Chapter 16
What Else Besides TBE and Borreliosis? Tick-Transmitted Pathogens in Germany and Beyond

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Abstract **Tick-borne diseases** are an important problem in European countries. In this chapter, we review the biology and distribution of five tick-transmitted pathogens in Germany and neighbouring countries Austria and Switzerland. We focus on the bacterial pathogens *Rickettsia* spp., *Anaplasma phagocytophilum* and *Francisella tularensis*, the protozoan parasite *Babesia* spp. as well as on Eyach virus. The diagnosis of these pathogens is difficult, because the majority of the infections result in mild or self-limited diseases. However, all these pathogens may induce severe clinical symptoms; therefore, their importance is not to be underestimated in the diagnosis of tick-borne diseases.

16.1 Introduction

Tick-borne encephalitis (TBE) and **Lyme Borreliosis** are probably the most common and best-known tick-borne diseases in Germany, Austria and Switzerland. Other pathogens have however gained more and more attention in recent years, because their potential to cause diseases in humans or their endemic occurrence in natural foci has been clearly demonstrated. Many tick species may act as vectors of bacterial, viral and protozoan pathogens. However, four species are of particular

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Fig. 16.1 Unfed female of *Ixodes ricinus* (From Mehlhorn and Mehlhorn 2009)

Fig. 16.2 Unfed female of *Dermacentor reticulatus* (From Mehlhorn and Mehlhorn 2009)

medical importance in central Europe: *Ixodes ricinus*, *Dermacentor marginatus*, *Dermacentor reticulatus* and *Rhipicephalus sanguineus* (Figs. 16.1–16.3).

The most prevalent tick-species in Germany, Austria and Switzerland is ***I. ricinus***. Typically, it inhabits mixed forests with herbaceous vegetation (Kimmig et al. 2000). Because of the wide distribution and the broad host range as well as its high affinity for humans, *I. ricinus* is the main vector of tick-transmitted pathogens in Europe.

Ticks of the genus *Dermacentor* (i.e. *D. marginatus* and *D. reticulatus*) are not as abundant as *I. ricinus* and prefer different habitats. *D. marginatus* needs warm and dry conditions; it mainly occurs on pastures and grasslands in river valleys. In Germany, its distribution is currently limited to the Rhine valley and parts of the

Fig. 16.3 Brown dog tick *Rhipicephalus sanguineus* (From Mehlhorn and Mehlhorn 2009)

Main valley (Liebisch and Rahmann 1976). *D. reticulatus* is adapted to colder and more humid areas and, therefore, shows a wider distribution. Both species are also distributed in Austria and Switzerland, but data about their precise distribution in these countries are not available.

Rhipicephalus sanguineus is a thermophilic tick, which is widely distributed in the Mediterranean area, but it has also spread to many other parts of the world. The occurrence of *R. sanguineus* in Austria is uncertain, but natural foci were detected in the canton Ticino in Switzerland (Bernasconi et al. 2002). The colder climate in central and northern Europe prevents this tick from breeding in the environment, but it can survive and breed inside houses and may become a pest problem. Up to now, the occurrence of *R. sanguineus* in Germany is mainly related to animal transports from Mediterranean countries. However, *R. sanguineus* reveals a different vector competence compared to *I. ricinus* and *Dermacentor* spp., and this has to be taken into account in the diagnosis of tick-borne diseases.

In order to study the distribution of tick-borne pathogens, ticks and potential mammalian hosts are examined. The results of such studies indicate (a) if the pathogen is established in natural foci and (b) if these pathogens may pose a risk for humans if these natural foci exist. To estimate if humans are actually exposed to these pathogens, seroepidemiological studies are conducted. These studies can be carried out with members of the general population or can be focussed on "high risk groups". The latter includes people that are constantly exposed to ticks and, therefore, have an increased risk to acquire tick-borne diseases. Hunters and forestry workers are members of these high risk groups and participate in such studies.

In this chapter, we review some tick-transmitted pathogens that are (or might be in the near future) of medical importance in Germany as well as in Austria and Switzerland. We focus on the biology and distribution of the bacterial pathogens *Rickettsia* spp., *Anaplasma phagocytophilum* and *Francisella tularensis*, the protozoan parasite *Babesia* spp. and the Eyach virus. To our knowledge, these data summarize the current status of distribution of these pathogens. The "status quo" is important because it provides the basis for further studies in order to elucidate and

to evaluate any changes in the distribution of these pathogens, which may occur in the future.

16.2 *Rickettsia* spp.

Rickettsia spp. are bacteria with worldwide distribution that are transmitted by various arthropod species. These pathogens have been known as causative agents of human diseases for several hundred years (Raoult and Roux 1997).

16.2.1 Taxonomy

Bacteria of the genus *Rickettsia* belong to the **α-Proteobacteria**, order *Rickettsiales*. Traditionally, the genus *Rickettsia* was divided into two subgroups (Raoult and Roux 1997). The **typhus group** includes only two species: *Rickettsia prowazekii*, the causative agent of epidemic typhus, and *R. typhi*, the causative agent of murine typhus. These species are transmitted by lice and fleas, respectively. The **spotted fever group** comprises more than 20 species that are transmitted by hard ticks (*Ixodidae*). For a long time, *R. akari* and *R. felis* were also included in the spotted fever group, although they are transmitted by mites and fleas, respectively. Recently, phylogenetic analyses revealed new insights into the taxonomic relationships in the genus *Rickettsia* and resulted in the reorganisation of subgroups. Gillespie et al. (2007) showed that *R. akari* and *R. felis* represent a cluster of its own called the transitional group. Additionally, non-virulent species such as *R. bellii* and *R. canadensis* are grouped in the ancestral group (Gillespie et al. 2007; Dobler and Wölfel 2009). Other studies propose even more subgroups, as they include also *Rickettsia* species that are symbionts of non-bloodfeeding arthropods (mainly beetles) and other animals such as amoeba and leeches (Weinert et al. 2009; Perlman et al. 2006). In summary, the classification of the numerous *Rickettsia* species is still a matter of controversy.

16.2.2 Biology

Rickettsiae are gram-negative, short rod-shaped or coccoid bacteria that are about 0.8–2 μm in length and about 0.3–0.5 μm in diameter (La Scola and Raoult 1997). The bacteria are obligate intracellular organisms and infect endothelial cells of small blood vessels as their main host cells (Parola et al. 2005).

Rickettsial species can be pathogenic or non-pathogenic for humans, and many species of (yet) unknown pathogenicity have been described (Raoult and Roux 1997). In recent years, several species that were thought to be non-pathogenic were

demonstrated to be associated with human diseases, for example *R. raoultii* (Parola et al. 2009) and *R. helvetica* (Nilsson et al. 1999). It is assumed that all rickettsiae may be pathogenic to humans, as long as their arthropod hosts are capable of feeding on humans (La Scola and Raoult 1997).

Spotted fever group rickettsiae can be transmitted both transovarially and transstadially in their arthropod hosts (Azad and Beard 1998); therefore, all developmental stages of ticks can serve as vectors.

16.2.3 Disease

After inoculation of the rickettsiae into the host, the bacteria proliferate in endothelial cells close to the inoculation site. This leads to dermal and epidermal necrosis, resulting in skin reactions that are called **eschar** or "**tache noire**". Further proliferations cause vasculitis and a typical rash that is characteristic for most rickettsioses (Martinez and Cossart 2004). Other common symptoms include fever, headache, muscle pain and local lymphadenopathy. The bacteria may be disseminated via lymph and blood to various organs including lungs, liver, spleen, kidney and heart (Martinez and Cossart 2004). The clinical symptoms and the severity of human diseases are different for the various rickettsial species. Rickettsioses may induce only mild symptoms if the infection remains localised, but they can also become life threatening or even lethal if infestations of inner organs result in internal bleeding (Parola et al. 2005). **Antibiotic therapy** is used to treat rickettsial infections, and **doxycycline** is the treatment of choice for all tick-transmitted rickettsioses (Parola et al. 2005).

16.2.4 Vertebrate Hosts

It is assumed that a broad range of mammals, including rodents, dogs, rabbits and deer, are susceptible hosts for rickettsiae (Azad and Beard 1998; Raoult and Roux 1997). But studies about the actual prevalence of *Rickettsia* spp. in wild animals are scarce and exist only for few species.

Dogs are known to be important hosts for *R. conorii*, the causative agent of **Mediterranean spotted fever** (Rovery et al. 2008). Recently, Menn et al. (2010) detected antibodies against *R. conorii* in 68.2% of dogs in an endemic area in Portugal. Wild boars seem to be important hosts for *R. slovaca*. Ortuno et al. (2007) showed that 52.2% of wild boars in northeastern Spain developed antibodies against *R. slovaca*. In 1992, Rehacek et al. identified different rodent species (including *Microtus arvalis* and *Apodemus flavicollis*), which are susceptible to infections with rickettsiae. Recently, spotted fever group rickettsiae were identified in 9.1% of rodents in China. Zhan et al. (2009) demonstrated by means of PCR of spleen samples that both *Arvicolidae* and *Muridae* were infected with rickettsiae.

Rodents from Bavaria and Baden-Wuerttemberg were studied for antibodies against *Rickettsia* spp. by serological methods (Schex and Essbauer, personal communication; Pluta, unpublished data). The preliminary results of these still ongoing projects indicate that rodents serve as hosts for *Rickettsia* spp. in Germany. Comparable data about the importance of certain vertebrates as hosts for rickettsiae in Austria or Switzerland are not available.

