febrile haemoglubinuria in cattle (Babes, 1888). Since the late 1950s, two species of *Babesia* in particular, the cattle species *Babesia divergens* in Europe and the rodent species *Babesia microti* in North America, have been shown to cause a significant number of infections in humans (Homer et al., 2000; Hunfeld and Brade, 2004). The frequent reports of human babesiosis cases in North America, however, are in striking contrast to only sporadic reports of the disease in Europe and other parts of the world. However, in many non-American regions, microbiological investigations and awareness of the clinical presentation of babesiosis in humans lag far behind those in the USA and Canada. In Germany, *Ixodes ricinus* is regarded the most important vector for tick-borne diseases in humans and, although it is not known for certain, there is circumstantial evidence that *I. ricinus* transmits at least *B. divergens* and *B. microti* to humans (Gray, 2006; Hunfeld and Brade, 2004). This tick is abundant throughout the country but no indigenous cases of human babesiosis have been documented in Germany so far. Here we report on detection and clinical management of the first autochthonous case of human babesiosis in Germany.

Materials and methods

Serological testing for *Babesia* spp.

Serological testing for specific IgG and IgM antibodies was performed using well-evaluated indirect immuno-fluorescence assays (IFA) for *B. microti* and *B. divergens* as described recently in more detail (Hunfeld et al., 2002). For detection and semiquantification of *B. microti*-specific antibodies, golden hamster erythrocytes infected with the *B. microti* GI strain, which was originally isolated from a human patient from the east coast of the United States, were used. For detection of antibodies to *B. divergens*, IFA antigens were prepared from the blood of jirds (*Meriones unguiculatus*) experimentally infected with a *B. divergens* isolate that was originally obtained from naturally infected cattle in northern Germany. All positive sera were titrated in triplicate on different days, and titres are reported as geometric mean titres. In addition, sera that were tested in IgM assays were pre-incubated with rheumatoid factor absorbance reagent (Focus, Cyprus, USA). Measurement of antibodies started at a serum dilution of 1:20 (IgM) or 1:16 (IgG). Sera were then diluted serially in twofold steps to determine end point titres (Hunfeld et al., 2002).

PCR for detection of *B. microti*

DNA extraction was performed by use of commercial DNA extraction kits (High Pure Template PCR Preparation Kit, Roche, Germany) according to the manufacturer's instructions. For the performance of PCR, the Taq DNA Polymerase Kit (Invitrogen, Germany) was applied. PCR was performed according to Persing et al. (1992), with some modifications. Each PCR run included a DNA preparation of the *B. microti* GI strain and a negative control. A separate preparation containing 8 µl DNA extracted from the corresponding clinical sample in addition to 2 µl of positive control DNA was co-amplified in each run to serve as inhibition control. The PCR mixture (100 µl) consisted of 10 µl of purified DNA preparation and 90 µl PCR mix [10 µl PCR buffer (10 × concentration: 200 mM Tris–HCl, pH 8.0, 500 mM KCl), 5 µl $MgCl_2$ (50 mM), 1 µl dNTPs (10 mM), 1 µl Bab1 primer (100 pmol), 1 µl Bab 4 primer (100 pmol), 71.5 µl distilled water, and 0.5 µl Taq DNA polymerase (5 U/µl)]. The amplification reaction was performed on a programmable Gene Amp PCR System 9600 (Perkin Elmer, Germany), with a three-step cycling programme as follows: 1 min of denaturation at 94 °C, 1 min of annealing at 55 °C, and 2 min of extension at 72 °C for a total of 35 cycles. The 238-bp product was then visualised on an ethidium bromide-stained 1.5% agarose gel by UV gel imaging after electophoresis on a Bio-Rad apparatus (Bio-Rad, Germany).

PCR for the detection of *Babesia* spp.

