks collected ranged from several to thousands (Fig. 2). Infection rates were very variable, ranging from less than 2% to 40%.

Other *Ornithodoros* vectors

Babudieri [25] reported that the tick *Ornithodoros coniceps*, a known parasite of chickens that often resides in stone chicken houses, was also a vector of a *Borrelia* spp., causing TBRF cases in the town of Nablus. Similarly, in Iran, *Ornithodoros lahorensis* was found to be infected with *Borrelia* spp. [22]. In Azerbijan, *Ornithodoros verrucosus* is a vector of *Borrelia caucasica*, which causes a very severe TBRF, and in Iran and the countries of Central Asia of the former USSR, *Ornithodoros tartakowskyi* is the vector of *Borrelia latyshewii*, which causes a very mild RF without apparent clinical relapses [17].

FIG. 1. CO_2 trap (used with dry ice) for tick collection.

FIG. 2. Thousands of *Ornithodoros* ticks collected using a dry ice trap.

The reservoir

O. tholozani mainly feeds on rodents and small mammals. According to Parola and Raoult [16], these animals constitute the natural reservoir. In Israel, no rodents or other mammals have been found to be infected with *Borrelia*, with the exception of a single badger [26]. It is known that transovarial transmission of the bacteria occurs from the adult to the offspring via the eggs [27]. Therefore, the tick may serve as both reservoir and vector. It is known that *O. tholozani* can remain infected for many years, even if does not feed [17]. In Jordan, a bat, *Pipistrellus kuhli*, was found to be infected with *Borrelia* that was morphologically identical to the *Borrelia* found in TBRF patients [28]. The fact that in Central Asia bats are reservoirs of the causative agent of TBRF transferred by *O. tholozani* [29] indicates the possibility that bats may be the reservoir of this *Borrelia* species in Jordan [30].

Epidemiology

In Israel, 230 cases of TBRF were recorded in the civilian population between the years 1980 and 2007 [11], an average of eight cases per year (range: 0–16). A great number of cases, averaging 6.4 per 100 000, were also found among Israeli soldiers between 1971 and 2002 [12]. As far as the civilian population is concerned, 86% of the infestation foci were caves and 5% were ruins, and individual cases were

recorded in areas of rocks and beside animal burrows. There have also been cases where persons who sat or lay on the ground at a distance of several metres from an infestation focus have been infected with *Borrelia* spp.

The number of TBRF cases in Israel decreased from 97 cases in 1947, in a population of 0.6 million inhabitants, to 0–8 cases per year since 1992 in a population of 6.57 million. The reasons for this decrease are: (i) awareness and education of the public about the danger of entering caves and the need to take preventive measures; (ii) preventive control measures carried out in caves and at other tourist sites; and (iii) expansion of urban areas with concomitant destruction of cave sites that were natural foci of TBRF infestation.

Among the people infected, 92% were hikers, and only 7.5% were professionals who entered infested habitats during the course of their work. The latter normally take the necessary precautions. Fifty per cent of the total cases were youths, up to the age of 18 years, most being infected during their summer vacation. In Israel, *O. tholozani* remains active during winter; consequently, infection is possible throughout the year.

In hot and dry countries such as Jordan, the disease characteristics are very similar to those described in Israel. The number of patients is directly related to the number of persons entering caves without taking any preventive measures. In Jordan, between 1959 and 1969, there were 723 cases of TBRF (72 cases annually), of which four were fatal [30]. This number includes cases recorded from the West Bank of the River Jordan, which at that time was in the Kingdom of Jordan (and which is presently under the Palestinian Authority). These figures show that, also in Jordan, there has been a significant decrease in the number of cases from the 230 cases recorded annually in 1951–1954 [25]. In Jordan, it is also probable that the disease can be contracted throughout the year. TBRF patients are again mainly young people, such as herdsmen, who are exposed to the ticks when entering caves.

