



**THE VECTOR-BORNE  
HUMAN INFECTIONS  
OF EUROPE**

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**THEIR DISTRIBUTION  
AND BURDEN  
ON PUBLIC HEALTH**

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# ABSTRACT

While the number of vector-borne diseases and their incidence in Europe is much less than that of the tropical, developing countries, there are, nevertheless, a substantial number of such infections in Europe. Furthermore, the incidence of many of these diseases has been on the rise, and their distribution is spreading.

This publication reviews the distribution of all of the vector-borne diseases of public health importance in Europe, their principal vectors, and the extent of their public health burden. Such an overall review is necessary to understand the importance of this group of infections and the resources that must be allocated to their control by public health authorities. Medical personnel must be aware of these infections and their distribution to ensure their timely diagnosis and treatment.

New combinations of diseases have also been noted, such as the appearance and spread of co-infections of HIV virus and leishmaniasis.

The effect of global warming may lead to the resurgence of some diseases or the establishment of others never before transmitted on the continent. Tropical infections are constantly being introduced into Europe by returning tourists and immigrants and local transmission of some of these, such as malaria, has already taken place as a result.

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Because the literature on these subjects is widely scattered throughout various public health, medical and entomological journals, extensive bibliographical references are provided.

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## INTRODUCTION

While the number of vector-borne diseases and their incidence in Europe is much less than that of the tropical, developing countries, there are, nevertheless, a substantial number of such infections in Europe. Furthermore, the incidence of many of these diseases has been on the rise, and their distribution is spreading. Several reviews have been made of the status in Europe of individual diseases or groups of diseases, e.g. the arboviruses, (Hubalek and Halouzka, 1996), (Lundstrom, 1999), malaria (Sabatinelli et al, 2001), Lyme disease (Weber, 2001) and others. This publication reviews the distribution of all of the vector-borne diseases of public health importance in Europe, their principal vectors, and the extent of their public health burden. Such an overall review is necessary to understand the importance of this group of infections and the resources that must be allocated to their control by public health authorities. Medical personnel must be aware of these infections and their distribution to ensure their timely diagnosis and treatment. Special reference will be made to both emerging diseases and to diseases once thought to be under control that are now resurging in Europe. Ecological changes have resulted in the virtual disappearance of some infections or the vectors that transmit them; now, other ecological and environmental changes are resulting in the re-emergence of some diseases. New combinations of diseases have also been noted, such as the appearance and spread of co-infections of HIV virus and leishmaniasis (Desjeux et al, 2001). The effect of global warming may lead to the resurgence of some diseases or the establishment of others never before transmitted on the continent. Tropical infections are constantly being introduced into Europe by returning tourists and immigrants and local transmission of some of these, such as malaria, has already taken place as a result.

Well into the twentieth century, vector-borne diseases were the cause of some of the most important public health problems in Europe. Malaria was a serious problem in much of southern and eastern Europe as well as in England after the First World War. The seasonal transmission of malaria extended as far as northern Europe. In 1927–1928, a massive epidemic of dengue with high mortality was witnessed in Athens, Greece Epidemic, or louse-borne typhus, relapsing fever and trench fever were scourges of armies and of civilians during the First World War, and, to a lesser extent, during World War II. This publication reviews vector-borne diseases in Europe and the extent to which they present public health problems; their epidemiology, incidence, and distribution, as well as the distribution of their vectors and reservoirs, is presented.

## ARBOVIRUSES

There are between 500 and 600 known arthropod-borne viruses, or arboviruses, in the world, of which some 100 may give rise to disease in humans. There are four families of arboviruses: Togaviridae, Flaviviridae, Bunyaviridae and Reoviridae. By 1996, 51 arboviruses had been reported from Europe and reviewed by Hubalek and Halouzka (1996 *ibid*). Many of these viruses are not known to cause human illness; some have only been isolated from arthropods, birds or animals, and their public health significance is unknown. Others may cause significant human illness. These arboviruses will be considered by the four groups of arthropods that transmit them: mosquitoes, sandflies, biting midges and ticks.

## MOSQUITO-BORNE VIRUSES

### West Nile virus

West Nile virus (WNV) is a member of the genus *Flavivirus*, which also includes yellow fever and Japanese encephalitis. The virus was first recovered from the blood of a woman in Uganda in 1937 (Smithburn et al, 1940). The virus is now known to be widely distributed across much of Africa, southern Europe, and the Middle East. In 1999, it invaded North America, and it has since spread across the country, reaching the West Coast in 2002. In that year, 3 389 reported cases of human WNV-associated illness were reported, 2 354 (69%) cases of which were West Nile meningoencephalitis. The epidemiology and virulence of West Nile virus has also changed in recent years. West Nile virus was, until recently, considered relatively benign, but increasing numbers of cases of encephalitis are being seen in all areas where the virus occurs. During a large-scale outbreak in Bucharest, Romania in 1996, of almost 1 000 clinically defined cases, 393 patients with neurological disease had laboratory evidence of West Nile virus infection; this outbreak will be further described below. WNV is widespread in Europe and is transmitted by several species of mosquitoes. It is the cause of periodic, often severe, outbreaks in man and horses. Table 1 shows the countries in which it has been reported as endemic between 1960-2000 (taken from Hubalek and Halouzka, 1999), while table 2 lists the mosquito species incriminated as vectors and the countries where this has been determined.