DNA extraction was performed as described above. PCR was performed as outlined by Armstrong et al. (1998), with some modifications. The forward primer PIRO-A and the reverse primer PIRO-B flank 407-, 408-, and 437-bp nucleotide regions of the 18S rRNA gene of *Babesia* spp. Each PCR run included a DNA preparation of the GI strain of *B. microti* and a negative control (water blank). A separate preparation containing 12 µl DNA extracted from the corresponding clinical sample in addition to 3 µl of positive control DNA was co-amplified in each run to serve as inhibition control (Fig. 1). For the PCR, the ELONGase Amplification System (Life Technologies, Germany) was used. The initial PCR mixture (40 µl) consisted of 15 µl of purified DNA preparation, 11 µl mix I [1 µl dNTPs (10 mM), 5 µl primer PIRO-A (100 pmol), and 5 µl primer PIRO-B (100 pmol)], and 14 µl distilled water. This mixture then was filled to a total volume of 100 µl by adding 60 µl of mix II (10 µl buffer A, 10 µl buffer B, 2 µl ELONGase enzyme mix, and 38 µl distilled water).

Thermocycling was performed on a programmable Gene Amp PCR System 9600 (Perkin Elmer, Germany) with a denaturation step of 1 min at 94 °C, followed by 40 cycles each consisting of 40 s at 94 °C, 45 s at 55 °C, and 45 s at 72 °C. The resulting amplification product was visualised as described above.

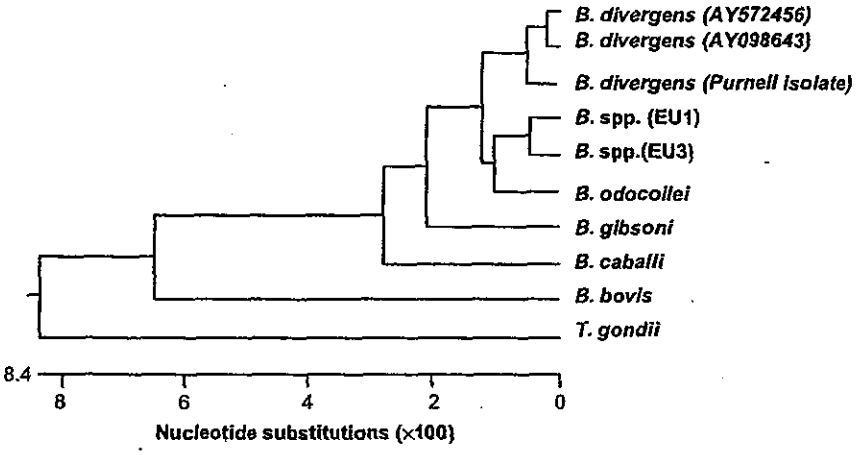

Fig. 1. Phylogenetic tree calculated for the 18S rRNA gene sequences as available from GeneBank for selected *Babesia* spp. and for our newly detected *Babesia* organism (EU3). The tree was computed by using the Clustal method with weighted residue weight table (MEGALINE program, DNASTAR, Lasergene, Germany). The accession numbers for the sequences obtained from GenBank that have been used in the analysis are as follows: *B. bovis*, L19077; *B. caballi*, Z15104; *B. divergens* (Purnell isolate), AY046576; *B. divergens*, AY572456; *B. divergens*, AY098643; *B. gibsoni* (genotype Asia 1), AF175300; *B. odocoilei*, AY046577; *B.* spp. (EU1), AY046575; and *T. gondii*, M64243.