In countries such as Iran and Uzbekistan, where *O. tholozani* infests both houses and cowsheds, people of all ages may be exposed to the disease [21,22,30]. The main endemic area of TBRF cases caused by *B. persica* in Iran is Ardabil, located in the northwest of that country. Between 1998 and 2001, 391 cases were recorded, and 83.4% of the patients were children or people not working away from home. More than 84% were from villages; 70% of the patients lived in old buildings, 64% of which also housed sheep or cattle [22].

Clinical Features

In 1919, Nicholson described a cluster of 14 cases of TBRF that occurred in British troops [4]. He performed a very nice epidemiological study in which he clearly distinguished between this tick-borne RF and the classic louse-borne fever. Interestingly, the Palestine war in 1918 began with an epidemic wave of several hundred cases of louse-borne RF that he described in the beginning of his paper.

This cluster of TBRF was closely related to a common location (Ras-el-Ain Castle), where all of the soldiers were at the same bivouac. Clinically, the TBRF attacks were similar to the louse-borne ones, but Nicholson pointed out that the accompanying symptoms of this new TBRF were much less severe. The borreliae seen in the patients' blood were indistinguishable from louse-borne borreliae. However, Nicholson mistakenly identified the tick vector as *Argas persicus*.

The complete description of the natural history of the disease, based on 45 serial cases, was published by Adler in 1937 [5]. The incubation period was between 5 and 9 days (median: 7–8 days). The number of tick bites (Fig. 3)

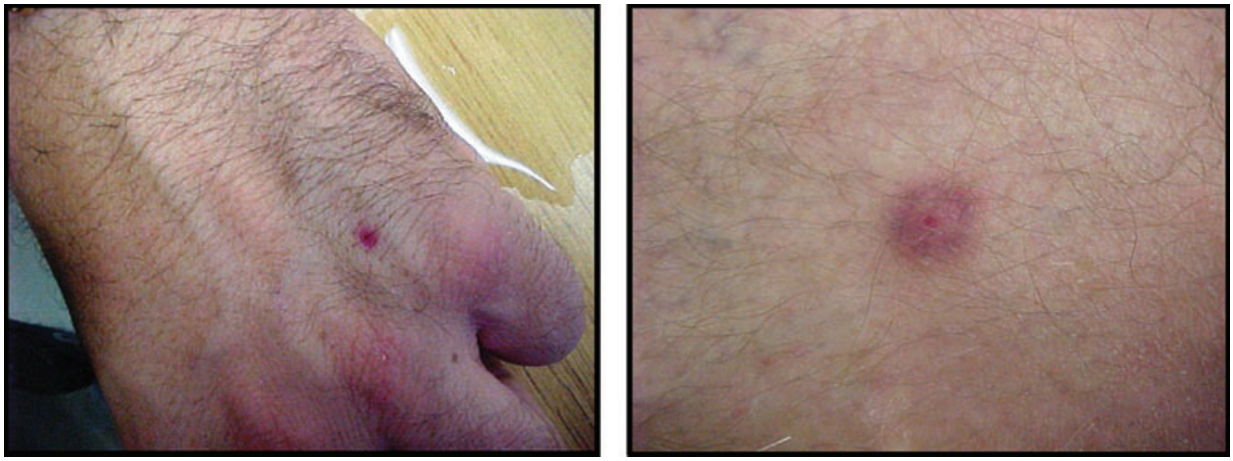

FIG. 3. Lesions caused by *Ornithodoros tholozani* bites.

appeared to correlate with a shorter period of incubation. The number of fever attacks ranged from 1 to 14, but 70% of cases had less than four attacks. Their duration varied from several hours to 4 days, and the attacks were often accompanied by intense eye pain, headache, nausea, vomiting, dyspnea, and joint pains. A slight enlargement of the spleen and liver and a hardly noticeable icterus occurred in one case. Complications were rare (three cases), and consisted of neurological and ophthalmological signs.

A report on TBRF in Jordan [25] described clinical aspects that do not differ significantly from those described by Adler. Arshi [22] reported cases from Iran that differed, being transmitted from a domestic environment. The inhabitants there lived in dwellings with earth floors, often in close contact with domestic animals. This fact certainly explains the very high incidence of the disease (average of 72 cases per year).