16.2.5 Distribution in Germany

16.2.5.1 Rickettsiae in Ticks

The first isolation of ***R. slovaca*** was published in Slovakia in 1969 and it was characterised as a new species in 1978 (Sekeyova et al. 1998). Since then, it has been found in ticks in several European countries (Parola et al. 2005). Rehacek et al. (1977) identified *R. slovaca* in 8 out of 51 *D. marginatus* ticks from southern Baden-Wuerttemberg in 1977.

From 2006 to 2009, we collected about 1,100 questing *D. reticulatus* and *D. marginatus* ticks in southern Germany. By PCR methods and DNA sequencing, we were able to identify *R. slovaca* in 16% of *D. marginatus* ticks from Aschaffenburg (Bavaria) and in 0.9% of *D. marginatus* ticks from Karlsruhe (Baden-Wuerttemberg), respectively (Pluta et al. 2009; Pluta, unpublished data). For a long time, *R. slovaca* was considered to be non-pathogenic for humans. However, Raoult et al. (1997) identified *R. slovaca* in a patient with febrile illness in France by PCR and serological methods. Because of the main symptom, enlarged and painful lymph nodes close to the tick bite, this rickettsiosis was subsequently named tick-borne lymphadenopathy (TIBOLA) (Lakos 1997). Other common symptoms include an eschar and/or erythema at the site of the tick bite, fever and local alopecia, whereas a rash is present only in few cases. Besides our detection of *R. slovaca* in *D. marginatus* ticks, we could recently identify this pathogen in a tick removed from a patient in Rhineland-Palatinate (Pluta et al. 2009). The patient was bitten by a *D. marginatus* tick and subsequently fell ill with fever, lymphadenopathy of submandibular lymph nodes and an exanthema at the site of the tick bite. IgG and IgM antibodies against rickettsiae of the spotted fever group were detected by an immunofluorescence assay (IFA), whereas an IFA detecting antibodies against typhus group rickettsiae remained negative. *R. slovaca* was identified in the tick removed from the patient by means of PCR and DNA sequencing. Therefore, we were able to confirm the first autochthonous case of tick-borne lymphadenopathy in Germany.

In 2008, ***R. raoultii*** was characterised as a new species (Mediannikov et al. 2008).

31.6% of *Dermacentor* ticks collected in the Rhine valley near Lörrach harboured *R. raoulti* (Pluta et al. 2010). This was confirmed by PCR methods followed by DNA sequencing. Additionally, 38.5, 39 and 3.2% of *Dermacentor*

ticks collected in the districts Karlsruhe (Baden-Wuerttemberg), Freiburg (Baden-Wuerttemberg) and Aschaffenburg (Bavaria), respectively, and five out of six ticks in the district Esslingen (Baden-Wuerttemberg) were infected with this pathogen (Pluta, unpublished data). In 2006, Dautel et al. studied *D. reticulatus* ticks that were removed from deer in southern and eastern Germany. They detected *R. raoultii* in 23% of ticks collected in the federal states of Bavaria, Brandenburg, Saxony and Saxony-Anhalt.

On the basis of these data, it can be assumed that *R. raoultii* is widely distributed in *Dermacentor* tick populations in Germany. *Rickettsia raoultii* has been regarded as non-pathogenic. However, Parola et al. (2009) studied samples of 86 patients with tick-borne lymphadenopathy in France. *Rickettsia raoultii* was the causative agent of the disease in 8% of the cases, whereas the other infections were due to *R. slovaca* infections. On the basis of these results, Parola et al. (2009) believe that *R. raoultii* can cause tick-borne lymphadenopathy but seems to be less pathogenic than *R. slovaca*, as it was shown to be prevalent in fewer patients. Although the prevalence of *R. raoultii* in *Dermacentor* ticks in Germany is very high, no cases of *R. raoultii* infection in humans have been reported until now.

Rickettsia helvetica was isolated for the first time from *I. ricinus* ticks in Switzerland (Burgdorfer et al. 1979). These bacteria have been frequently found in *I. ricinus* ticks in many areas of Germany with infection rates up to 13%. Hartelt et al. (2004) studied about 1,100 *I. ricinus* from various districts in southern Baden-Wuerttemberg. In these areas, the *R. helvetica* infection rate was 8.9% on average, ranging from 5.6 to 13.3%. In Bavaria, a prevalence of 12% was detected in 2006 (Wölfel et al. 2006), whereas Silaghi et al. (2008b) revealed a lower prevalence of 4.8%. In a forest near Berlin, 14.2% of *I. ricinus* nymphs were infected with *R. helvetica* (Pichon et al. 2006).

Hildebrandt et al. (2010) detected *Rickettsia* spp. in 14.7% of *I. ricinus* ticks in Thuringia and identified *R. helvetica* by DNA sequencing in some of the samples. In Germany, *R. helvetica* has been detected in *I. ricinus* ticks only, but *Dermacentor* ticks are also possible vectors of this pathogen. Dobec et al. (2009) detected *R. helvetica* in 10% of *D. reticulatus* ticks in Croatia. *Rickettsia helvetica* was considered a non-pathogenic species for a long time (Raoult and Roux 1997). However, it was associated with two cases of perimyocarditis and sudden cardiac death in Sweden in 1999 (Nilsson et al. 1999). It has also been detected in a patient with meningitis in Sweden (Nilsson et al. 2010) and in patients with febrile illnesses in France and Italy (Fournier et al. 2000, 2004). Up to now, no cases of *R. helvetica* infection have been reported in Germany.

Rickettsia monacensis was isolated for the first time in 2002 from an *I. ricinus* tick collected in the English Garden in Munich, and was subsequently characterised as a new species (Simser et al. 2002). Since then, this pathogen has been found now and then in *I. ricinus* ticks in different parts of Germany. Silaghi et al. (2008b) detected *R. monacensis* in 0.5% of ticks from southern Bavaria, and Hildebrandt et al. (2010) demonstrated this pathogen in ticks in Thuringia. This indicates that *R. monacensis* is distributed in ticks throughout Germany, but apparently with a low prevalence. In Spain, Jado et al. (2007) reported infections of two patients with

R. monacensis. Both patients had a rash and unspecific flu-like symptoms after tick bites. The authors isolated the pathogen and characterised it by DNA sequencing as *R. monacensis*, showing that it is able to cause disease in humans. Up to now, there are no reports about *R. monacensis* infections in humans in Germany.

Antibody Prevalences in Humans

Until now, there is only one report of an autochthonous rickettsiosis caused by *R. slovaca* in Germany (Pluta et al. 2009). In contrast, no cases of infection with *R. raoultii*, *R. helvetica* or *R. monacensis* have been found, although they were frequently detected in ticks in Germany. However, in 2008, Jansen et al. conducted a seroepidemiological study with 286 hunters from all over Germany. They detected antibodies against *Rickettsia* spp. in 9.1% and antibodies specific for *R. helvetica* in two of the participating hunters. Nearly all participants noted at least one tick bite within the year before the study, and some of them remembered having symptoms that are compatible with rickettsiosis, but none of them was diagnosed with an acute rickettsial infection.

16.2.5.2 Distribution in Austria

In Austria, only very few data about the occurrence of *Rickettsia* spp. in ticks are available.

Until now, only *R. helvetica* was detected in *I. ricinus* ticks. Dobler et al. (2008) identified *R. helvetica* in 5.6% of *I. ricinus* ticks from the federal state of Burgenland in the eastern part of Austria. Blaschitz et al. (2008b) collected ticks in different areas of Austria and showed that 35.6% of the ticks harboured *Rickettsia* spp. Further studies revealed that the ticks were infected with *R. helvetica* only, although not all of the samples were sequenced. To our knowledge, the antibody prevalence in humans is not known and there are no reports about rickettsial infections.

16.2.5.3 Distribution in Switzerland

Rickettsiae in Ticks

Three different rickettsial species have been identified in *I. ricinus* and *Rhipicephalus* spp. ticks. In 1979, Burgdorfer et al. detected a new *Rickettsia* species in 8.4% of *I. ricinus* ticks, which was subsequently characterised as ***R. helvetica***. Boretti et al. (2009) identified this species in 12% of unfed and 36% of engorged *I. ricinus* from the canton of Zurich. Additionally, ***R. monacensis*** was found, but only in one tick. Furthermore, Bernasconi et al. (2002) identified ***R. massiliae*** in three *R. sanguineus* ticks from southern Switzerland (canton Ticino). This species has recently been linked to human disease (Parola et al. 2005).

Human Infections

In 2003, Baumann et al. examined patients with febrile illnesses following tick bites for various tick-borne pathogens. In eight patients, they were able to show antibodies against spotted fever group rickettsiae, and assumed that these antibodies were directed against *R. helvetica*. This study indicates that infections with tick-borne rickettsiae occur in Switzerland.

16.2.6 Conclusions

The numerous detections of various pathogenic species of rickettsiae in ticks in Germany, Austria and Switzerland revealed that there are considerable risks for humans to acquire rickettsioses. This is supported by the detection of autochthonous cases of rickettsioses in Germany and Switzerland as well as by seroepidemiological studies of hunters in Germany. The results of these studies emphasize that tick-borne rickettsioses have to be included in the differential diagnosis of tick-borne diseases in these countries.

16.3 *Anaplasma phagocytophilum*

The bacterial pathogen *A. phagocytophilum* is distributed in the northern hemisphere, and ixodid ticks of the genera *Ixodes* and *Dermacentor* act as vectors. The bacterium is well known as an agent of veterinary importance, but in the last years, it has received more and more attention as a pathogen causing disease in humans.