Molecular characterisation of the pathogen and sequencing of PCR products

Amplification of the complete 18S rRNA gene was performed using *Babesia* DNA extracted from the patient's blood and by use of a generic apicomplexan 18S rDNA-specific PCR as described recently in more detail (Herwaldt et al., 2003) yielding a specific product of 1700 base pairs. The sequencing of all PCR amplification products was performed in both directions by use of an "ABI PRISM™ Dye Terminator Cycle Sequencing Ready Reaction Kit" in accordance with the manufacturer's specifications. Products were sequenced by a commercial specialist laboratory (GATC, Stuttgart, Germany). Obtained sequences were analysed using DNASTAR version 4.0 (Lasergene, Germany) and then submitted to GenBank (NIBC) for comparison with known sequences of reference organisms. A phylogenetic tree (Fig. 1) was then calculated for the 18S rRNA gene sequences as available from GenBank for selected *Babesia* spp. and for our newly detected *Babesia* organism (EU3) by using the Clustal method with weighted residue weight table (MEGALINE program, DNASTAR, Lasergene, Germany).

Case report

In October 2005, a 63-year-old German patient, who had undergone splenectomy in 1973 because of Hodgkin's disease, was admitted to the hospital. He suffered from mild anaemia and enlarged iliacal lymph nodes. Subsequently, a relapse of Hodgkin's disease manifesting itself as paragranuloma (stage: IIa, IPI1) was diagnosed based upon histopathology of a lymph node biopsy. Reactivation of the disease was treated with intravenous application of a chimeric anti-CD20 antibody preparation (Rituximab, MabThera) for 4 weeks. In late November, the patient showed progressive weakness, shortness of breath, and lethargy finally resulting in re-hospitalisation on December 4, 2005 because of haemolytic anaemia (erythrocyte count: 2.7 mio/µl; Hb: 8.6 g/dl), elevated serum lactate dehydrogenase (LDH: 3569 U/l) and bilirubin levels (2.6 mg/dl), and dark urine from haemoglobinuria. His body temperature was slightly elevated (37.8 °C; Table 1). A positive direct Coombs test led to the initial diagnosis of autoimmune haemolytic anaemia potentially owing to ongoing Hodgkin's disease. Therefore, treatment with prednisolone 30 mg per os (p.o.) once daily was initiated. However, the patient did not improve clinically and continued to show elevated leukocyte counts (17,000/µl). Moreover, an elevated C-reactive protein of 14.2 mg/dl and procalcitonin levels of 3.1 µg/dl suggested ongoing infection. Forty-eight hours after admission, haematological examination of peripheral blood smears finally revealed parasitic inclusions (parasitaemia: 4%) in erythrocytes (Fig. 2a–c). The patient admitted doing regular outdoor recreation but he had not travelled beyond his home town recently. Suspicion of malaria was ruled out by a negative dip stick antigen test result (Binax Now Malaria®, Inverness Medical GmbH, Germany). On questioning, he did not recall a tick bite in his recent medical history and no blood products had been administered prior to hospital admission. Presumptive diagnosis of babesiosis was established based

Table 1. Summary of important clinical data, laboratory findings, and microbiological test results in a splenectomised German patient with babesiosis