In this study, all symptoms were statistically quantified, including a comparison among children, residents, and visitors. Fever, chills, headache, nausea and vomiting, sweating, abdominal pain, arthralgia and cough were found at similar frequencies in these three groups. Interestingly, photophobia, epistaxis, jaundice, haematuria and petichiae were found in the resident group (19.1%, 9.6%, 4.5%, 4%, and 2.9%, respectively) but not in the visitor group. In conclusion, all the above clinical features caused by *B. persica* seem very similar.

There is very little information on the other species of *Borrelia* reported to occur in Eurasia. According to Rodhain [10], *B. latyschevii* is the causative agent of a very benign borreliosis in humans, with fever lasting 1 day, or otherwise an occult sickness. Although the bacteraemia is undetectable, the blood can infect a newborn rabbit [10]. In contrast, the infection in humans caused by *B. caucasica* is severe, causing 10–15 relapses in the space of 3 months. Finally, *Borrelia baltazardii* [31] was isolated from the blood of a patient suffering from thrombocytopenic purpura.

Taxonomy

TBRF caused by *Borrelia* species is generally called 'Asian or Asiatic TBRF' [17,32]. It seems that the geographical distribution of the borelliae more or less corresponds to Eurasia. The most important is *B. persica* [1], which causes the large majority of human cases and has the widest distribution. Two other species are regularly cited, i.e. *B. caucasica* and *B. latyschewii* [2,27]. *Borrelia microtii* is considered to belong to the *Crocidurae* group, and was described in 1946 [10]. Another species, described 30 years ago, is *B. baltazardi* [31].

In 1976, Rodhain summarized [10] the then current knowledge of TBRF-causing species from all over the world.

This review, written in French, was translated into English (Brooks Air Force Base, Texas) and is available at http://lrs.afpmb.org/rlgn_app/ar_login/guest/guest. Rodhain presents a very precise description of a great number of 'binomes' comprising each species of tick and its associated RF-causing *Borrelia*. This association is defined as the 'co-speciation concept', and is the basis of RF *Borrelia* taxonomy. In this approach, the only characters that can be used in taxonomy were: (i) the vector species; (ii) the geographical location; (iii) the spectrum of laboratory animal pathogenicity; and (iv) the experimental transmission of *Borrelia* by different arthropods. This approach contributes to creating great complexity [17], because these characters do not allow differentiation between two *Borrelia* species with sufficiently great precision. To simplify this complexity, Rodhain regrouped the numerous binomes into several great complexes (Table 1). On the basis of electron microscopic findings, ultrastructural differences, and experimental pathogenicity, Karimi *et al.* [31] described the new species *B. bartarzardi*.

The fastidious culture requirements of TBRF-causing species have prevented the use of DNA-relatedness studies, which are otherwise widely used for taxonomic purposes. For these reasons, and to avoid selection bias, PCR amplification combined with gene sequencing offers great promise for taxonomic studies. The first study that included one Eurasian TBRF species (*B. persica*) was conducted by Narti *et al.*, using 16S rRNA gene sequencing [33], and compared 20 strains of RF *Borrelia*. The nucleotide similarity within each species was 100%. The similarity between *B. persica* and other species was 98.4–98.7%. This was not sufficient to place it in a separate cluster. Narti *et al.* concluded that the status of *B. persica* is uncertain. The flagellin gene (*flaB*) was subsequently used for taxonomic studies of borreliae causing RF and Lyme borreliosis [34]. It has also separated into two clusters, one for RF in the New World and one in the Old

TABLE 1. Pathogenicity for experimental animals of Eurasian TBRF-causing *Borrelia*e

Borrelia species	Experimental animal			
	Guinea-pig adult	Rabbit newborn	Rat newborn	Mice adult
B. persica	+++	+++	–	+
B. microtti	+	++++	++++	++
B. latyschevi	–	+++	++	+
B. bartalzardi	–	+	+	+/–
B. causica	–	++	–	–