16.3.1 Taxonomy

Anaplasma phagocytophilum is classified as **α-Proteobacterium** and belongs to the order *Rickettsiales*, family *Anaplasmatacae*. Recent studies (Dumler et al. 2001; Taillardat-Bisch et al. 2003) based on the analysis of the 16S rDNA gene, the heat shock protein (GroEL) and the β-subunit of the RNA-polymerase, initiated a reorganisation within the genera *Ehrlichia, Anaplasma* and *Neorickettsia*. The former genus *Ehrlichia* was divided into three groups based on the nucleotide sequence of the 16S rDNA gene: *Ehrlichia canis* genogroup, *Ehrlichia phagocytophila* genogroup and *Ehrlichia sennetsu* genogroup. All members of the *E. phagocytophila* genogroup, which included *E. phagocytophila, Ehrlichia equi* and the agent of human granulocytic anaplasmosis (HGA) (formerly known as **human granulocytic ehrlichiosis**), are now described as *A. phagocytophilum*.

16.3.2 Biology

Anaplasma phagocytophilum is a small (0.4–1.9 μm), coccoid, **gram-negative bacterium**. It infects granulocytes and multiplies in intracytoplasmatic vacuoles, so-called morulae. According to its target cells, the disease is known as human granulocytic anaplasmosis (Maurin et al. 2003).

16.3.3 Disease

Infections with *A. phagocytophilum* remain asymptomatic in 60% of cases. Symptomatic infections are usually mild and self-limited with unspecific symptoms. After an incubation period of 2–7 days, the infection is characterised by **flu-like symptoms** with fever, arthralgia and malaise; thrombocytopenia and elevation of liver enzymes are typically observed. An exanthema can be present in some cases, and severe disease courses can lead to neurological disorders such as meningitis or meningoencephalitis. *Anaplasma phagocytophilum* may suppress the immune system; this is often followed by secondary infections such as candidiasis and pneumonia. The severity of disease depends on the age of the patients, the capability of their immune system and the timely administration of **antimicrobial therapy** that consists of **tetracyclines, fluoroquinolones or rifampicin** (Maurin et al. 2003). Severe and fatal infections mainly occur in patients with a deficient immune system. According to criteria of the WHO, human granulocytic anaplasmosis is confirmed if (a) an at least fourfold increase of IgG antibodies is observed, (b) *A. phagocytophilum* is detected by PCR, or (c) *A. phagocytophilum* can successfully be grown in cell culture (Bakken and Dumler 2000).

16.3.4 Vertebrate Hosts

It is supposed that *A. phagocytophilum* may infect a broad range of mammals, including wild and domestic animals as well as several rodent species (Strle 2004).

Anaplasma phagocytophilum infections were detected by PCR in 5.3% of rodents from southern Germany and in 7% of rodents from western Switzerland (Hartelt et al. 2008; Liz et al. 2000). In both studies, infection rates of *Myodes glareolus* were considerably higher than those of *Apodemus* spp. or *Microtus* spp. This indicates that *M. glareolus* is a particularly suitable host for *A. phagocytophilum.* Recently, Skuballa et al. (2010) studied different organs of 31 hedgehogs (*Erinaceus europaeus*) from various regions in Germany by means of PCR and sequencing. They detected *A. phagocytophilum* in eight of these hedgehogs (25.8%) and discussed the importance of hedgehogs as hosts for this pathogen. *Anaplasma phagocytophilum* was also detected in cervids in Switzerland and Austria with prevalences ranging from 29 to 60% (Liz et al. 2002; Petrovec et al. 2003; Polin

et al. 2004). However, sequencing revealed differences in the amplified genes of the pathogens isolated from cervids and humans. Therefore, the question whether *A. phagocytophilum* of cervids are responsible for human infections remains open.

16.3.5 Distribution in Germany

16.3.5.1 Ticks

In different studies carried out in Baden-Wuerttemberg, *A. phagocytophilum* was detected in 1.2, 2.8 and 1% of *I. ricinus*, respectively (Baumgarten et al. 1999; Oehme et al. 2002; Hartelt et al. 2004). The pathogen was also identified in *I. ricinus* in different parts of Bavaria. Baumgarten et al. (1999) described an infection rate of 2.6% in ticks from Frankonia in the northern part of Bavaria. Silaghi et al. (2008a) collected about 3,000 ticks in different areas in the south of Bavaria and observed a similar prevalence of 2.9%. Several reports confirmed that *A. phagocytophilum* is also widespread in eastern parts of Germany (Hildebrandt et al. 2002, 2010; Pichon et al. 2006). The infection rates vary between 2.3 and 5.4%. In 2003, von Loewenich et al. collected *I. ricinus* ticks in different parts of Germany and described a prevalence of 4.1%.

16.3.5.2 Antibody Prevalences in Humans

Hunfeld and Brade (1999) studied serum samples of 270 patients from the Rhine-Main area with history of a tick bite or confirmed Lyme Borreliosis and detected antibodies against *A. phagocytophilum* in 5.5% of all samples. In 2002, Oehme et al. screened sera from 4,368 forestry workers from Baden-Wuerttemberg for antibodies against *A. phagocytophilum*. The prevalences ranged from 5 to 16% in different areas with a mean prevalence of 10.7%. In a similar study, Bätzing-Feigenbaum et al. (2002) detected antibodies against *A. phagocytophilum* in 3.1 and 3.9% of forestry workers from Hesse and Berlin, respectively. In Berlin and Brandenburg, Kowalski et al. (2006) demonstrated *A. phagocytophilum* antibodies in 4.5% of patients with confirmed Lyme Borreliosis.

16.3.6 Distribution in Austria

16.3.6.1 Ticks

Anaplasma phagocytophilum was detected in 5.1 and 8.7% of questing *I. ricinus* ticks from various areas in Austria (Sixl et al. 2003; Polin et al. 2004). Additionally, Sixl et al. (2003) collected 178 *D. reticulatus* ticks, but none of them revealed an

infection with *A. phagocytophilum*, indicating that *D. reticulatus* is not a suitable vector for this pathogen in Austria.

16.3.6.2 Antibody Prevalences in Humans

Walder et al. (2003b) detected antibodies against *A. phagocytophilum* in 9% of sera from healthy blood donors from western Austria. Deutz et al. (2003) studied blood samples of 149 hunters from southern Austria. Interestingly, the prevalence of IgG antibodies against *A. phagocytophilum* was 15% and, therefore, remarkably higher than in people less exposed to ticks.

Human infections: Several cases of HGA were reported in Austria. Walder et al. (2003a) detected very high levels of both IgG and IgM antibodies in a patient with fever, flu-like symptoms and thrombocytopenia after a tick bite in Tyrol (southern Austria). The IgG antibody titre increased further in the following 6 weeks, whereas the IgM titre decreased. Therefore, Walder et al. confirmed the first autochthonous case of human granulocytic anaplasmosis in Austria. Further cases of HGA were identified by Walder et al. (2006) in five patients with febrile illness after tick bites and by Vogl et al. (2010) in a patient from eastern Austria.

16.3.7 Distribution in Switzerland

16.3.8 Ticks

In the cantons Zürich and Schaffhausen, *A. phagocytophilum* was detected in 1.3 and 2% of questing *I. ricinus* ticks, respectively (Pusterla et al. 1999; Liz et al. 2000). Additionally, the pathogen was identified in 1.4% of ticks collected in western Switzerland (cantons Bern and Neuchatel) (Liz et al. 2000). Wicki et al. (2000) screened 6,071 *I. ricinus* from various regions of Switzerland. They demonstrated *A. phagocytophilum* infections in 2.95% of adult ticks and in 0.94% of nymphs, respectively.

16.3.8.1 Human Infections

In 2000, Weber et al. detected antibodies against *A. phagocytophilum* in 8 out of 80 patients with febrile illness following tick bites and in 12 out of 48 patients who were seropositive for TBE or Lyme Borreliosis. Additionally, Baumann et al. (2003) revealed antibodies in seven patients with fever after tick bites.

Neither Weber et al. (2000) nor Baumann et al. (2003) were able to detect the pathogen by microscopic or molecular biological methods, and no fourfold increase in IgG antibody titres was observed. All of the described cases were probably due to

A. phagocytophilum infections, but it has to be pointed out that these infections did not match the WHO case definitions completely.

16.3.9 Conclusions

Anaplasma phagocytophilum was frequently detected in ticks and mammals in Germany, Austria and Switzerland. Moreover, high seroprevalences especially in persons that are highly exposed to tick bites were reported. Surprisingly, only few cases of HGA occurred in Austria and Switzerland, and no case has been reported from Germany so far. Because of the often unspecific flu-like symptoms, it might be possible that human infections are overlooked or misdiagnosed in some cases. However, *A. phagocytophilum* infections should be considered in cases of febrile illness after tick bites in these countries.

16.4 *Babesia* spp.

Babesiosis caused by the protozoan parasite *Babesia* spp. is a well-known disease of veterinary importance that attracts increasing attention as an emerging tick-borne disease in humans (Homer et al. 2000; Kjemtrup and Conrad 2000). More than 100 *Babesia* species are known, but only a few were identified as pathogens for humans.

16.4.1 Taxonomy

Parasites of the genus *Babesia* belong to the phylum Apicomplexa, order *Piroplasmida*.