Clinical information	2005		2006								
	December 4 Admission, weakness, haemoglobinuria, shortness of breath	December 6 Start of treatment with quinine and clindamycin	January 3 Follow-up 10 days after conclusion of treatment, clinical improvement	January 20 Relapse of babesiosis, initiation of re-treatment with atovaquone and azithromycin	January 30 Follow-up, clinical improvement	March 15 Follow-up, clinical improvement	April 5 Control visit, stop of azithomycin therapy, maintenance treatment with atovaquone only, clinical improvement	May 17 Follow-up, physical well-being	June 26 Follow-up, seroconversion, physical well-being	August 9 Follow-up, clearance of parasite, physical well-being	September 7 Follow-up, stop of maintenance therapy
Laboratory data											
CRP (mg/dl)	**14.2**	**11.7**	0.6	**6.1**	0.15	0.3	0.3	n.d.	0.1	n.d.	0.1
Erythrocytes (mio./µl)	**2.7**	**2.5**	**3.6**	**3.7**	n.d.	**4.7**	**4.9**	**4.7**	**4.7**	**4.9**	**4.9**
Haemoglobin (g/dl)	**8.6**	**7.6**	**11.7**	**11.4**	n.d	**14.5**	**14.5**	**14.4**	**14.6**	**15.2**	**15.0**
LDH (U/l)	**3569**	**3263**	**337**	**3030**	**519**	**270**	**401**	**286**	**197**	**207**	**197**
Bilirubin (mg/dl)	**2.6**	**2.3**	0.3	**1.7**	0.6	n.d	0.8	0.7	**1**	0.8	n.d.
Microbiology data											
Parasite count	n.d	+ (4%)	+ (<1‰)	+ (3%)	+ (<1‰)	+ (<1‰)	+ (<1‰)	+ (<1‰)	–	–	–
Babesia spp. PCR	n.d	+	+	+	+	+	+	+	±	–	–
IgM-*B. microti*-IFA	n.d	–	–	–	–	–	–	–	**1:20**	**1:20**	**1:20**
IgG-*B. microti*-IFA	n.d.	–	–	–	–	–	–	–	–	–	**1:16**
IgM-*B. divergens*-IFA	n.d.	–	–	–	–	–	–	–	**1:20**	**1:40**	**1:20**
IgG-*B. divergens*-IFA	n.d.	–	–	–	–	–	–	–	–	**1:32**	**1:128**

LDH: Lactate dehydrogenase; n.d.: not determined; (–): negative; (+): positive; ±: borderline; %: per cent; ‰: per mille; abnormal findings are given in bold type.

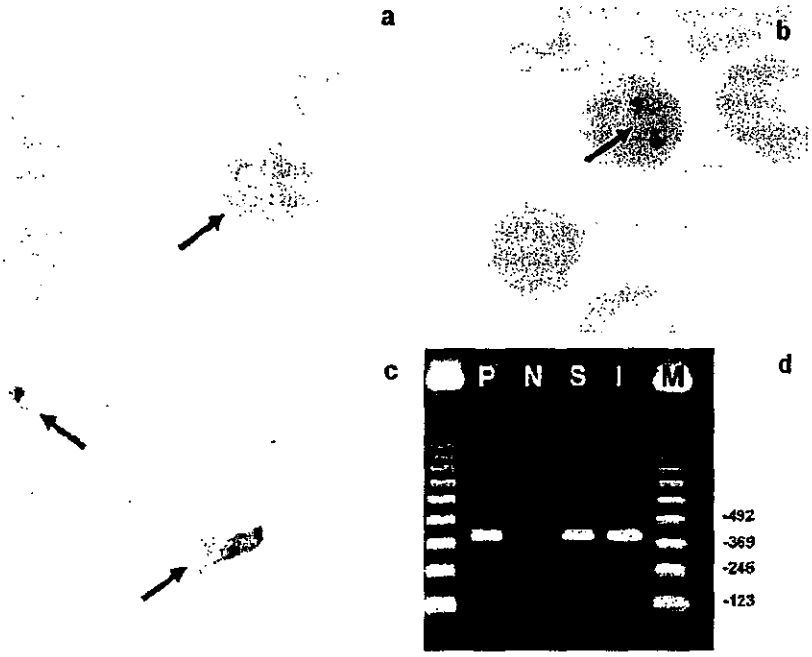

Fig. 2. (a–c) Photomicrographs of *Babesia* (EU3) spp. on a Giemsa-stained smear of peripheral blood showing characteristic piriform inclusions and band forms (trophozoites and merozoites) in infected erythrocytes (denoted by black arrows). Parasites are 1–2.5 μm in diameter. (d) Babesia spp.-specific PCR (PIRO-A and PIRO-B primers) designed for amplification of a highly specific region of the 18S rRNA gene. P: positive control, N: negative control, S: patient sample, I: inhibition control, M: 123-bp marker.