Adapted from [31] and [32]

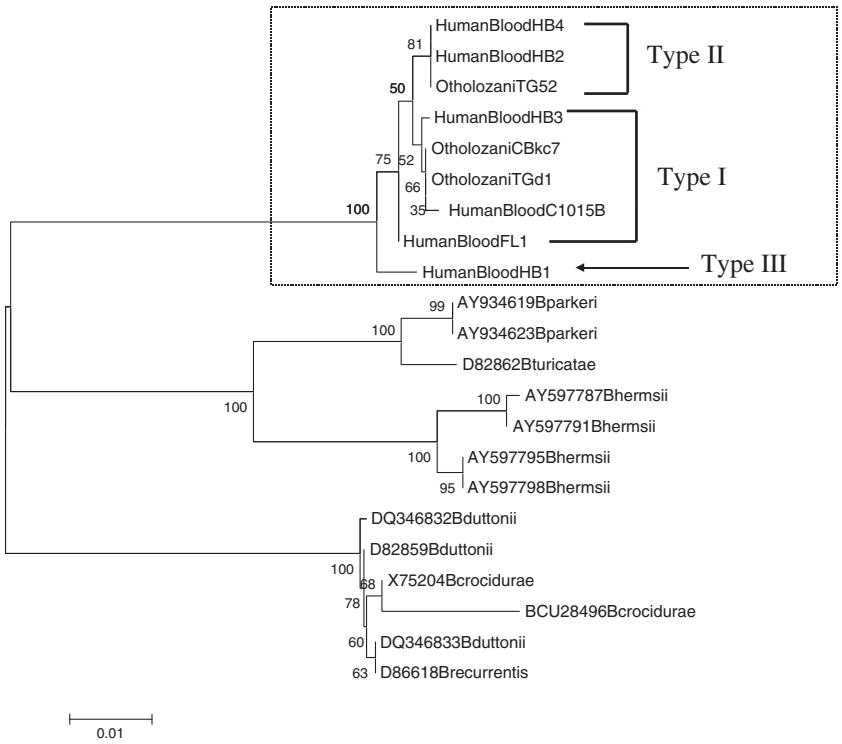

FIG. 4. Phylogenetic tree based on *flaB* nucleotide sequences. The tree was constructed using the neighbour-joining method with a pairwise deletion procedure. Distances were calculated according to Jukes and Cantor. Numbers at nodes correspond to the percentage confidence level in a bootstrap test performed on 1000 replicates. The scale bar corresponds to a distance of 0.01. The GenBank accession numbers for nucleotide sequences of *Borrelia persica flaB* shown here are as follows: Human Blood FL1, DQ673617; Human Blood C1015B, DQ679904; *Ornithodoros tholozani* CBkc7, DQ679905; Human Blood 1, DQ679906; Human Blood 2, DQ679907; Human Blood 3, DQ679908; Human Blood 4, DQ679909; *O. tholozani* TG52, DQ679910; and *O. tholozani* TGd1, DQ679911.

TABLE 2. Amino-acid variations in, and type definition of the flagellin FlaB in 14 samples of TBRF-causing *Borreliae persica*

Type	Amino Acid Position*								Number of strains
	86	105	134	195	216	217	228	231	
Type I	V	A	R	A	-	A	I	I	7
Type II	V	A	R	S	A	A	I	I	6
Type III	I	S	H	A	-	A	T	V	I

*: Numbering according the amino acid sequence of FlaB of *Borrelia. hermsii* (GenBank accession: gi|1311448|)

World, but, regrettably, *B. persica* strains were not included in this study. A more recent study [15] on Israeli TBRF specimens demonstrated a third cluster corresponding to the Eurasia strains (Fig. 4). The *flaB* gene sequences from human and tick samples were 98–100% identical. All of the translated amplicon sequences showed a specific signature, in that they had a seven amino acid gap at position 216, when compared with previously described *flaB* genes of TBRF borreliae. In addition, the amino acid sequences of FlaB of local TBRF borreliae could be grouped into three subtypes according to variations at seven amino acid positions. The results for 14 strains are given in Table 2. It would be very interesting to complete these gene analyses for other regions in the Middle East and to include other Eurasian pathogenic species.