A geographical variation exists in the status of mosquito species incriminated as vectors of WNV in Europe. Studies conducted in the Camargue, southern France, during a WNV outbreak there from 1962-1965 incriminated *Cx. modestus* as the vector (Mouchet et al, 1970). In the summer of 1969, WNV, or a virus antigenically very closely related to it, was isolated from female *An. maculipennis* collected in Beja, southern Portugal, and was named the Roxo strain. This is the first record of the isolation of an arbovirus from mosquitoes in Portugal (Filipe, 1972). Isolations of West Nile Virus were made from *Cx. pipiens* in Romania during the outbreaks of 1996 to 2000 (Tsai et al, 1998), and this species was probably the major, if not only, vector, particularly in urban areas. In the Czech Republic, WNV has been isolated from *Ae. vexans*, *Ae. cinereus* and *Cx. pipiens* (Hubalek et al, 2000). In Moldavia, reports have been made of the isolation of the virus from the ticks *Dermacentor marginatus* and *Ixodes ricinus*, (Chumakov, 1974, Kononov, 1977), as well as from *I. ricinus* in Hungary (Molnar, et al, 1976) and from *Ornithodoros capensis* in Azerbaijan (Gromashevskii et al, 1973) and the Caucasus (Lvov, 1973). Lvov et al (2002) also reported isolating WNV

**Table 1. Countries in Europe in which WNV endemic activity has been detected**

Countries	Reported activity or outbreaks
Albania	1958
Austria	1964-1977 / 1988
Belarus	1972-1973* / 1977
Bosnia	1980s
Bulgaria	1960-1970 / 1978*
Croatia	1978-1980
Czech Republic	1978* / 1980s* / 1990* / 1997
France	1962-65 / 1975-1980 / 2001 / 2003
Germany	1990s*
Greece	1970-1978 / 1980-1981
Hungary	1970s / 1984
Italy	1966-1969 / 1981* / 1998*
Poland	1996*
Portugal	1967 / 1969 / 1973 / 1976-1970
Romania	1966-1970 / 1975 / 1980 / 1984 / 1996-2000
Russia	1962-1976 / 1977* / 1981-1986 / 1989 / 1991 / 1992* / 1999
Serbia	1970s (?)
Spain	1960s / 1979* / 1980 / 1998
Slovakia	1970-1973* / 1984-1987 / 1998
Ukraine	1980s / 1998

\* birds, animals or arthropods only

from *Hyalomma marginatum* ticks found on the great cormorant (*Phalacrocorax carbo*) and the crow (*Corvus corone*) of the Astrakhan region of the Volga delta. Despite these findings, the overall vectorial importance of ticks in the transmission of WNV appears to be minor. It is possible that ticks may have a role in maintaining the virus in endemic foci, but it is unlikely that they would be of vectorial importance during epidemic outbreaks.

**Table 2. Arthropod species confirmed as vectors or with isolations of WNV**

Country	Species
Bulgaria	<i>Mansonia uniformis</i>
Czech Republic	<i>Aedes cinereus</i> , <i>Ae. vexans</i> , <i>Cx. pipiens</i>
France	<i>Culex modestus</i> , <i>Cx. pipiens</i>
Portugal	<i>Anopheles maculipennis</i>
Slovakia	<i>Ae. cantans</i>
Romania	<i>Cx. pipiens</i>
Russian Federation	<i>Ae. vexans</i> , <i>Cx. modestus</i> , <i>Cx. univittatus</i> , <i>Dermacentor marginatus</i> , <i>Ixodes ricinus</i>
Ukraine	<i>An. maculipennis</i>