upon the piriform shape (Fig. 2a–c) and the *Plasmodium*-like appearance of the intraerythrocytic parasites. Testing for specific IgM and IgG antibodies against *B. microti* and *B. divergens* by IFA proved negative. The diagnosis was subsequently confirmed by a positive *Babesia*-specific 18S rDNA PCR from EDTA-blood (Fig. 2d). A *B. microti*-specific PCR yielded a negative result. Subsequent sequence analysis of the 18S rRNA gene, amplified by using a generic apicomplexan 18S rDNA-specific PCR (Herwaldt et al., 2003), revealed a 99.7% sequence homology of the PCR product with the recently described EU1 isolate clustering within the *B. divergens/Bodocoilei odocoilei* complex (Fig. 1), and the organism was designated EU3. On December 7, treatment with prednisolone was discontinued and specific anti-parasitic chemotherapy with quinine (650 mg, 3 × /day, p.o.) and clindamycin (600 mg, 3 × / day, p.o.) was initiated. However, the interval between onset of symptoms attributed to babesiosis and the initiation of specific therapy after presumptive diagnosis of the disease was at least 6 days. Attempts to obtain an isolate of the parasite, by injecting several specimens into jirds and mice, were unsuccessful and periodic smears as well as PCR analysis of animal blood remained negative.

The patient initially showed a rapid clinical response to treatment and parasites could no longer be detected in conventional blood smears. After 1 week, however, the application of quinine had to be discontinued because of side effects and treatment was continued with clindamycin only for an additional 10 days. Ten days after therapy, the patient remained well clinically but blood samples became positive for *Babesia* again, both in blood smears and in PCR examination. Four weeks, after the conclusion of treatment, the patient relapsed with recurrent anaemia, sweats, haemoglobinuria, and a parasitaemia of 3% (Table 1). Upon serological examination by IFA the patient remained negative for specific antibodies. Re-treatment was initiated with azithromycin (500 mg, 1 × /day, p. o.) plus atovaquone (750 mg, 2 × /day, p. o.) resulting in rapid clinical improvement of the patient. Nevertheless, direct smears and PCR analysis continued to demonstrate persistent low-level parasitaemia (< 1‰) in follow-up blood samples despite re-treatment for eleven weeks. In addition, the patient remained seronegative upon serological examination for anti-*Babesia* antibodies. To avoid a relapse of babesiosis, atovaquone maintenance therapy was therefore continued for an additional 5 months. The patient continued to improve clinically since February 2006 and laboratory parameters returned to normal levels (Table 1). He finally seroconverted for IgM antibodies (titre: IgM: 20) both, in the *B. microti* and *B. divergens* IFA in late June and

for *B. divergens* IgG antibodies (IgG: 32) in early August. In August 2006, he eventually cleared the parasite as demonstrated in direct blood smears and by negative PCR analysis. Following an additional 4 weeks of atovaquone maintenance therapy, laboratory examinations revealed increasing IgG antibody titres (*B. divergens* IFA titre: IgM: 20, IgG: 128; *B. microti* IFA titre: IgM: 20, IgG: 16) and no evidence for persistence of the pathogen. Thus, treatment was discontinued in September 2006 and the patient remained well thereafter.