Microbiological Diagnosis

With standard microscopy, *B. persica* appears very similar to other TBRF borreliae (Fig. 5). Using dark-field microscopy of blood from human clinical cases and mice inoculated with *Borrelia*-positive human blood, we have observed that *B. persica* isolates have the tendency to adhere to one red blood cell. Borreliae can survive for 1 or 2 days at room temperature, but when kept at 4°C, they rapidly lose motility, and animal inoculations become unsuccessful.

Thin and thick blood smears are most frequently used for laboratory diagnosis. In our experience, the sensitivity of the microscopic methods averages 80%. The morphology of *Borrelia* is better conserved in thin blood smears (Fig. 5a,b), but thick blood smears (Fig. 5c,d) can improve the sensitivity. Dark-field microscopy of fresh blood samples (Fig. 6) can also improve the sensitivity, as the motility of *Borrelia* can help in the detection of discrete bacteraemia.

A list of experimental animals is given in Table 1. We have succeeded in inoculating *B. persica* into mice (ICR, Harlan, Israel) via the intraperitoneal route with 200 μL of blood from human cases and positive mouse blood samples. Attempts at *in vitro* cultivation in BSK-H complete medium (B8291, Sigma-Aldrich, Rehovot, Israel) and BSK-H (B3528, Sigma-Aldrich, Rehovot, Israel) supplemented with rabbit