Traditionally, the genus *Babesia* is divided into two groups based on their morphology and their size: the large *Babesia* species, including *B. bigemina* and *B. canis*, and the small *Babesia* species, for example *B. microti* and *B. gibsoni* (Homer et al. 2000). Phylogenetic analyses confirmed the separation of large *Babesia* species (also referred to as *Babesia* sensu stricto) and small *Babesia* species (or *B. microti*-like *Babesia*) (Gray et al. 2010).

16.4.2 Biology

Babesia spp. are obligate intracellular, pleomorph organisms that infest erythrocytes. Large *Babesia* species are about 2.5–5.0 μm in diameter, whereas small *Babesia* measure 1.0–2.5 μm in diameter (Hunfeld et al. 2008).

The life cycle of *Babesia* spp. includes an obligate host switch with ticks as definitive hosts and vertebrates as intermediate hosts. The asexual reproduction (merogony) takes place in the erythrocytes of the vertebrate, whereas sexual reproduction (gamogony) and further asexual proliferation (sporogony) occur in the tick. In contrast to small *Babesia* species, large *Babesia* species are transmitted transovarially in their tick vectors (Gray et al. 2010). All European *Babesia* species use *I. ricinus* as definitive host, but their intermediate hosts differ. *Babesia divergens* mainly infects cattle, whereas *B. microti* is found in rodents. The main host for *B. venatorum* seems to be the deer (Gray et al. 2010).

16.4.3 Disease

Babesiosis in Europe is mainly caused by *B. divergens*. Most patients are splenectomised, and severe, often lethal cases are observed frequently. *Babesia microti*, which causes many infections in North America, is rarely diagnosed in Europe. However, infections with this species also affect immunocompetent persons, and the course of disease is usually mild (Granström 1997; Kjemtrup and Conrad 2000). *Babesia venatorum* (previously known as strain *Babesia* sp. EU1) is also linked to human babesiosis in Europe. This species belongs to the large *Babesia* species and is closely related to *B. divergens* (Hunfeld et al. 2008). Most infections with *Babesia* spp. remain subclinical. Clinical manifestations have been observed mainly in immunocompromised patients and are often found in splenectomised patients. However, the number of infections in otherwise healthy persons has increased in the last years (Granström 1997; Kjemtrup and Conrad 2000).

After an incubation period of 1–3 weeks, a flu-like illness with fever, arthralgia and weakness emerges. Haemolysis leads to the main symptoms of acute infection, which are haemoglobinuria, haemolytic anaemia, hepatosplenomegaly and jaundice. In mild cases, the disease is self-limited and patients recover without any further problems. In immunocompromised or splenectomised and elderly patients, complications including acute pulmonary failure, congestive heart failure and renal failure may occur and may be lethal (Homer et al. 2000; Wang et al. 2000; Hunfeld et al. 2002a). Patients with severe babesiosis need **rapid treatment** with a combination of either **clindamycin** and **quinine or atovaquone** and **azithromycin** (Krause 2003). Additionally, a blood exchange transfusion may be necessary to reduce the number of parasites in the blood and to prevent further haemolysis. *Babesia* spp. infections are mainly due to tick bites, but transmission via blood transfusion may also occur (Leiby 2006).

16.4.4 Distribution in Germany

The information about the distribution of *Babesia* species in ticks as well as mammals is often restricted to certain areas in Germany. Hartelt et al. (2004)

screened more than 3,000 *I. ricinus* ticks in Baden-Wuerttemberg and identified *B. divergens* and *B. microti* in 0.9 and 0.1% of ticks, respectively. Additionally, they trapped 508 rodents in the same areas (Hartelt et al. 2008). 1.6% of *Arvicolidae* (*M. glareolus* and *M. arvalis*) were infected, but none of the *Muridae*. In 2002, Hunfeld et al. showed that exposure to *Babesia* spp. must frequently occur in Germany. They screened serum samples of 467 persons from the Rhine-Main area for antibodies against *Babesia* spp. IgG antibodies against *B. microti* and *B. divergens* were detected in 5.4 and 3.6% of participants, respectively. Additionally, antibody prevalences were considerably higher in persons with previous tick bites (11.5%) than in persons without tick exposure (1.7%) (Hunfeld et al. 2002b). The first report about an autochthonous case of human babesiosis in Germany was published in 2005 (Häselbarth et al. 2007). The splenectomised patient living in the south of Baden-Wuerttemberg showed typical signs of babesiosis, including haemolytic anaemia and haemoglobinuria. *Babesia venatorum* was detected in the peripheral blood by microscopy and PCR. Hildebrandt et al. (2007) confirmed another case of human babesiosis due to *B. microti* in a patient with acute myeloid leukaemia in Thuringia by PCR and microscopy of peripheral blood smears. They assumed that the patient acquired the infection via blood transfusion. This was confirmed by the detection of *B. microti* antibodies in serum samples of the blood donor. Neither the patient nor the donor travelled recently to countries with high risk of *B. microti* infections (especially North America). The authors assumed that this is the first autochthonous case of a *B. microti* infection in Germany.

16.4.5 Distribution in Austria

Blaschitz et al. (2008a) studied 853 *I. ricinus* from different sampling sites in Austria. The results of their study revealed a surprisingly high infection rate with *Babesia* spp. of 51.7%. Infection rates ranged from 0 to 100% in the different sampling areas. All positive samples were sequenced and identified as *B. divergens* or *B. divergens*-like strains, respectively. Blaschitz et al. assumed that the striking differences in prevalences might be due to a very focal distribution of the pathogen, and that the high overall infection rate could be explained by high tick population densities. In 2003, Herwaldt et al. reported the first autochthonous case of human babesiosis in Austria. According to PCR and DNA sequencing, the disease of a splenectomised patient was due to an infection with *B. venatorum*.

16.4.6 Distribution in Switzerland

Several studies concerning *Babesia* spp. infections in ticks are available. Foppa et al. (2002) detected *B. microti* in 3.4% of *I. ricinus* nymphs from eastern Switzerland. Casati et al. (2006) examined *I. ricinus* ticks from various regions in Switzerland and identified *B. microti*, *B. divergens* and *B. venatorum* in 0.2, 0.2 and

0.4% of ticks, respectively. Hilpertshauser et al. (2006) studied ticks that were removed from wild and domestic ruminants (sheep, goat, cattle and deer) in southern Switzerland. They identified *B. divergens* and *B. venatorum* in 0.9 and 2% of ticks, respectively. Additionally, they found strains of *Babesia* spp. of yet unknown pathogenicity.

In 2002, Foppa et al. confirmed that the exposure of humans to *Babesia* spp. occurs in Switzerland more frequently than expected, because they detected IgG antibodies against *B. microti* in 1.5% of healthy blood donors from eastern Switzerland.

The first autochthonous case of **human babesiosis** in Switzerland was published in 2004 (Meer-Scherrer et al. 2004). *Babesia microti* was identified as the causative agent by PCR. Additionally, the patient suffered from concurrent *Borrelia burgdorferi* infection.

16.4.7 Conclusions

Pathogenic *Babesia* species are prevalent in ticks in all three countries and cases of human babesiosis were reported from Germany, Austria and Switzerland. The detection of antibodies against *Babesia* spp. indicates that people are frequently exposed to this pathogen without developing symptomatic infections. *Babesia divergens*, *B. microti* and *B. venatorum* were identified as causative agents not only in immunocompromised or splenectomised patients but also in healthy people.

16.5 *Francisella tularensis*

16.5.1 Biology

Francisella tularensis belongs to the **γ-proteobacteria**, family *Francisellaceae*. It is a facultative intracellular, small gram-negative bacterium. Because of its high infectivity and low infection dose, it was classified as a possible bioterrorist agent and, therefore, has gained increasing attention in recent years. Two subspecies are responsible for human infections. *Francisella tularensis* subspecies *tularensis* occurs only in North America, whereas *F. tularensis* subsp. *holarctica* is distributed in the northern hemisphere (Ellis et al. 2002).

16.5.2 Disease

Generally, *F. tularensis* subsp. *holarctica* induces mild infections, whereas severe forms of tularaemia (typhoid and pneumonic forms) are almost exclusively related to infections with *F. tularensis* subsp. *tularensis*.

The **symptoms of tularaemia** differ depending on the route of infection. Ulceroglandular tularaemia is the most common form and usually follows transmission by arthropod bites or inoculation of the bacteria through skin lesions. It is characterised by a sudden onset with flu-like symptoms such as fever, chills and headache, followed by the development of an ulcer at the site of infection that can persist for several months. Dissemination of the bacteria via lymph fluid leads to an enlargement of regional lymph nodes and lymphadenopathy. This form is usually mild and self-limited, but a spread of the pathogen to tissues of inner organs may lead to complications such as pneumonia. Ingestion of contaminated food or water leads to oropharyngeal tularaemia with a painful sore throat, enlargement of tonsils and swollen cervical lymph nodes or to gastrointestinal infection. Depending on the infection dose, a gastrointestinal infection can lead to mild and persistent diarrhoea or to severe intestinal ulceration that can be lethal. The most severe forms of tularaemia are the typhoid form without an identified route of infection, characterised by septicaemia and a mortality rate of 30–60%, and the pneumonic form that follows inhalation of *F. tularensis* and appears as pneumonia with very variable clinical signs (Ellis et al. 2002).

Tularaemia is usually treated with **streptomycin** or **gentamicin**. Because of the unspecific symptoms, the diagnosis of mild infections might often be missed.