Discussion

The genus *Babesia* is phylogenetically related to other sporozoan genera, i.e. *Toxoplasma* and *Plasmodium*. To date, about 100 species of *Babesia* have been described world-wide based on intraerythrocytic stages detected in mammals (Levine, 1988). However, their pleomorphism in different species of mammalian hosts and the results of recent molecular systematic studies render some of these descriptions dubious (Gray, 2006; Hunfeld and Brade, 2004). It is now assumed that some species of *Babesia* are less host-specific than believed previously and that a number of species of *Babesia* will be reclassified as more information becomes available on them (Gray, 2006; Homer et al., 2000; Hunfeld and Brade, 2004). During the last decade, new *Babesia* spp. of unknown identity currently designated as WA1-type organisms (WA1-WA3 and CA1-CA6), MO1, and EU 1 have been established to be pathogens of considerable concern for humans in the USA and Europe (Herwaldt et al., 2003; Hunfeld and Brade, 2004; Conrad et al., 2006), with recent case reports suggesting that new species are emerging and that *Babesia* infections in European countries are more common than believed previously, especially in the immunocompromised host (Herwaldt et al., 2003; Hunfeld et al., 2002). Here, we describe the first reported human case of babsiosis in Germany and provide molecular evidence that the causative pathogen detected in our patient is virtually indistinguishable from the recently described *Babesia* organism designated as EU1 (Herwaldt et al., 2003). Molecular characterisation of the pathogen revealed that EU1 is not closely related to *Babesia* organisms such as *B. microti* or the recently established species *B. duncani* (formerly dubbed 'WA1' and 'CA5') that are known to have infected humans (Herwaldt et al., 2003; Conrad et al., 2006). Upon phylogenetic analysis, the newly discovered pathogen EU 1 instead clusters with *B. odocoilei*, a parasite of white-tailed deer, and these two organisms form a sister group with *B. divergens* (Herwaldt et al., 2003). Provisionally, the species name "*Babesia venatorum*" has been proposed for EU1 organisms (Herwaldt et al., 2003).

In the past, human babesiosis has been thought to occur rarely in Europe, with only about 30 reported cases and all but four clinical cases have been attributed to *B. divergens*, which has been diagnosed mainly in splenectomised patients in former Yugoslavia, France, and the British Isles (Gorenflot et al., 1998; Gray 2006; Homer et al., 2000). However, microbiological diagnosis of human babesiosis in Europe, so far, has been based mainly on the detection of the parasites in Giemsa-stained blood smears of patients with clinical symptoms of disease. Although helpful for diagnostic purposes, detection of parasites in blood smears by microscopy alone without additional molecular analysis of the pathogen does not provide reliable species identification. Therefore, it remains to be clarified whether many cases of human babesiosis in Europe that would have been attributed to *B. divergens* in the past based on traditional methods, in reality, are caused by other *Babesia* organisms (Gray, 2006; Herwaldt et al., 2003). In Europe, patients with *B. divergens* infection mainly presented with acute febrile haemolytic disease, and in the initial reports their clinical courses were almost always fatal. In contrast to the findings in human *B. divergens* infection, the first two cases of EU1 babesiosis in Italy and Austria, which occurred in two asplenic men with Hodgkin's disease and large B-cell lymphoma, respectively, were different in that the disease manifestation ranged from mild to moderately severe and both patients were cured after successful chemotherapy with clindamycin and/or quinine (Herwaldt et al., 2003). Whether this observation is typical of the clinical course of EU1 babesiosis, or whether differences in the pathogenicity of strains endemic to different geographic areas may explain the variable clinical disease manifestations, remains to be determined.

Similar to the manifestation in our patient clinical symptoms of the disease in the Italian and Austrian patients included elevated body temperature, chills, anaemia, weakness, fatigue, anorexia, and headache followed by jaundice and dark urine from haemoglobinuria. As with our patient, there was a significant delay of several days between the onset of symptoms, the detection of parasites in blood smears suggesting babesiosis, and the initiation of chemotherapy. Such a delay of treatment can be fatal because human babesiosis can be further complicated by central nervous system involvement, or severe complications, such as congestive heart failure, intravascular coagulation, renal failure, and respiratory distress syndrome if left untreated (Homer et al., 2000; Mylonakis, 2001). Patients with babesiosis, most of whom are immunocompromised or asplenic, therefore, should be regarded as medical emergencies and require immediate treatment to arrest haemolysis and prevent renal failure (Gelfand, 2000; Homer et al., 2000). Our case, however, is unique in that the patient remained seronegative for specific