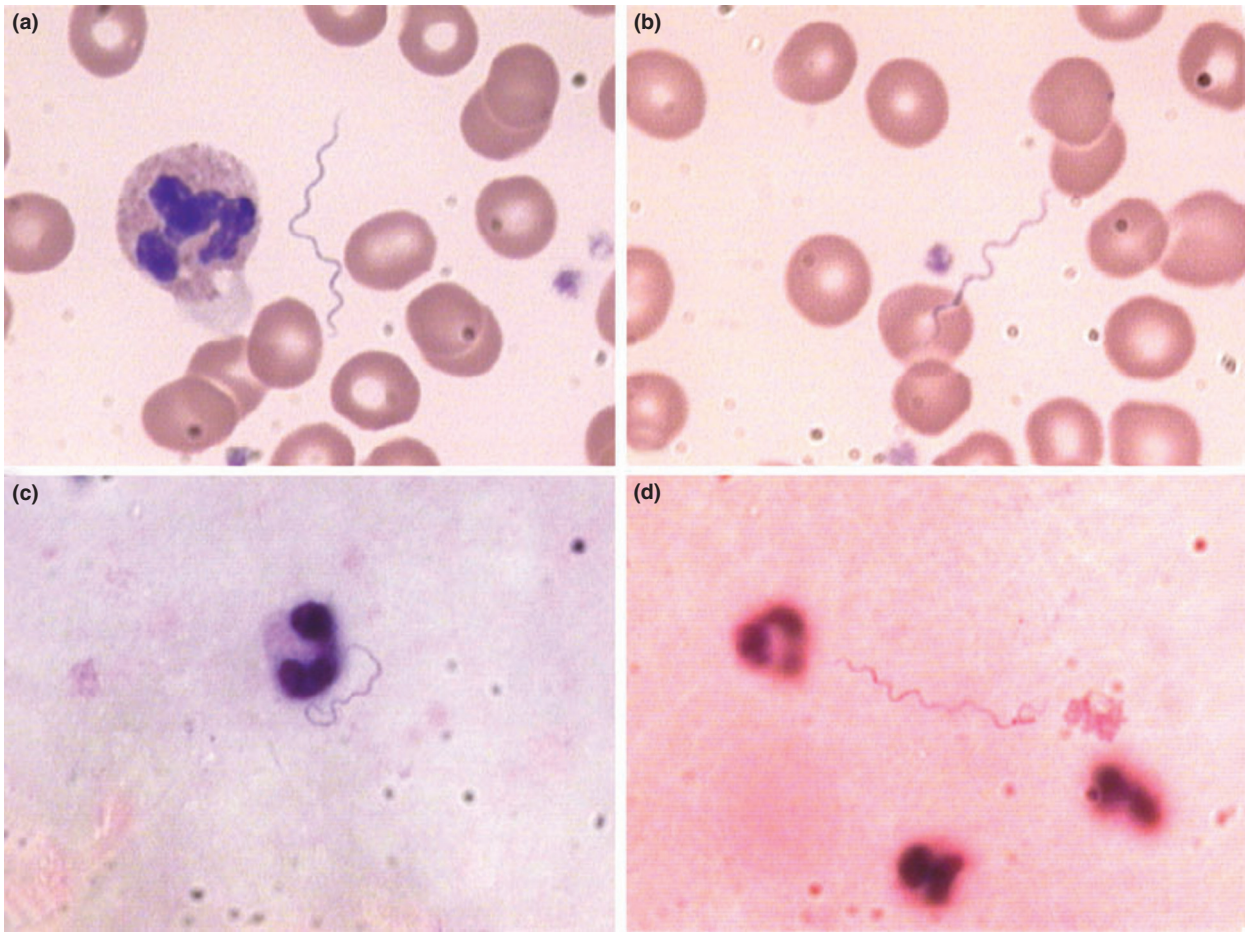

FIG. 5. Thin (a, b) and thick (c, d) blood smears showing *Borrelia persica* (×1000, Giemsa stain).

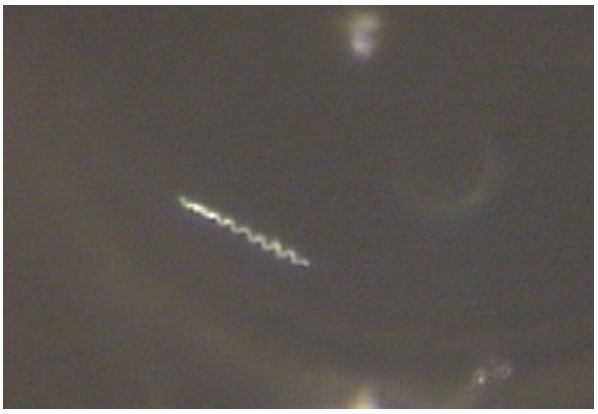

FIG. 6. *Borrelia persica* in patient's blood under dark-field examination.

serum were unsuccessful. One explanation could be that bacteraemia did not exceed five to ten organisms per 10 μL.

Molecular analysis is the most sensitive diagnostic method, and has the advantage of allowing species identification by sequencing [13,15] or on the basis of restriction patterns [33]. This type of analysis can also be performed on frozen blood or samples kept for several days at 4°C, and three sequences of genes (*flaB* [15], *glpQ* and 16S rRNA genes [13]) have been successfully used for PCR.

To our knowledge, specific serology for *B. persica* is not available. Some authors have reported the usefulness of Lyme borreliosis ELISA serology, taking advantage of the interspecies cross-reactions with sensitivities of 50% [35] and 89% [14]. Serological GlpQ assays have been used for RF [36]. However, serological methods could not differentiate between active and past disease.

Treatment and Prevention

Treatment of TBRF caused by *B. persica* does not differ from that of TBRF caused by other borreliae, and is based on doxycycline [10,17]. A high frequency of Jarisch–Herxheimer reactions, approximately 80%, has been reported [14].

Public education concerning the risks involved in entering caves, combined with prevention measures in countries in

which *O. tholozani* lives primarily in caves and similar sites, is effective in reducing the number of TBRF cases. Persons entering caves must wear appropriate shoes and clothes covering all the body. It is recommended to spray shoes and the trouser bottoms with a repellant. Avoidance of long stays in caves reduces the opportunities for ticks to identify the host. Sleeping in caves or at nearby sites must be avoided. If it is necessary to stay in caves or at archaeological or similar sites for an extended period, it is necessary to monitor whether the place is infested with ticks, and to spray the site with suitable residual insecticides. It is recommended to spray the ground until it is wet and the walls of the cave up to a height of 1 m. If prolonged work is necessary, the work should be stopped for several days for respraying.