16.5.3 Epidemiology

Francisella tularensis has been identified in a broad range of mammals, but only some species seem to be able to maintain the pathogen in enzootic cycles. *Francisella tularensis* subsp. *tularensis* mainly infects lagomorphs (rabbits and hares), while *F. tularensis* subsp. *holarctica* is detectable in lagomorphs as well as in rodent species. Various arthropods are able to transmit the pathogen to animals and humans. Tabanids and mosquitoes (*Aedes* spp., *Culex* spp., *Anopheles* spp.) are frequently involved in larger outbreaks of tularaemia. They often bite multiple hosts in short time periods, and, therefore, contribute to a rapid spread of the disease. It is assumed that both tabanids and mosquitoes are mechanical vectors and that the bacteria cannot survive in these arthropods for more than a few days. In hard ticks, however, the bacteria are present and multiply in the gut and in haemolymph, and they are transmitted transstadially. Therefore, ticks are capable of maintaining *F. tularensis* for a long time in nature. Transovarial transmission may occur exceptionally (Petersen et al. 2009).

In North America and Scandinavia, arthropod bites are the most important mode of transmission (Petersen et al. 2009). Only few studies were conducted in central Europe. Hubalek et al. (1998) detected *F. tularensis* in 2.8% of *D. reticulatus* in Austria, whereas Wicki et al. (2000) identified this pathogen in 0.12% of *I. ricinus* nymphs in Switzerland. In 2009, *F. tularensis* was found in 0.9% of *I. ricinus* ticks from Baden-Wuerttemberg (Oehme et al. unpublished data). Moreover, Hanke et al. (2009) reported a case of tularaemia in a 1-year-old

child living in the Southwest of Germany. They assumed that the toddler acquired the infection via a mosquito bite. These studies indicate that *F. tularensis* is distributed in arthropods in Germany, and that transmission of this pathogen via arthropod bites may occur.

However, in central Europe, hares and rodents seem to be the most important sources of human infections (Ellis et al. 2002). In Germany, the pathogen has been detected in 4.92% of rodents (*M. glareolus*, *Arvicola terrestris*, *Microtus* spp., *A. flavicollis*) trapped in areas with previous tularaemia outbreaks (Kaysser et al. 2008). Since 2005, the number of *F. tularensis* infections in hare increased in Germany. In summary, 25 infected hare were found between 2005 and 2009 in various federal states (P. Otto, personal communication). Additionally, specific antibodies were detected in 3.1% of wild boar (*Sus scrofa*) from Mecklenburg-Western Pomerania (Al Dahouk et al. 2005). It was also detected in 3 out of 167 hares in Switzerland (Friedl et al. 2005). Data about *F. tularensis* infections in mammals are not available for Austria so far. Besides sporadic cases of tularaemia, there are outbreaks with high numbers of patients from time to time. Such outbreaks often occur concurrently in humans and wild animals (Ellis et al. 2002). Infections are mainly acquired via skin lesions while handling infected animals, or by inhalation of aerosolised bacteria. In 2005, there was an outbreak of airborne tularaemia among participants of a hare hunt in Hesse (Hauri et al. 2010). It was subsequently shown that nine hunters got infected by inhalation of aerosols containing *F. tularensis* while they rinsed carcasses of infected hare.

Hunters have an increased risk of acquiring *F. tularensis* infection via contact to infected animals. Jenzora et al. (2008) detected antibody prevalence of 1.7% in hunters from western Germany, and Winter et al. (2010, unpublished data) showed a very high prevalence of 4.5% in hunters from Baden-Wuerttemberg. In Austria, 3.0% of hunters from the federal states of Styria and Burgenland revealed antibodies against *F. tularensis* (Deutz et al. 2003).

Similar seroprevalence studies in the general population indicate that infections with *F. tularensis* occur frequently, despite the low number of reported cases. In Germany, seroprevalences of 0.23, 3.0 and 2.32% in the general population were reported (Porsch-Özcürümez et al. 2004; Schmitt et al. 2005; Splettstoesser et al. 2008).

The seroprevalence data of both hunters and the general population contradict the very low number of reported cases. In Germany, an average number of three cases are reported per year, with most infections occurring in Baden-Wuerttemberg, Hesse and North Rhine-Westphalia (Grunow and Priebe 2007). However, the number of human cases in Germany has increased in the last years; in 2007, 21 cases were reported, which is the highest case number since 1958 (Splettstoesser 2008). The average number of infections in Austria is stated as 10–15 cases (Deutz et al. 2003). In Switzerland, only sporadic cases occur (Friedl et al. 2005).

16.5.4 Conclusions

The distribution of *F. tularensis* in arthropods in central Europe is still not known. Therefore, it is not certain if transmission by arthropod bites plays an important role in transmitting *F. tularensis* in these countries. More studies are necessary to clarify the epidemiology of this pathogen and its occurrence in natural foci.

16.6 Eyach Virus

In 1976, Rehse-Küpper et al. isolated a virus from *I. ricinus* in the Eyach valley in Baden-Wuerttemberg, which was subsequently named the Eyach virus. Sequence analyses revealed a close relationship with the Colorado tick bite fever virus (CTF virus) that was isolated in Colorado in the 1940s and identified as a disease agent causing a febrile illness after tick bites.

16.6.1 Biology and Disease

CTF and Eyach virus belong to the family **Reoviridae,** genus *Coltivirus*. They are non-enveloped, spherical, often icosahedral particles that measure about 75–80 nm in diameter. Target cells for the CTF virus are human haematopoietic precursor cells. The virus can persist in the erythrocytes and can be transported in other organs such as brain, spleen, bone marrow and myocardium. It is assumed that the Eyach virus shows the same characteristics (Charrel et al. 2004). To date, nothing is known about the disease course in human Eyach-virus infections, but it is supposed that it resembles that of CTF-virus infections. Colorado tick bite fever is usually a mild and self-limited disease with a characteristic biphasic fever that is present in half of the patients (Bowen 1988). After an incubation period of 3–6 days, a febrile illness with unspecific symptoms such as retroorbital headache, myalgia and arthalgia, pharyngitis and anorexia develops. Typically, fever lasts for 2–5 days, followed by an afebrile and asymptomatic interval of 2–7 days. Subsequently, a second febrile period with higher temperatures and involvement of inner organs may follow (Klasco 2002). Complications due to secondary infections, such as meningitis, encephalitis or myocarditis, are relevant in about 5% of patients and are mainly seen in children (Braun et al. 1999). No specific treatment against Colorado tick bite fever exists at the moment.

It is suspected that the Eyach virus causes similar symptoms in humans. This was supported by studies with experimentally infected new-borne mice that showed neurological symptoms, and most of them died due to encephalitis (Rehse-Küpper et al. 1976; Chastel et al. 1984).

16.6.2 Epidemiology

The Eyach virus was first isolated in Germany in 1976 (Rehse-Küpper et al. 1976). In 2004, Hartelt screened 3,260 ticks in Baden-Wuerttemberg and detected the virus in three of them, i.e. 0.1%. The pathogen was also identified in *I. ricinus* and *Ixodes ventalloi* from northwest France (Chastel et al. 1984). Up to now there have been no reports about this pathogen in other European countries. At the moment, nothing is known about mammalian hosts of the Eyach virus. Dobler et al. (2006) studied 166 sera of brown hare from northern Germany, but did not find any evidence for Eyach-infected animals. The pathogenicity of the Eyach virus for humans is unknown, for no human infections have been reported so far. But antibodies against this pathogen were detected in patients with meningoencephalitis in the Czech Republic (Malkova et al. 1980). This indicates that the Eyach virus is indeed pathogenic for humans. However, as no cases of Eyach-virus infection were reported in Europe and the infection rate of ticks in Germany seems to be rather low, it is very likely that an infection risk for humans does not exist at the moment. But the virus should be kept in mind for future studies.

16.7 General Conclusions of the Chapter

The data reported in this review summarise the current status of the distribution of some tick-transmitted pathogens in natural foci. However, these distribution patterns may change in the future, for example due to climate change and increasing average temperatures. It is generally assumed that changes in temperature have an important influence on ticks (Gray et al. 2009). If temperatures rise due to climate change, the distribution and abundance of some tick species (especially *Dermacentor* spp. and *R. sanguineus*) may be extended, and tick-borne pathogens might spread with them. Therefore, continuing studies are necessary to monitor any changes in the distribution and abundance of tick-transmitted pathogens. Future infection risks for humans can only be evaluated on the basis of these studies.

Ticks and pathogens that are not endemic in central Europe may establish in natural foci if the climate conditions become more suitable for them. For example, *R. sanguineus* could be imported and build up populations in Germany if the average temperatures rise in the future, and *Rickettsia conorii* may be introduced together with its main vector. Dogs are the main hosts for both *R. sanguineus* and *R. conorii*; therefore, dogs from endemic areas in the Mediterranean region can act as carriers for both the vector and the pathogen. Menn et al. (2010) detected antibodies against *R. conorii* in 68.2% of dogs from an endemic area in Portugal. This shows that the risk of introducing this specific pathogen with imported or travelling dogs is quite high.

All tick-borne diseases mentioned in this review can manifest as mild, self-limited illnesses with unspecific symptoms. Therefore, their diagnosis might often

be missed, and the current infection risk for humans may be underestimated. But infections with the above-mentioned pathogens can also lead to severe or even life-threatening disease courses. Hence, their medical importance should not be treated lightly, and they have to be kept in mind in the differential diagnosis of tick-borne diseases.