Many species of migratory and non-migratory birds are reservoirs of WNV, and their role in the epidemiology of WNV is important. Malkinson and Banet (2002) observed that in Europe, some species of seropositive birds were nonmigrators, while others were hatchlings of migrating species. Persistently infected avian reservoirs are potential sources of viruses for mosquitoes that multiply in the temperate European zone in hot, wet summers. The unusual findings of anti-WNV antibodies in a population of storks maintained in northern Germany could be interpreted as evidence of local infection. The unique susceptibility of young domestic geese in Israel in 1997–2000 to WNV and the isolation of similar strains from migrating White storks in Israel and Egypt suggest that the recent isolates are more pathogenic for certain avian species, and that migrating birds do play a crucial role in the geographical spread of the virus. The authors considered that the appearance of the disease in western European equine populations (Italy and France) required that other birds and their migratory routes be investigated once more. They considered that it remains to be determined whether the European endemic foci of WNV are in themselves sources of infection for other birds that migrate across Europe but do not necessarily reach sub-Saharan Africa. Migratory birds were probably responsible for the introduction of the virus into Europe from Africa, Israel, or Egypt but, by now, local European foci may now be the source of infection to birds. Birds also migrate to the UK and potential vector species are found there; however, the population density of mosquitoes is relatively low, and therefore, the risk of WNV transmission in the UK is thought to be low (Crook et al, 2002). Retrospective sampling of domestic fowl in the vicinity of case-patient residences during the years 1997–2000 in Romania demonstrated seroprevalence rates of 7.8%–29%. Limited wild bird surveillance showed seroprevalence rates of 5%–8% (Ceianu et al, 2001). Hubalek (2000) observed that natural (exoanthropic, sylvatic) foci of WNV characterized by the wild bird-ornithophilic mosquito cycle probably occur in many wetlands of climatically warm as well as some temperate parts of Europe; these foci remain silent but could be activated under circumstances supporting an enhanced virus circulation due to appropriate abiotic (weather) and biotic (increased populations of vector mosquitoes and susceptible avian hosts) factors. In any event, it is probable that WNV strains are transported between sub-Saharan Africa and Europe by migratory birds. After the major outbreak of WNV in Romania in 1996, phylogenetic analyses were compatible with the introduction of the virus into Romania by birds migrating from sub-Saharan Africa, to northern Africa, and into southern Europe (Savage et al, 1999). In August 2001, Al'khovskii et al (2003) surveyed the degree to which 315 birds collected in the lower and middle delta region of the Volga River within the Astrakhan region had antibodies to WNV. Positive results were found in coots (15.1%) and in cormorants (14.3%) in the lower delta. As for the middle delta, the infection rate among coots, herons, sea-gulls and terns was found to be identical and amounted to 8–13%, whereas it was mark-

edly higher in cormorants 42%. The infection rate of land-based birds did not exceed 5%. The obtained results are indicative of a high activity of circulation of WNV among the birds of the water and near-water complexes in the region. The isolation of WNV from the great cormorant *Phalacrocorax carbo* and the crow *Corvus corone* by L'vov et al (2002 *ibid*) has already been referred to above.

### THE PUBLIC HEALTH IMPORTANCE OF WEST NILE VIRUS

The first outbreaks of WNV in France occurred in the south, in the Carmargue region, in 1962–1965, the virus having apparently been introduced into the country in 1962. There was a high mortality rate among horses, with some 50 dying during this period (Panthier, 1968a). Between 1962 and 1964, 13 human cases of WNV were reported near Montpellier and in the Carmargue, regions where *Ae. caspius* and *Cx. modestus* are common. Symptoms ranged from benign pyrexia to fatal meningoencephalitis. WNV was isolated from two mild cases at the onset of the febrile phase in 1964. In the other cases, serological studies showed that WNV was responsible for the illness. In the outbreak in the Carmargue in 1962, severe cases of human illness were observed; after a winter intermission, the epidemic again developed in 1963, but with a lower incidence. In 1964, only a few mild human cases were seen in the Camargue in areas not covered by the mosquito control programme (Panthier et al, 1968b).

In the year 2000, an outbreak again occurred in the south of France in which horses were the principal victims. The disease was first confirmed in August 2000 in two horses in the Hérault region. By December 2000, out of a total of 1992 horses tested, 76 clinical cases and 21 deaths were recorded, and 227 serologically positive horses were detected. Restrictions on the movement of horses in the Bouches-du-Rhône, Gard and Hérault departments were put in place, and no human cases were reported during this equine outbreak (Zientara et al, 2001). It is interesting to note that a case of West Nile Virus was diagnosed in an 82-year old man recently arrived in France from Atlanta, Georgia, USA, who complained of chills and fever in late August 2002. He left Atlanta on 26 August 2002, and spent a week in Paris before he reached Burgundy. On day 9, after his arrival in the town of Dijon, he had chills and fever (40°C), weakness, malaise, diarrhea, and headache. He was then admitted to Dijon University Hospital where WNV was serologically diagnosed (Charles et al, 2003).

The most serious European outbreak of WNV occurred in Romania in 1996–1997. Seroprevalence data suggest that West Nile Virus activity in southern Romania dates to the 1960s or earlier (Campbell et al, 2001). In the 1996–1997 outbreak, 767 clinical cases of WNV were reported, with 17 deaths, representing a case fatality rate of 10%. However, it is estimated that about 70 000 (range 43 000–96 000) residents had probably been infected during the epidemic, 0.5% of whom developed encephalitis (Hubalek, 2001 unpublished report). Following the outbreak, a surveillance system for WNV in Romania was established, and

it detected a total of 39 clinical human WN fever cases during the period 1997–2000: 14 cases in 1997, 5 cases in 1998, 7 cases in 1999, and 13 cases in 2000. Thirty-eight of the 39 case-patients lived in the greater Danube Valley of southern Romania, and one case-patient resided in the district of Vaslui, located on the Moldavian plateau. The estimated annual case incidence rate for the surveillance area during the period 1997–2000 was 0.95 cases per million residents. Thirty-four cases were serologically confirmed, and five cases were classified as probable. Twenty-four case-patients presented with clinical symptoms of meningitis (62%), 12 with meningoencephalitis (31%), 1 with encephalitis (3%), and 2 with febrile exanthema (5%). Five of the 39 cases were fatal (13%). Fourteen case-patients resided in rural areas and 25 in urban and suburban areas, including seven case-patients who resided in Bucharest. The surveillance data suggest that WN virus persists focally for several years in poorly understood transmission cycles after sporadic introductions, or that WNV is introduced into Romania at relatively high rates and persists seasonally in small foci (Ceianu et al, 2001 *ibid*). WNV transmission continued in southeastern Romania, and in 1997–1998, neurologic infections were diagnosed serologically as WN encephalitis in 12 of 322 patients in 19 southeastern districts and in 1 of 75 Bucharest patients, and sentinel chickens continued to convert to WNV, indicating local zoonotic transmission (Cernescu et al, 2000).