antibodies for several months and suffered from relapse after the conclusion of initial treatment. Moreover, re-treatment with atovaquone and azithromyin for 2 months was unsuccessful in clearing the parasite and low-level parasitaemia persisted for several months despite maintenance therapy with atovaquone, possibly due to the previous combined application of rituximab and prednisolone, which have highly immunosuppressive effects. It is well known that treatment with corticosteroids and depressed cellular immunity are associated with severe clinical illness in human babesiosis (Telford and Maguire, 2005; Meldrum et al., 1992; Rosner et al., 1984). Humoral immunity, however, appears to be less important than cellular immunity in controlling the disease as demonstrated for example in a mouse model of *B. microti* infection because B-cell-deficient mice remain less susceptible to infection, whereas T-cell receptor-deficient mice are readily infected (Clawson et al., 2002). Whether such data hold true also for human infection with EU1 organisms remains to be demonstrated in future experiments. It is interesting to note though, that following prednisolone treatment and rituximab-induced depletion of CD20-positive cells, it took our patient 7 months to finally develop a *Babesia*-specific antibody response. At the same time, he obviously started clearing the parasite from his blood stream and smears turned negative upon microscopic examination. Six weeks later, PCR which had been used to monitor the success of treatment turned negative also (Table 1). The question whether seroconversion in our patient was simply a sign of immune reconstitution or whether the production of anti-*Babesia* antibodies significantly contributed to clearing the parasite, however, cannot be answered from our data.

So far, Giemsa-stained blood smears (Fig. 2a–c) remain the mainstay for the detection of parasites in patients with clinical symptoms of babesiosis. In addition, indirect detection of the pathogen can be performed by IFA for IgG and IgM antibodies. Obviously, in our patient, antibodies directed against the infecting parasite predominantly cross-reacted with *B. divergens* antigen in the IFA. This phenomenon was initially reported also by Herwaldt et al. (2003) in previous cases of EU 1 infection and suggests that assays using *B. divergens* antigen preparations can be helpful in the laboratory diagnosis of antibodies in such patients. One drawback of serology, however, is the fact that the production of antibodies in the non-immunocompromised host can take up to 14 days after the infection, and immunocompromised individuals can remain seronegative for even longer periods after the onset of clinical symptoms (Homer et al., 2000).

PCR is a new, rapid diagnostic technique for the detection of *Babesia* spp. that has not yet been standardised and systematically evaluated (Homer et al., 2000; Hunfeld and Brade, 2004). As with our case, however, diagnostic results with this method are promising and show PCR to be a sensitive and specific tool in the diagnosis of human babesiosis (Armstrong et al., 1998; Homer et al., 2000; Persing et al., 1992). Whether PCR indeed can be useful in monitoring the success of specific treatment in patients with prolonged persistent parasitaemia awaits further evidence from clinical studies.

Therapy of human babesiosis with a combination of quinine and clindamycin for 7–10 days is the most commonly used treatment. A recent prospective, randomised study in humans compared the efficacy of this treatment regimen with the clinical outcome of atovaquone and azithromycin in cases of *B. microti* infection. Although the clinical outcome was similar for the two patient groups, the application of atovaquone plus azithromycin lowered the relative number of side effects to 15% versus 72% in the group of patients receiving quinine and clindamycin (Krause et al., 2000). In our case, the application of atovaquone and azithromycin as re-treatment and maintenance therapy was well tolerated and proved effective in treating the clinical symptoms of the patients although it did not immediately clear the parasite from the blood stream. We did not use exchange transfusion in addition to conventional chemotherapy because this treatment is reserved for those individuals who are extremely ill, i.e., those with massive haemolysis, asplenia, immunosuppression, and blood parasitaemia of more than 10% (Mylonakis, 2001).