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References

Al Dahouk S, Nöckler K, Tomaso H, Splettstoesser WD, Jungersen G, Riber U, Petry T, Hoffmann D, Scholz HC, Hensel A, Neubauer H (2005) Seroprevalence of brucellosis, tularemia, and yersiniosis in wild boars (*Sus scrofa*) from north-eastern Germany. J Vet Med B 52:444–455

Azad AF, Beard CB (1998) Rickettsial pathogens and their arthropod vectors. Emerg Infect Dis 4(2):179–186

Bakken JS, Dumler JS (2000) Human granulocytic ehrlichiosis. Clin Infect Dis 31:554–560

Bätzing-Feigenbaum J, Brenner H, Kallischnigg G, Rüden H, Talaska T (2002) Seroprevalence of antibodies against the agent of the "Human Granulocytic Ehrlichiosis" (HGE) in high risk populations of foresters in the Federal Laender of Hesse (northern part), Brandenburg and Berlin, Germany. Int J Med Microbiol 291(Suppl 33):194–195

Baumann D, Pusterla N, Peter O, Grimm F, Fournier PE, Schär G, Bossart W, Lutz H, Weber R (2003) Fieber nach Zeckenstich: Klinik und Diagnostik von akuten Zeckenstich-assoziierten Infektionskrankheiten in der Nordostschweiz. Dtsch Med Wochenschr 128:1042–1047, In German

Baumgarten BU, Röllinghoff M, Bogdan C (1999) Prevalence of *Borrelia burgdorferi* and granulocytic and monocytic ehrlichiae in *Ixodes ricinus* ticks from southern Germany. J Clin Microbiol 37(11):3448–3451

Bernasconi MV, Casati S, Peter O, Piffaretti JC (2002) *Rhipicephalus* ticks infected with *Rickettsia* and *Coxiella* in Southern Switzerland (Canton Ticino). Infect Genet Evol 2:111–120

Blaschitz M, Narodoslavsky-Gföller M, Kanzler M, Stanek G, Walochnik J (2008a) *Babesia* species occurring in Austrian *Ixodes ricinus* ticks. Appl Environ Microbiol 74(15):4841–4846

Blaschitz M, Narodoslavsky-Gföller M, Kanzler M, Walochnik J, Stanek G (2008b) First detection of *Rickettsia helvetica* in *Ixodes ricinus* ticks in Austria. Vector Borne Zoonotic Dis 8(4):561–563

Boretti FS, Perreten A, Meli ML, Cattori V, Willi B, Wengi N, Hornok S, Honegger H, Hegglin D, Woelfel R, Reusch CE, Lutz H, Hofmann-Lehmann R (2009) Molecular investigations of *Rickettsia helvetica* infection in dogs, foxes, humans and *Ixodes* ticks. Appl Environ Microbiol 75(10):3230–3237, 27

Bowen GS (1988) Colorado tick fever. In: Monath TP (ed) The arboviruses: epidemiology and ecology, vol II. CRC Press, Florida, pp 159–176

Braun R, Hassler D, Kimmig P (1999). Seltenere Zecken-übertragene Krankheiten Teil II: Viren, Tularämie und Babesiose. Available at www.baxter.de/fachkreise/artikel/ellipse_fsme_teil2.pdf. In German

Burgdorfer W, Aeschlimann A, Peter O, Hayes SF, Philip RN (1979) *Ixodes ricinus*: vector of a hitherto undescribed spotted fever group agent in Switzerland. Acta Trop 36:357–367

Casati S, Sager H, Gern L, Piffaretti JC (2006) Presence of potetially pathogenic *Babesia* sp. for human in *Ixodes ricinus* in Switzerland. Ann Agric Environ Med 13:65–70

Charrel RN, Attoui H, Butenko AM, Clegg JC, Deubel V, Frolova TV, Gould EA, Gritsun TS, Heinz FX, Labuda M, Lashkevich VA, Loktev V, Lundkvist A, Lvov DV, Mandi CW, Niedrig M, Papa A, Petrov VS, Plyusnin A, Randolph S, Süss J, Zlobin VI, de Lamallerie X (2004) Tick-borne virus diseases of human interest in Europe. Clin Microbiol Infect 10:1040–1055

Chastel C, Main AJ, Couatarmanac'h A, Le Lay G, Knudson DL, Ouillen MC, Beaucournu JC (1984) Isolation of Eyach virus (*Reoviridae*, Colorado Tick Fever group) from *Ixodes ricinus* and *I. ventalloi* in ticks in France. Arch Virol 82:161–171

Dautel H, Dippel C, Oehme R, Hartelt K, Schettler E (2006) Evidence for an increased geographical distribution of *Dermacentor reticulatus* in Germany and detection of *Rickettsia* sp. RpA4. Int J Med Microbiol 296(Suppl 1):149–156

Deutz A, Fuchs K, Schuller W, Nowotny N, Auer H, Aspöck H, Stünzner D, Kerbl U, Klement C, Köfer J (2003) Seroepidemiologische Untersuchung von Jägern auf Zoonosen in Südösterreich – Prävalenzen, Risikopotentiale und Vorbeugemaßnahmen. Berl Münch Tierärztl Wochenschr 116:306–311, In German

Dobec M, Golubic D, Punda-Polic V, Kaeppeli F, Sievers M (2009) *Rickettsia helvetica* in *Dermacentor reticulatus* ticks. Emerg Infect Dis 15(1):98–100

Dobler G, Wölfel R (2009) Typhus and other rickettsioses. Dtsch Arztebl Int 106(20):28

Dobler G, Wölfel R, Schmüser H, Essbauer S, Pfeffer M (2006) Seroprevalence of tick-borne and mosquito-borne arboviruses in European brown hares in Northern and Western Germany. Int J Med Microbiol 296(Suppl 1):80–83

Dobler G, Essbauer S, Terzioglu R, Thomas A, Wölfel R (2008) Häufigkeit des Frühsommer-Meningoenzephalitis-Virus und von Rickettsien in Zecken aus dem Burgenland (Österreich). Wien Klin Wochenschr 120(Suppl 4):45–48, In German

Dumler JS, Barbet AF, Bekker CPJ, Dasch GA, Palmer GH, Ray SC, Rikihisa Y, Rurangirwa FR (2001) Reorganisation of genera in the families *Rickettsiaceae* and *Anaplasmataceae* in the order *Rickettsiales*: unification of some species of *Ehrlichia* with *Anaplasma*, *Cowdria* with *Ehrlichia* and *Ehrlichia* with *Neorickettsia*, description of six new species combinations and designation of *Ehrlichia equi* and 'HGE agent' as subjective synonyms of *Ehrlichia phagocytophila*. Int J Syst Evol Microbiol 51:2145–2165

Ellis J, Oyston PCF, Green M, Titball RW (2002) Tularemia. Clin Microbiol Rev 15(4):631–646

Foppa JM, Krause PJ, Spielman A, Goethert H, Gern L, Brand B, Telford SR 3rd (2002) Entomologic and serologic evidence of zoonotic transmission of *Babesia microti*, eastern Switzerland. Emerg Infect Dis 8(7):722–726

Fournier PE, Grunnenberger F, Jaulhac B, Gastinger G, Raoult D (2000) Evidence of *Rickettsia helvetica* infection in humans, eastern France. Emerg Infect Dis 6(4):389–392

Fournier PE, Allombert C, Supputamongkol Y, Caruso G, Brouqui P, Raoult D (2004) Aneruptive fever associated with antibodies to *Rickettsia helvetica* in Europe and Thailand. J Clin Microbiol 42(2):816–818

Friedl A, Heinzer I, Fankhauser H (2005) Tularemia after a dormouse bite in Switzerland. Eur J Clin Microbiol Infect Dis 24:352–354

Gillespie JJ, Beier MS, Rahman MS, Ammermann NC, Shallom JM, Purkayastha A, Sobral BS, Azad AF (2007) Plasmids and rickettsial evolution: insights from *Rickettsia felis*. PLoS ONE 2 (3):e266

Granström M (1997) Tick-borne zoonoses in Europe. Clin Microbiol Infect 3:156–167

Gray JS, Dautel H, Estrada-Pena A, Kahl O, Lindgren E (2009) Effects of climate change on ticks and tick-borne diseases in Europe. Interdiscip Perspect Infect Dis 2009:593232. Epub ahead of print

Gray J, Zintl A, Hildebrandt A, Hunfeld KP, Weiss L (2010) Zoonotic babesiosis: overview of the disease and novel aspects of pathogen identity. Ticks Tick-borne Dis 1:3–10

Grunow R, Priebe HS (2007) Tularämie - zum Vorkommen in Deutschland. Epidemiologisches Bulletin 7/2007. Available from http://www.rki.de/cln_160/nn_264978/DE/Content/Infekt/EpidBull/Archiv/2007/07__07.html?__nnn=true. Cited 10 May 2010. In German. 29

Hanke CA, Otten JE, Berner R, Serr A, Splettstoesser W, von Schnakenburg C (2009) Ulceroglandular tularemia in a toddler in Germany after a mosquito bite. Eur J Pediatr 168:937–940

Hartelt K (2004) Epidemiologie Arthropoden-übertragener Infektionen in Baden-Württemberg. Doctoral thesis at the University of Hohenheim, Germany. In German

Hartelt K, Oehme R, Frank H, Brockmann SO, Hassler D, Kimmig P (2004) Pathogens and symbionts in ticks: prevalence of *Anaplasma phagocytophilum* (*Ehrlichia* sp.), *Wolbachia* sp. *Rickettsia* sp. and *Babesia* sp. in Southern Germany. Int J Med Microbiol 293(Suppl 37):86–92

Hartelt K, Pluta S, Oehme R, Kimmig P (2008) Spread of ticks and tick-borne diseases in Germany due to global warming. Parasitol Res 103(Suppl 1):109–116