The WN virus is endemic over large areas of Russian Federation and Ukraine. Platonov (2001) reviewed the status of WNV in European Russia and Siberia and the following observations are excerpted from his article. In 1963–1993, several strains of West Nile virus (WNV) were isolated from ticks, birds, and mosquitoes in the southern area of European Russia and western Siberia. In the same regions, anti-WNV antibody was found in 0.4 to 8% of healthy adult donors. Sporadic human clinical cases were observed in the delta of the Volga River. In spite of this, WNV infection was not considered by the health authorities as a potentially emerging infection, and the large WNV outbreak in southern Russia, which started in late July 1999, was not recognized in a timely fashion. The first evidence suggesting a WNV etiology of the outbreak was obtained by IgM ELISA on 9 September 1999. Two weeks later, a specific WNV RT-PCR study was carried out and the presence of WNV disease was confirmed in all 14 non-survivors from whom brain tissue samples were available. Retrospective studies of serum samples by IgM ELISA indicated WNV etiology in 326 of 463 survivors, with aseptic meningitis or encephalitis. Moreover, 35 of 56 patients who contracted aseptic meningitis in 1998 had a high titre of WNV IgG antibody. WNV infection seems to have been introduced into the Volgograd region before 1999. A complete sequence (AF317203) of WN viral RNA, isolated from the brain of one Volgograd fatality, and partial sequences of an envelope E gene from other fatal cases, showed that the Volgograd isolate had the greatest homology (99.6%) with WN-Romania-1996 mosquito strain RO97-50.

The recent introduction of WNV into the USA and its rapid spread from where it first appeared in New York in 1999 to California and Washington State on the West Coast by 2002 further illustrates the epidemic potential of the infection. By November of 2002, at least 3 737 cases had been reported for that year, 214 deaths were recorded, and evidence of infection was found in 43 states of the USA (WHO, 2002a). In 2001, dead birds were found in Canada, and by 2002, human cases appeared in that country. Infected birds have recently been found in the Caribbean, and the infection will no doubt continue to spread through the Americas.

Further serological surveys are likely to indicate that the virus is endemic in countries and territories in Europe other than those in which it has been reported to date; antibodies, but no human cases, have been reported from Austria and Poland, and a human case from Belarus (Voinov et al, 1981) has been registered. From the 1990s to the present, encephalitis has been a more prominent feature of West Nile virus infection in Europe, the Middle East, and the United States, suggesting the emergence of more neurovirulent strains (Johnson and Irani, 2002). A growing number of cases involving central nervous system manifestations and deaths have been reported in elderly people in Algeria and Romania. Deaths have also been recorded in migrating birds in zones where the virus is emerging (Zeller, 1999). Outbreaks of the diseases may occur after long periods of silence, and continued surveillance of WNV is essential.

## **OTHER MOSQUITO-BORNE VIRUSES OF PUBLIC HEALTH IMPORTANCE**

### **Batai virus (Calovo virus)**

Batai or Calovo virus, a bunyavirus, was first isolated in Europe in Slovakia from *An.s maculipennis* in 1960. Batai virus, or closely related viruses, has been identified from several countries in Asia and Africa. It has been isolated as far north as Norway, Sweden, Finland and in the northern part of Russian Federation, and has been found in Ukraine, the Czech Republic, Slovakia, Austria, Hungary, Portugal, Romania, and in the south of the Russian Federation. The western European vectors appear to be mainly *An. maculipennis* and *An. claviger*, and it has been isolated from *Ae. communis* and several other *Aedes* and *Culex* species. Lundstrom (1994) did not associate the Batai or Calovo viruses with human diseases in western Europe, and considered their potential for human disease low (Lundstrom, 1999). Chaporgina et al (1995) reported a human focus of Batai virus in the Lake Baikal region, but considered that the epidemiological significance of the virus was insignificant. Danielova (1990) observed that Calovo virus had a very low prevalence in humans in the Czech Republic due to the marked zoophilia of its vectors.