For single exposures, the classic pre-exposure prophylaxis based on doxycycline is used; it can be similarly used for post-exposure prevention [14]. In this study, no Jarisch–Herxheimer reactions occurred with pre-exposure or post-exposure use of doxycycline. However, this drug has many side effects. For this reason, we used amoxycillin in our field studies for pre-exposure and post-exposure treatment, and this proved to be successful.

Acknowledgements

We are very grateful to H. Schnur for editorial assistance.

Transparency Declaration

The authors declare no conflict of interest in relation to this paper.

References

1. Dschunkowsky E. Das Rückfallfieber in Persien. *Dtsch Med Wochenschr* 1913; 39: 419–420.
2. Euzeby JP. List of bacterial names with standing in nomenclature: a folder available on the Internet. Last full update: December 06, 2008. URL: http://www.bacterio.net). *Int J Syst Bacteriol* 1997; 47: 590–592.
3. Theodorides J. [A great Franco-Mauritian epidemiologist: Joseph Desire Tholozan (1820–1897)]. *Bull Soc Pathol Exot* 1998; 91: 104–108.
4. Nicholson FD. Tick fever in Palestine. *BMJ* 1919; 2: 811.
5. Adler S, Theodor O, Schieber H. Observations on tick-transmitted human spirochaetosis in Palestine. *Ann Trop Med Parasitol* 1937; 31: 25–35.
6. Kalra SL, Rao KN. Observations on the epidemiology of relapsing fever in Kashmir. *Indian J Med Res* 1951; 39: 313–321.
7. Davis G, Hoogstraal H. The relapsing fevers: a survey of the tick-borne spirochetes of Egypt. *J Egypt Public Health Assoc* 1954; 29: 138–140.
8. Ozsan K, Akyay N. Relapsing fever in Turkey; presence in the South (Turko-Syrian border) of Ornithodorus erraticus infected with a spirochete of the Crocidurae group. *Bull Soc Pathol Exot Filiales* 1954; 47: 501–503.
9. Babudieri B. *Survey of relapsing fever in Jordan, final report*. Geneva: WHO World Health Organization Regional Office for the Eastern Mediterranean, 1955.
10. Rodhain F. Borrelia et fievres recurrentes aspects epidemiologiques actuels. *Bull Inst Pasteur* 1976; 74: 173–218.
11. Wilamowski A, Assous M, Anis E, Marva E. Tick-borne relapsing fever in the civilian population of Israel, 1980–2002. In: Robinson C-Y, La WH, eds. *Proceedings of the Fifth International Conference on Urban Pests*. Singapore: Executive committee of the International Conference of Urban Pests, 2005; 399–407.
12. Sidi G, Davidovitch N, Balicer RD, Anis E, Grotto I, Schwartz E. Tick-borne relapsing fever in Israel. *Emerg Infect Dis* 2005; 11: 1784–1786.
13. Halperin T, Orr N, Cohen R *et al.* Detection of relapsing fever in human blood samples from Israel using PCR targeting the glycerophosphodiester phosphodiesterase (GlpQ) gene. *Acta Trop* 2006; 98: 189–195.
14. Hasin T, Davidovitch N, Cohen R *et al.* Postexposure treatment with doxycycline for the prevention of tick-borne relapsing fever. *N Engl J Med* 2006; 355: 148–155.
15. Assous MV, Wilamowski A, Bercovier H, Marva E. Molecular characterization of tickborne relapsing fever Borrelia, Israel. *Emerg Infect Dis* 2006; 12: 1740–1743.
16. Parola P, Raoult D. Ticks and tickborne bacterial diseases in humans: an emerging infectious threat. *Clin Infect Dis* 2001; 32: 897–928.
17. Goubau PF. Relapsing fevers. A review. *Ann Soc Belg Med Trop* 1984; 64: 335–364.
18. Lidror R. Relapsing fever tick, ways of prevention and extermination. *Tavruah* 1964; 24: 26–30 (in Hebrew).
19. Avivi A. *Biology of the relapsing fever tick Ornithodoros tholozani (Labouldene & megnin, 1982) in Israel*. WHO Seminar on the Ecology, Biology and Control of Ticks and Mites of Public Health Importance. Geneva, Dec. 1967. WHO/VBC/68.57. Geneva: WHO, 1968; 85–90.
20. Avivi A, Warburg M, Galun R. Ecological studies on the cave tick *Ornithodoros tholozani* and its distribution in Israel. *Israel J Entomol* 1973; 8: 109–129.
21. Abidov ZI, Vasil'eva IS, Rakhimov NR, Gutova VP, Parpiev AM. Tick-borne relapsing fever morbidity in Namangan. *Med Parazitol (Mosk)* 1993; 1: 32–35.
22. Arshi S, Majidpoor A, Sadeghi H, Asmar M, Emdadi D, Derakhshan MH. Relapsing fever in Ardabil, a northwestern province of Iran. *Arch Iranian Med* 2002; 5: 141–145.
23. Katznelson D, Brook U, Gross S. Relapsing fever in the area of Kefar-Saba. *Harefuah* 1976; 90: 231.
24. Pospelova-Shtrom MV. *Ornithodorini ticks and their epidemiological significance*. Washington, DC: Joint Publications Research Service, 1962.
25. Babudieri B. *Relapsing fever in Jordan. Bull. World Health Organ (Naplus and West Bank)*. Geneva: WHO, 1957.
26. Costa M. *Insects anti man*. Israel: Hakibbutz Hameuchad, 1978 (in Hebrew).
27. Barbour AG, Hayes SF. Biology of *Borrelia* species. *Microbiol Rev* 1986; 50: 381–400.
28. De Zulueta J, Nasrallah S, Karam JS, Anani AR, Sweatman GK, Muir DA. Finding of tick-borne relapsing fever in Jordan by the Malaria Eradication Service. *Ann Trop Med Parasitol* 1971; 65: 491–495.
29. Pospelova-Shtrom MV. On the ecology of *Alectorobius cholodkovskvi* Pavl. *Medicin Parazit* 1946; 15: 55. (in Russian).
30. Vasil'eva IS, Ershova AS, Vilisov GM *et al.* The current status of foci of tick-borne relapsing fever in the western Pamirs. *Med Parazitol (Mosk)* 1990; 6: 31–34.