Häselbarth K, Tenter AM, Brade V, Krieger G, Hunfeld KP (2007) First case of human babesiosis in Germany – clinical presentation and molecular characterisation of the pathogen. Int J Med Microbiol 297:197–204

Hauri AM, Hofstetter I, Seibold E, Kaysser P, Eckert J, Neubauer H, Splettstoesser WD (2010) Investigating an airborne tularemia outbreak, Germany. Emerg Infect Dis 16(2):238–243

Herwaldt BL, Caccio S, Gherlinzoni F, Aspöck H, Slemenda SB, Piccaluga PP, Martinelli G, Edelhofer R, Hollenstein U, Poletti G, Pampiglione S, Löschenberger K, Tura S, Pieniazek NJ (2003) Molecular characterization of a non-*Babesia divergens* organism causing zoonotic Babesiosis in Europe. Emerg Infect Dis 9(8):942–948

Hildebrandt A, Schmidt KH, Fingerle V, Wilske B, Straube E (2002) Prevalence of granulocytic ehrlichiae in *Ixodes ricinus* ticks in Middle Germany (Thuringia) detected by PCR and sequencing of a 16S ribosomal DNA fragment. FEMS Microbiol Lett 211:225–230

Hildebrandt A, Hunfeld KP, Baier M, Krumbholz A, Sachse S, Lorenzen T, Kiehntopf M, Fricke HJ, Straube E (2007) First confirmed autochthonous case of human *Babesia microti* infection in Europe. Eur J Clin Microbiol Infect Dis 26:595–601

Hildebrandt A, Krämer A, Sachse S, Straube E (2010) Detection of *Rickettsia* spp. and *Anaplasma phagocytophilum* in *Ixodes ricinus* ticks in a region of middle Germany (Thuringia). Ticks Tick-borne Dis 1:52–56

Hilpertshauser H, Deplazes P, Schnyder M, Gern L, Mathis A (2006) *Babesia* spp. identified by PCR in ticks collected from domestic and wild ruminants in southern Switzerland. Appl Environ Microbiol 72(10):6503–6507, 30

Homer MJ, Aguilar-Delfin I, Telford SR 3rd, Krause PJ, Persing DH (2000) Babesiosis. Clin Microbiol Rev 13:451–469

Hubalek Z, Sixl W, Halouzka J (1998) *Francisella tularensis* in *Dermacentor reticulatus* ticks from the Czech Republic and Austria. Wien Klin Wochenschr 110(24):909–910

Hunfeld KP, Brade V (1999) Prevalence of Antibodies against the human granulocytic ehrlichiosis agent in Lyme Borreliosis patients from Germany. Eur J Clin Microbiol Infect Dis 18:221–224

Hunfeld KP, Cinatl J, Tenter AM, Brade V (2002a) Granulocytic *Ehrlichia*, *Babesia* and spotted fever *Rickettsia*: not yet widely known tick-borne pathogens of considerable concern for humans at risk in Europe. Biotest Bull 6:321–344

Hunfeld KP, Lambert A, Kampen H, Albert S, Epe C, Brade V, Tenter AM (2002b) Seroprevalence of *Babesia* infections in humans exposed to ticks in midwestern Germany. J Clin Microbiol 40(7):2431–2436

Hunfeld KP, Hildebrandt A, Gray JS (2008) Babesiosis: recent insights into and ancient disease. Int J Parasitol 38:1219–1237

Jado I, Oteo JA, Aldamiz M, Gil H, Escuerdo R, Ibarra V, Portu J, Portillo A, Lezaun MJ, Garcia-Amil C, Rodriguez-Moreno I, Anda P (2007) *Rickettsia monacensis* and human disease, Spain. Emerg Infect Dis 13(9):1405–1407

Jansen A, La Scola B, Raoult D, Lierz M, Wichmann O, Stark K, Schneider T (2008) Antibodies against *Rickettsia* spp. in hunters, Germany. Emerg Infect Dis 14(12):1961–1963

Jenzora A, Jansen A, Ranisch H, Lierz M, Wichmann O, Grunow R (2008) Seroprevalence study of *Francisella tularensis* among hunters in Germany. FEMS Immunol Med Microbiol 53:183–189

Kaysser P, Seibold E, Mätz-Rensing K, Pfeffer M, Essbauer S, Splettstoesser WD (2008) Re-emergence of tularemia in Germany: presence of *Francisella tularensis* in different rodent species in endemic areas. BMC Infect Dis 8:157

Kimmig P, Hassler D, Braun R (2000) Zecken - kleiner Stich mit bösen Folgen. Ehrenwirth (Hrsg), 2. Auflage. ISBN 3-431-04018-7. In German

Kjemtrup AM, Conrad PA (2000) Human babesiosis: an emerging tick-borne disease. Int J Parasitol 30:1323–1337

Klasco R (2002) Colorado tick fever. Med Clin North Am 86:435–440

Kowalski J, Hopfenmüller W, Fingerle V, Malberg H, Eisenblätter M, Wagner J, Miksits K, Hahn H, Ignatius R (2006) Seroprevalence of human granulocytic anaplasmosis in Berlin/Brandenburg, Germany: an 8-year survey. Clin Microbiol Infect 12(9):924–927, 31

Krause PJ (2003) Babesiosis diagnosis and treatment. Vector Borne Zoonotic Dis 3:45–51

La Scola B, Raoult D (1997) Laboratory diagnosis of rickettsioses: current approaches to diagnosis of old and new rickettsial diseases. J Clin Microbiol 35(11):2715–2727

Lakos A (1997) Tick-borne lymphadenopathy - a new rickettsial disease? Lancet 350:1006

Leiby DA (2006) Babesiosis and blood transfusion: flying under the radar. Vox Sang 90:157–165

Liebisch A, Rahmann MS (1976) Zum Vorkommen und zur vektoriellen Bedeutung der Zecken *Dermacentor marginatus* (Sulzer, 1776) und *Dermacentor reticulatus* (Fabricius, 1794) in Deutschland. Tropenmed Parasitol 27:393–404, In German

Liz JS, Anderes L, Sumner JW, Massung RF, Gern L, Rutti B, Brossard M (2000) PCR detection of granulocytic ehrlichiae in *Ixodes ricinus* ticks and wild small mammals in western Switzerland. J Clin Microbiol 38(3):1002–1007

Liz JS, Summer JW, Pfister K, Brossard M (2002) PCR detection and serological evidence of granulocytic ehrlichial infection in roe deer (*Capreolus capreolus*) and chamois (*Rupicapra rupicapra*). J Clin Microbiol 40(3):892–897

Malkova D, Holubova J, Kolman JM, Marhoul Z, Hanzal F, Kulkova H, Markvart K, Simkova L (1980) Antibodies against some arboviruses in persons with various neuropathies. Acta Virol 24(4):298

Martinez JJ, Cossart P (2004) Early signaling events involved in the entry of *Rickettsia conorii* into mammalian cells. J Cell Sci 117:5097–5106

Maurin M, Bakken JS, Dumler JS (2003) Antibiotic susceptibilities of *Anaplasma* (*Ehrlichia*) *phagocytophilum* strains from various geographic areas in the United States. Antimicrob Agents Chemother 47:413–415

Mediannikov O, Matsumoto K, Samoylenko I, Drancourt M, Roux V, Rydkina E, Bavoust B, Tarasevich I, Brouqui P, Fournier PE (2008) *Rickettsia raoultii* sp. nov. a spotted fever group rickettsia associated with *Dermacentor* ticks in Europe and Russia. Int J Syst Evol Microbiol 58:1635–1639

Meer-Scherrer L, Adelson M, Mordechai E, Lottaz B, Tilton R (2004) *Babesia microti* infection in Europe. Curr Microbiol 48:435–437

Mehlhorn B, Mehlhorn H (2009) Zecken auf dem Vormarsch. Düsseldorf University Press, Düsseldorf

Menn B, Lorentz S, Naucke TJ (2010) Imported and travelling dogs as carriers of canine vector-borne pathogens in Germany. Parasit Vectors 3:34

Nilsson K, Lindquist O, Pahlson C (1999) Association of *Rickettsia helvetica* with chronic perimyocarditis in sudden cardiac death. Lancet 354:1169–1173, 32

Nilsson K, Elfvig K, Pahlson C (2010) *Rickettsia helvetica* in patient with meningitis, Sweden, 2006. Emerg Infect Dis 16(3):490–492

Oehme R, Hartelt K, Backe H, Brockmann S, Kimmig P (2002) Foci of tick-borne diseases in Southwest Germany. Int J Med Microbiol 291(Suppl 33):22–29

Ortuno A, Quesada M, Lopez-Claessens S, Castella J, Sanfeliu I, Anton E, Segura-Porta F (2007) The role of wild boar (*Sus scrofa*) in the eco-epidemiology of *R. slovaca* in northeastern Spain. Vector Borne Zoonotic Dis 7(1):59–64

Parola P, Paddock CD, Raoult D (2005) Tick-borne rickettsioses around the world: emerging diseases challenging old concepts. Clin Microbiol Rev 18(4):719–756

Parola P, Rovery C, Rolain JM, Brouqui P, Davoust B, Raoult D (2009) *Rickettsia slovaca* and *R. raoultii* in tick-borne rickettsioses. Emerg Infect Dis 15(7):1105–1108

Perlman SJ, Hunter MS, Zchori-Fein E (2006) The emerging diversity of *Rickettsia*. Proc Biol Sci 273:2097–2106