### Ockelbo virus

Ockelbo virus is a Sindbis-related virus. It was first described in Sweden in the 1960s, and it is probably identical to Pogosta disease in Finland and to Karelian fever in western Russia (Francy et al, 1989 *ibid*). In the 1980s, Ockelbo disease caused considerable human morbidity in portions of northern Europe, with outbreaks involving hundreds of cases. In 1981, the Russian Federation and Finland reported 200 and 300 laboratory confirmed cases respectively. A major outbreak occurred once again in Finland in 1995, when 1400 laboratory confirmed cases were reported. In Sweden, an annual average of 31 laboratory confirmed cases were diagnosed during the period 1981–1988, although Lundstrom et al (1991) believe that as many as 600 to 1200 cases a year occur in the country. The virus has been isolated from many different species of mosquitoes including *Ae. cantans*, *Ae. cinereus*, *Ae. communis*, *Ae. excrucians*, *Ae. intrudens*, *Cx. pipiens*, *Culiseta morsitans* and *Cx. torrentium*, particularly species which feed upon the Passeriformes bird reservoirs and man. Arthralgia is the dominating feature of Ockelbo disease, and it may immobilize patients for a week or up to a month or more (Niklasson et al, 1988).

The many strains of the Sindbis group of arboviruses are widely distributed throughout Europe, Asia and Africa, and, as noted above, they are closely related to Ockelbo and other viruses in northern Europe. The virus is maintained in nature in a mosquito-bird transmission cycle and is transmitted throughout Europe by migratory birds and ornithophilic *Culex* species and *Culiseta morsitans* as vectors (Lundstrom et al, 2001). In Finland, the yearly incidence of Sindbis virus is 2.7/100 000 (18 in the most endemic area of Northern Karelia). The annual average was 136 (varying from 1 to 1282), with epidemics occurring in August–September in a seven year interval (Brummer Korvenkontio et al, 2002). As with other viral infections of the group, the main symptom in humans is a febrile arthritis-like disease.

### Inkoo virus

Inkoo virus is a member of the California serogroup of the bunyaviruses; it is broadly distributed in northern Europe and has been reported in Norway, Sweden, Finland, Estonia and the Russian Federation. Inkoo virus is transmitted by *Ae. communis* and *Ae. punctor* in Scandinavia, and has been isolated from *Ae. communis* in Sweden (Francy et al, 1989). In the Russian Federation, the virus has been isolated from *Ae. hexodontus* and *Ae. punctor* (Mitchell et al, 1993). Inkoo virus is quite common in Finland, with its prevalence increasing towards the north, where it rises to 69% (Brummer Korvenkontio and Saikku, 1975). The antibody prevalence is also high in Sweden (Niklasson and Vene, 1996), but there is no evidence of human disease caused by this virus in either country. In the Russian Federation, however, Demikhov (1995) noted patients with antibodies to Inkoo virus had chronic neurologic disease; Demikhov and Chaitsev (1995)

described severe illness ascribed to infection with the virus, although there was no mortality. Inkoo, and, as will be seen below, Tahyna virus are the most common California group viruses in Eurasia, and must remain the subject of close public health surveillance.

### **Tahyna virus**

Tahyna virus is also a member of the California complex of arboviruses. It is similar to Inkoo virus, but antigenically distinct (Butenko et al, 1991). It was isolated for the first time in Europe in 1958 in a village in the present day Slovakia (Bardos and Danielova, 1958). The virus appears to be present in most countries of Europe. In human patients, the virus may present with influenza-like symptoms, and, in some cases, meningoencephalitis and atypical pneumonia has been observed. No cases of death have been reported (Bardos, 1976). Demikhov (1995) followed up patients in Russian Federation who had been ill with Inkoo and Tahyna viruses; one to 2.5 years after the disease, 16.7% of convalescents who had had the febrile form of the disease and 30.7% of convalescents with the neuroinfectious form showed asthenoneurologic disturbances and microfocal neurologic symptoms. Of the 37 patients examined, 70.3% had disseminated encephalomyelitis, and the author emphasized that these findings point to the necessity of further study of the possible role of California encephalitis group viruses in the etiology of chronic neuroviral infections. In another clinical study of patients with infections due to Inkoo and Tahyna virus (Demikhov and Chaitsev, 1995), two principal forms of the disease were observed; 61% with fever, 31.7% with neuroinfection, and in 7.3% of cases, both were present. Of the patients with the neuroinfectious form of the disease, three presented with aseptic meningitis, two with meningoencephalitis, and five with encephalitis. Inasmuch as Tahyna virus is widespread in Europe and may cause severe disease, it must be considered of public health importance at present, bearing in mind its even greater potential for increased incidence, especially as its vectors are so widespread.

The vectors of Tahyna virus are mainly pasture-breeding species of the genus *Aedes*; most of the isolations reported have been made from *Aedes vexans*. The anthropophilic nature of this species accounts for the high antibody rates in humans in countries where the infection is endemic in human populations (Danielova et al, 1990 *ibid*). Table 3 presents a listing of countries in which Tahyna virus has been isolated or in which antibodies have been detected.