In Europe, *Babesia* spp. such as *B. microti*, *B. divergens*, *B. odocoilei*-like, and the newly described EU1 *Babesia* organism are known to be prevalent in *I. ricinus* (Duh et al., 2005; Hartelt et al., 2004). In Germany, *I. ricinus* is widely distributed and is regarded as the chief vector of tick-borne infections to humans (Hunfeld and Brade, 2004). *B. microti* has been identified in rodents, *B. divergens* in cattle, and both species in *I. ricinus* ticks in Germany (Hartelt et al., 2004; Huwer et al., 1994; Walter, 1984). Moreover, the potential relevance of *Babesia* species for tick-exposed German individuals was substantiated very recently by demonstrating the presence of *B. microti* or *B. divergens* in 31 (1%) out of 3113 investigated *I. ricinus* ticks collected in south western Germany by PCR and subsequent nucleotide sequence analysis of the small subunit ribosomal RNA gene (Hartelt et al., 2004). Few systematic studies have been conducted on potentially infected humans as yet, but recent seroepidemiological investigations using *B. divergens* and *B. microti* as surrogate antigens suggest that infections with *Babesia* spp. may occur more frequently than previously believed in tick-exposed patients in Europe, with overall seroprevalence rates ranging between 3.6% and 5.4% in the population investigated (Hunfeld et al., 2002). However, no such data are currently available for potentially emerging *Babesia* organisms such as EU1. When dealing with the actual frequency of *Babesia* infections in

European countries, it is also likely that in most immunocompetent individuals suffering from babesiosis the disease probably is self-limiting and milder than in the immunocompromised host (Hunfeld and Brade, 2004). The apparent existence and high prevalence of babesial pathogens in ticks, however, may become increasingly important as the number of immunocompromised individuals and organ transplant recipients is increasing steadily and because, although a rarity, asymptomatic but chronically infected blood donors are now known to be a source of transfusion-transmitted babesiosis in areas where *Babesia* spp. with zoonotic potential are endemic (Homer et al., 2000; Popovsky, 1991). Consequently, further seroepidemiological and molecular epidemiological studies on *Babesia* spp. in general and EU1-like organisms in particular are urgently needed to learn more about the true distribution and medical relevance of such pathogens in the various parts of Europe.

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医薬品 研究報告 調査報告書

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研究報告の概要

○広範囲薬剤耐性結核(超薬剤耐性結核)の世界的新興

薬剤耐性結核(MDR TB)の治療に使用される第二選択剤に耐性を増しつつある*Mycobacterium tuberculosis*株は、世界各国の公衆衛生の脅威となりつつある。我々は、2000年～2004年の期間中に第二選択抗結核剤に耐性を示した*M. tuberculosis*分離菌株について、国際的に認知された結核研究施設(Supranational Reference Laboratories;SRL)のネットワークを調査した。広範囲薬剤耐性結核(XDR TB)は、第二選択剤6クラスのうち3つ以上に耐性を持つMDR TBと定義した。該当施設23のうち、14(61%)施設から分離菌株17,690のデータが提供され、これは48カ国の薬剤感受性結果を反映するものであった。MDR TB 分離菌株3,520(19.9%)のうち、347(9.9%)がXDR TBの基準を満たした。公衆衛生を守り、結核を制圧するには、集団での傾向をさらに調査し、薬剤耐性を防ぎMDR TB患者を効果的に治療するための努力を拡大することが極めて重要である。

使用上の注意記載状況・その他参考事項等

合成血「日赤」
照射合成血「日赤」
合成血-LR「日赤」
照射合成血-LR「日赤」

血液を介するウイルス、細菌、原虫等の感染
vCJD等の伝播のリスク

報告企業の意見	今後の対応
2000年～2004年の期間中に第二選択抗結核剤に耐性を示した*M. tuberculosis*分離菌株について、国際的に認知された結核研究施設のネットワークを調査したところ、該当施設23のうち、14(61%)施設から分離菌株17,690のデータが提供され、347(9.9%)が広範囲薬剤耐性結核菌だったとの報告である。	日本赤十字社は、問診で結核の既往、薬剤の使用を確認し、既往がある場合は治癒するまで献血不可としている。また、体調不良者を献血不可としている。今後も引き続き情報の収集に努める。