31. Karimi Y, Hovind-Hougen K, Birch-Andersen A, Asmar M. *Borrelia persica* and *B. baltazardi* sp. nov.: experimental pathogenicity for some animals and comparison of the ultrastructure. *Ann Microbiol (Paris)* 1979; 130B: 157–168.
32. Geigy R. *Relapsing fevers. Infectious blood of man and animals*. New York: Academic Press Inc., 1968; 175–216.
33. Ras NM, Lascola B, Postic D *et al.* Phylogenesis of relapsing fever *Borrelia* spp. *Int J Syst Bacteriol* 1996; 46: 859–865.
34. Fukunaga M, Okada K, Nakao M, Konishi T, Sato Y. Phylogenetic analysis of *Borrelia* species based on flagellin gene sequences and its application for molecular typing of Lyme disease borreliae. *Int J Syst Bacteriol* 1996; 46: 898–905.
35. Berger SA, Samish M, Kletter Y, Tinghitella T, Heering S, Edberg SC. Lyme disease acquired in Israel: report of a case and studies of serological cross reactivity in relapsing fever. *Isr J Med Sci* 1993; 29: 464–465.
36. Schwan TG, Schrumpf ME, Hinnebusch BJ, Anderson DE Jr, Konkel ME. GlpQ: an antigen for serological discrimination between relapsing fever and Lyme borreliosis. *J Clin Microbiol* 1996; 34: 2483–2492.