### **Dengue virus**

Dengue was at one time endemic in the countries of southern Europe in which the *Ae. aegypti* vector was present. A massive epidemic of dengue with high mortality in Athens, Greece in 1927–1928 has already been mentioned. Today, dengue is the most important arboviral human disease globally, although the disease has disappeared from Europe, mainly due to the nearly universal use of piped

**Table 3. Reports of Tahyna virus found in surveys in Europe**

Country	Results: isolations or antibodies	Reference
Austria	<i>Ae. caspius</i>	Pilaski & Mackenstein, 1989
Croatia	humans	Vesenjal Hirjan et al, 1989
Croatia	bears	Madic et al, 1993
Czech Rep.	<i>Ae. cinereus</i> , <i>Ae. vexans</i>	Danielova et al, 1977
Czech Rep.	<i>Ae. sticticus</i> , <i>Cx. modestus</i>	Danielova & Holubova, 1977
Czech Rep.	birds	Hubalek et al, 1989
Czech Rep.	birds: swallows, martins	Jurikova et al, 1989
Czech Rep.	<i>Ae. spp</i> , humans	Danilov, 1990
Czech Rep.	game animals: deer, boars	Hubalek et al, 1993
Czech Rep.	birds: cormorants	Juricova et al, 1993
Czech Rep.	birds: ducks	Juricova & Hubalek, 1993
Czech Rep.	<i>Ae. cinereus</i> , <i>Ae. vexans</i> , humans	Hubalek et al, 1999
Czech Rep.	birds: sparrows	Juricova et al, 2000
France	<i>Ae. caspius</i> , humans	Joubert, 1975
Germany	<i>Ae. caspius</i>	Pilaski & Mackenstein, ibid
Germany	domestic animals, humans	Knuth et al, 1990
Hungary	<i>Ae. caspius</i>	Molnar, 1982
Italy	small mammals	Le lay Rogues et al, 1983
Poland	birds: sparrows	Juricova et al, 1998
Portugal	cattle and sheep	Filipe & Pinto 1969
Russian Federation	<i>An. hyrcanus</i>	L'vov, 1973
Russian Federation	humans	Kolobukhina et al, 1989
Russian Federation	humans	Butenko et al, 1990
Russian Fed	humans	Glinskikh et al, 1994
Russian Federation	<i>Ae. communis</i> , <i>Ae. excrucians</i>	L'vov et al, 1998
Romania	<i>Cx. pipiens</i>	Arcan et al, 1974
Romania	cattle, sheep, goats, humans	Draganescu & Girjabu, 1979
Slovakia	humans, hares (?)	Bardos, 1976 ibid
Serbia	<i>Ae. vexans</i>	Gligic & Adamovic, 1976
Slovakia	<i>Ae. vexans</i>	Danielova et al, 1978
Slovakia	humans	Kolman et al, 1979
Slovakia	sheep	Juricova et al, 1986
Slovakia	<i>Culiseta annulata</i> larvae	Bardos, 1998
Spain	rodents	Chastel et al, 1980

water supplies. Piped water has led to the virtual disappearance of containers such as jars and barrels for the storage of water for household use and, consequently, *Ae. aegypti* as a species has not been reported in Europe for many years. Grist and Burgess (1994) pointed out that while the spread of *Ae. aegypti* in Europe is limited by its cold intolerance, this is obviously not the case with *Ae. albopictus*,

and the reintroduction of dengue transmission must be considered a possibility. *Ae. albopictus* is a vector of dengue in some parts of the world, and strains from Albania have readily transmitted dengue in laboratory transmission studies (Vazeille Falcoz et al, 1999). Dengue is frequently introduced into Europe by travelers returning from dengue-endemic countries, and a viremic traveler bitten by *Ae. albopictus* could well be the source of renewed dengue transmission in Europe (Ciufolini and Nicoletti, 1997).

## MOSQUITO-BORNE DISEASES – MALARIA

Until after the end of World War II, malaria was endemic throughout much of southern Europe. The Balkans, Italy, Greece, and Portugal were particularly affected, although seasonal epidemics or outbreaks occurred as far north as Scandinavia, e.g. Finland in 1944 (Bonsdorff, 1991), Norway (Fossmark, Bergstrom, 1994) and southern Sweden. The area of malaria distribution in Europe peaked at the beginning of the twentieth century. At that time, the northernmost limit of malaria in Europe ran from Central England to Southern Norway, Central Sweden, Central Finland and Northern European Russia along the 64°N parallel.

Soon after the war, intensive control measures were initiated, and by 1970, malaria transmission had been virtually eradicated from the continent, a considerable achievement which contributed to the economic development of the some of the worst affected areas in south-east Europe. The last indigenous cases at the time occurred in Macedonia in 1974, and in 1975, the World Health Organization declared malaria eradicated from Europe.

However, populations of potential *Anopheles* vectors of malaria remain high in many countries of the continent, and their presence poses the risk of renewed transmission, should infected human hosts be available. Romi et al (1997) reported human landing rates of anophelines in Grosseto, Italy, with peaks of >200 landings per human per night. In some areas of Europe, particularly in Italy and Greece, the expansion of rice cultivation has resulted in great increases in the population densities of potential malaria vectors. On the other hand, in the Netherlands, ecological changes in water quality have greatly reduced the populations of what was once the most important vector of malaria in that country, *An. atroparvovus*, (Takken et al, 2002).