Petersen JM, Mead PS, Schriefer ME (2009) *Francisella tularensis*: an arthropod-borne pathogen. Vet Res 40(2):7

Petrovec M, Sixl W, Schweiger R, Mikulasek S, Elke L, Wüst G, Marth E, Strasek K, Stünzner D, Avsic-Zupanc T (2003) Infections of wild animals with *Anaplasma phagocytophila* in Austria and the Czech Republic. Ann NY Acad Sci 990:103–106

Pichon B, Kahl O, Hammer B, Gray JS (2006) Pathogens and host DNA in *Ixodes ricinus* nymphal ticks from a German forest. Vector Borne Zoonotic Dis 6(4):382–387

Pluta S, Tewald F, Hartelt K, Oehme R, Kimmig P, Mackenstedt U (2009) *Rickettsia slovaca* in *Dermacentor marginatus* ticks, Germany. Emerg Infect Dis 15(12):2077–2078

Pluta S, Hartelt K, Oehme R, Mackenstedt U, Kimmig P (2010) Prevalence of *Coxiella burnetii* and *Rickettsia* spp. in ticks and rodents in southern Germany. Ticks Tick-borne Dis 1 (3):145–147. doi:10.1016/j.ttbdis.2010.04.001

Polin H, Hufnagl P, Haunschmid R, Gruber F, Ladurner G (2004) Molecular evidence of *Anaplasma phagocytophilum* in *Ixodes ricinus* ticks and wild animals in Austria. J Clin Microbiol 42(5):2285–2286

Porsch-Özcürümez M, Kischel N, Priebe H, Splettstösser W, Finke EJ, Grunow R (2004) Comparison of enzyme-linked immunosorbent assay, western blotting, microagglutination, indirect immunofluorescence assay, and flow cytometry for serological diagnosis of tularemia. Clin Diagn Lab Immunol 11(6):1008–1015, 33

Pusterla N, Leutenegger CM, Huder JB, Weber R, Braun U, Lutz H (1999) Evidence of the human granulocytic ehrlichiosis agent in *Ixodes ricinus* ticks in Switzerland. J Clin Microbiol 37 (5):1332–1334

Raoult D, Roux V (1997) Rickettsioses as paradigms of new or emerging infectious diseases. Clin Microbiol Rev 10(4):694–719

Raoult D, Berbis PH, Roux V, Xu W, Maurin M (1997) A new tick-transmitted disease due to *Rickettsia slovaca*. Lancet 350:112–113

Rehacek J, Liebisch A, Urvölgyi J, Kovacova E (1977) Rickettsiae of the spotted fever isolated from *Dermacentor marginatus* ticks in South Germany. Zentralbl Bakteriol Orig A 239:275–281

Rehacek J, Urvölgyi J, Kocianova E, Jedlicka L (1992) Susceptibility of some species of rodents to rickettsiae. Folia Parasitol 39(3):265–284

Rehse-Küpper B, Casals J, Rehse E, Ackermann R (1976) Eyach – an arthropod-borne virus related to Colorado tick fever virus in the federal republic of Germany. Acta Virol 20:339–342

Rovery C, Brouqui P, Raoult D (2008) Questions on mediterranean spotted fever a century after its discovery. Emerg Infect Dis 14(9):1360–1367

Schmitt P, Splettstösser W, Porsch-Özcürümez M, Finke EJ, Grunow R (2005) A novel sreening ELISA and a confirmatory Western blot useful for diagnosis and epidemiological studies of tularemia. Epidemiol Infect 133:759–766

Sekeyova Z, Roux V, Xu W, Rehacek J, Raoult D (1998) *Rickettsia slovaca* sp. nov. a member of the spotted fever group rickettsiae. Int J Syst Bacteriol 48:1455–1462

Silaghi C, Gilles J, Höhle M, Fingerle V, Just FT, Pfister K (2008a) *Anaplasma phagocytophilum* infection in *Ixodes ricinus*, Bavaria, Germany. Emerg Infect Dis 14(6):972–974

Silaghi C, Gilles J, Höhle M, Pradel I, Just FT, Fingerle V, Küchenhoff H, Pfister K (2008b) Prevalence of spotted fever group rickettsiae in *Ixodes ricinus* (Acari: *Ixodidae*) in southern Germany. J Med Entomol 45(4):948–955

Simser JA, Palmer AT, Fingerle V, Wilske B, Kurtti TJ, Munderloh UG (2002) *Rickettsia monacensis* sp. nov., a spotted fever group *Rickettsia*, from ticks (*Ixodes ricinus*) collected in a European city park. Appl Environ Microbiol 68(9):4559–4566

Sixl W, Petrovec M, Marth E, Wüst G, Stünzner D, Schweiger R, Avsic-Zupanc T (2003) Investigation of *Anaplasma phagocytophila* infections in *Ixodes ricinus* and *Dermacentor reticulatus* ticks in Austria. Ann NY Acad Sci 990:94–97, 34

Skuballa JD, Petney T, Pfäffle M, Taraschewski H (2010) Molecular detection of *Anaplasma phagocytophilum* in the European hedgeog (*Erinaceus europaeus*) and its ticks. Vector Borne Zoonotic Dis 10(10):1055–1057, Epub 28 Apr 2010

Splettstoesser W (2008)Zur Häufung von Tularämie-Erkrankungen in Deutschland im Jahr 2007. Epidemiologisches Bulletin 4/2008. Available from http://www.rki.de/cln_160/nn_969736/DE/Content/Infekt/EpidBull/Archiv/2008/04/Tabelle.html?__nnn=true. Cited 10 May 2010. In German

Splettstoesser WD, Piechotowski I, Buckendahl A, Frangoulidis D, Kaysser P, Kratzer W, Kimmig P, Seibold E, Brockmann SO (2008) Tularemia in Germany: the tip of the iceberg? Epidemiol Infect 137:736–743

Strle F (2004) Human granulocytic ehrlichiosis in Europe. Int J Med Microbiol 293(Suppl 37):27–35

Taillardat-Bisch AV, Raoult D, Drancourt M (2003) RNA polymerase β-subunit-based phylogeny of *Ehrlichia* spp., *Anaplasma* spp., *Neorickettsia* spp. and *Wolbachia pipientis*. Int J Syst Evol Microbiol 53:455–458

Vogl UM, Presterl E, Stanek G, Ramharter M, Gattringer KB, Graninger W (2010) First described case of human granulocytic anaplasmosis in a patient in eastern Austria. Wien Klin Wochenschr 160(3–4):91–93

von Loewenich FD, Baumgarten BU, Schröppel K, Geißdörfer W, Röllinghoff M, Bogdan C (2003) High density of *ankA* sequences of *Anaplasma phagocytophilum* among *Ixodes ricinus* ticks in Germany. J Clin Microbiol 41(11):5033–5040

Walder G, Falkensammer B, Aigner J, Tiwald G, Dierich MP, Würzer R, Lechleitner P (2003a) First documented case of human granulocytic ehrlichiosis in Austria. Wien Klin Wochenschr 115(7–8):263–266

Walder G, Tiwald G, Dierich MP, Würzner R (2003b) Serological evidence for human granulocytic ehrlichiosis in western Austria. Eur J Clin Microbiol Infect Dis 22:543–547

Walder G, Fuchs D, Sarcletti M, Berek K, Falkensammer B, Huber K, Petrovec M, Dierich MP, Würzner R (2006) Human granulocytic anaplasmosis in Austria: epidemiological, clinical, and laboratory findings in five consecutive patients from Tyrol, Austria. Int J Med Microbiol 296 (Suppl 1):297–301

Wang TJ, Liang MH, Sangha O, Phillips CB, Lew RA, Wright EA, Berardi V, Fossel AH, Shadick NA (2000) Coexposure to *Borrelia burgdorferi* and *Babesia microti* does not worsen the long-term outcome of Lyme disease. Clin Infect Dis 31:1149–1154

Weber R, Pusterla N, Loy M, Leutenegger CM, Schär G, Baumann D, Wolfensberger C, Lutz H (2000) Serologische und klinische Daten weisen auf das endemische Vorkommen der humanen granulozytären Ehrlichiose in der Nordostschweiz hin. Schweiz Med Wochenschr 130:1462–1470, In German

Weinert LA, Werren JH, Aebi A, Stone GN, Jiggins FM (2009) Evolution and diversity of *Rickettsia* bacteria. BMC Biol 7:6

Wicki R, Sauter P, Mettler C, Natsch A, Enzler T, Pusterla N, Kuhnert P, Egli G, Bernasconi M, Lienhard R, Lutz H, Leutenegger CM (2000) Swiss army survey in Switzerland to determine the prevalence of *Francisella tularensis*, members of the *Ehrlichia phagocytophila* genogroup, *Borrelia burgdorferi* sensu lato, and tick-borne encephalitis virus in ticks. Eur J Clin Microbiol Infect Dis 19:427–432

Wölfel R, Terzioglu R, Kiessling J, Wilhelm S, Essbauer S, Pfeffer M, Dobler G (2006) *Rickettsia* spp. in *Ixodes ricinus* ticks in Bavaria, Germany. Ann NY Acad Sci 1078:509–511

Zhan L, Cao W, Chu C, Jiang B, Zhang F, Liu W, Dumler JS, Wu X, Zuo S, Zhang P, Huang H, Zhao Q, Jia N, Yang H, Richardus JH, Habbema JDF (2009) Tick-borne agents in rodents, China, 2004-2009. Emerg Infect Dis 15(12):1904–1908