### RECRUDESCENCE OF AUTOCHTHONOUS MALARIA IN EUROPE

Malaria was at one time endemic throughout much of Italy. *P. falciparum* transmission disappeared from the country in 1950 after an intensive vector control campaign; *P. vivax* persisted somewhat longer, and the last autochthonous case was documented in 1955, near the river Esaro in Calabria (Coluzzi, 2000). The last endemic focus of *P. vivax* was reported in Sicily in 1956 (Sabatinelli and Majori, 1998). Much of southern and central rural Italy remains receptive to malaria transmission, due to the presence of capable malaria vectors such as *An. labranthiae*. While the overall malariogenic potential of Italy appears to be low, and the reintroduction of malaria is unlikely in most of the country (Romi and Sabatinelli, 2001), the densities of *An. labranthiae* remain very high in many parts

**Table 4. Number of autochthonous malaria cases registered in the countries of the WHO European Region\***

Country	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999
Armenia	0	0	0	0	1	0	149	567	542	329
Azerbaijan	24	113	27	23	667	2840	13 135	9911	5 175	2311
Bulgaria	0	0	0	0	0	11	7	0	0	0
Georgia	0	0	0	0	0	0	3	0	14	35
Greece	0	0	0	0	0	0	0	0	n/a	1
Italy	0	0	0	0	0	0	0	2	0	0
Kazakhstan	0	0	1	0	1	0	1	0	4	1
Kyrgyzstan	0	0	0	0	0	0	1	0	5	0
Republic of Moldova	0	0	0	0	0	0	2	0	0	0
Russian Federation	7	0	0	1	1	4	10	31	63	77
Tajikistan	175	294	404	619	2411	6 103	16 561	29 794	19 351	13 493
Turkey	8 675	12 213	18 665	47 206	84 321	81 754	60 634	35 376	36 780	20 905
Turkmenistan	0	13	5	1	1	0	3	4	115	10
Uzbekistan	3	1	0	0	0	0	0	0	0	7
<b>Total</b>	<b>8 884</b>	<b>12 634</b>	<b>19 102</b>	<b>47 850</b>	<b>87 403</b>	<b>90 712</b>	<b>90 506</b>	<b>75 685</b>	<b>62 049</b>	<b>37 169</b>

Table adapted from the Centralized Information System of Infectious Diseases (CISID) website of the WHO Regional Office for Europe

\* The remaining 37 Member States of the WHO European Region registered no autochthonous cases during this period

of Italy, along with other such potential vectors as *An. maculipennis*, *An. atroparvovus* and *An. superpictus* (Romi et al, 1997 *ibid*, Zamburlini and Cargnus, 1999). Fortunately, most of these species are not particularly receptive to African strains of *P. falciparum*. In Maremma, Italy in 1977, a woman with no history of travel to malarious regions developed *P. vivax* malaria. She lived in a rural area where indigenous *An. labranchiae* were present. House-to-house investigation identified a 7-year-old girl who had a feverish illness a few days after her arrival in Italy from India, and, three months later, still had *P. vivax* in her blood; both she and her mother had antimalarial antibodies. The child's father later developed a high fever and parasitaemia. It is suggested that the index case of malaria was caused by local anophelines infected with exogenous *P. vivax*. These were considered to be among the first cases of introduced malaria in Italy in 20 years (Baldari et al, 1998).

No cases of indigenous malaria have been reported from the Netherlands since the early 1960s; this was a result of a combination of factors which included the active detection and treatment of patients and parasite carriers, the targeted use of insecticides in vector control, changes in farming practices and in the quality of housing of man and cattle, the pollution of surface water with phosphates, and the fact that surface waters have become fresher. These factors reduced the *Anopheles* mosquito population that is dependent on brackish water. The Dutch

malaria vector cannot transmit *P. falciparum*. However, the mosquito population could possibly increase due to measures to ‘develop nature’, but the number of parasite carriers, the acute disease manifestations, the quality and organization of the health care system make it extremely unlikely that local transmission will occur. Fears that malaria may become endemic and that the population in the western parts of the country will have to apply malaria chemoprophylaxis in the near future are unfounded (Taken et al, 1999). To confirm these observations, Takken et al (2002, *ibid*) examined a previously malaria endemic area in the delta of the rivers Rhine and Meuse. They found that the study area had undergone a dramatic ecological change since the previous anopheline investigations in 1935, and this had caused the near extinction of *An. atroparvus*. As this species was the only malaria vector in The Netherlands, it is not expected that malaria would return to its former endemic status in the coastal areas of the country.

Throughout large areas of the Russian Federation, including the Moscow Region, malaria was endemic until a DDT vector control program, combined with active case detection, was begun in 1945. Malaria transmission was prevalent in the regions of the Russian Federation where average daily temperatures were above 15° C for more than 30 days a year. However, since 1966, the number of imported cases of malaria has increased and has led to renewed local transmission. Cases of local malaria now outnumber imported cases in the European part of the Russian Federation. During the year 2000, a total of 763 cases of malaria were registered in the Russian Federation, 47 of which were autochthonous (Sokolova and Snow, 2002), including locally transmitted cases of *P. vivax* in the Moscow area (Makhnev, 2002). The incidence of autochthonous malaria cases in the Moscow region has risen from 112 in 1997 to 214 in 2001, and has necessitated the implementation of an active vector control programme. While transmission may have started as a result of imported cases, it has now become endemic in a limited area.

In Spain, a case of *P. ovale* was recently reported in the central area of the country. The patient was a woman who had never traveled outside of Spain and had no other risk factors for malaria. This case is the first locally acquired *P. ovale* infection connected with Europe. There were international airports 4 and 18 km from the patient’s home, possibly within the range of a mosquito introduced aboard an aircraft. Transmission may also have occurred after one of the potential local vectors, *An. labranchiae* or *An. atroparvus*, had bitten a migrant worker (Cuadros et al, 2002).

The most serious problems of resurgent malaria occur in the Newly Independent States and in Turkey, due to a number of factors including an influx of refugees from malaria endemic areas, the breakdown in health services, and lack of vector control measures in most of these states, as well as in the failure to carry out adequate malaria surveillance and control measures. There has now been a return of malaria to countries in which it had previously disappeared.

While considerable effort is now being made, with the assistance of WHO and donors, to curb transmission by control of the vectors, the incidence of autochthonous malaria for the period 1996–2000 remains quite high in some countries, as seen in Table 5.

**Table 5. Autochthonous malaria reported in eastern Europe**

Country	1996	1997	1998	1999	2000
Armenia	149	567	542	329	56
Azerbaijan	13 135	9911	5 175	2 311	1 526
Georgia	3	0	14	15	244
Russian Federation	10	31	63	77	43
Tajikistan	16 561	29 794	19 351	13 493	19 064
Turkey	60 634	35 376	36 780	20 908	11 381
Turkmenistan	3	4	115	10	18

Most of the resurgent malaria cases are due to *P. vivax*, although there have been an increasing number of cases of *P. falciparum*. In view of the mobility of the human population, the increased number of malaria cases constitutes a threat to those areas of Europe, particularly the Balkans.

### IMPORTED MALARIA

Between 10,000 and 12,000 cases of imported malaria are notified in the European Union each year (crude rate ~ 2–3/100 000 population); inasmuch as

**Table 6. Imported cases of malaria in Europe 1996–2000**

Country	1996	1997	1998	1999	2000
Austria	87	75	80	93	62
Belgium	n.a	n.a	334	369	337
Denmark	191	213	174	207	202
France	5 109	5 377	5 940 <sup>1</sup>	6 127 <sup>1</sup>	8 056 <sup>1</sup>
Germany	1 021	1 017	1 008	918	732
Italy	760	814	931	1 006	986
Netherlands	308	223	250	263	691
Norway	101	107	88	74	79
Russian Federation	601	798	1 018	715	752
Spain	224	291	339	260	333
Sweden	189	183	172	153	132
Switzerland	292	319	339	313	317
United Kingdom	2 500	2 364	2 073	2 045	2 069

<sup>1</sup> Preliminary data

Table adapted from the Centralized Information System of Infectious Diseases (CISID) website of WHO Regional Office for Europe

at least an equal number of cases are not properly diagnosed or reported, the actual number of imported cases may be high as 20 000 per year. The WHO Regional Office for Europe reported a total of 15 528 cases of imported malaria in Europe in the year 2000. The vast majority of these cases are imported from countries of Africa, particularly West Africa. A study by Muentener et al (1999) on the reliability of the reporting of imported malaria cases in Europe showed gross underreporting and marked heterogeneity in the type and availability of national data. Only Finland, France, and the Netherlands estimated the level of underreporting (respectively 20%, 55%, 59%) (Legros and Danis, 1998). The largest numbers of cases are recorded in continental France and the United Kingdom. Almost all the cases are of malaria acquired while visiting endemic areas by tourists, businessmen, military personnel or other travellers. These imported cases constitute both a serious public health problem for the recipient countries and often a grave medical problem for the infected patients. Most of the cases are of *P. falciparum* and the most common area of origin is Africa. The number of imported cases has been steadily increasing, and there has been an eight-fold increase in imported cases since the 1970s: 1 500 cases were reported in 1972 vs 13 000 cases in 1999. France, Germany, Italy, and the United Kingdom represent the west European countries with the largest numbers of cases (Sabatinelli et al, 2001 *ibid*). Within a decade (1989–1999), 680 people died from imported cases of *P. falciparum* infection in the WHO European Region; death is often a result of delayed diagnosis, as most physicians are not confronted with malaria very often and may have relatively little familiarity with its symptoms. The increasing frequency of drug-resistant strains of *P. falciparum* among the imported cases complicates treatment of infected individuals and has probably led to an increase in mortality among the imported cases. Table 6 provides figures on the number of cases of malaria from 1996 to 2000 in the most affected countries, although imported cases are reported from virtually every country of Europe. The situation in some of the countries for which important surveillance data are available will be discussed below.

### **Austria**

During the period 1990–1999, a total of 862 cases of malaria were reported as introduced into Austria. The country, with a population of 8.1 million, registers an average of 84 cases of malaria per year. Within the period mentioned, eight individuals died of malaria. Of the imported malaria cases for which data are available, almost half had taken no chemoprophylaxis (333/691); of those travelers who did take prophylaxis, 88 people (30%) had taken insufficient prophylaxis, and 29 patients (10%) had stopped their prophylactic regimen before the full course. Among the reasons given for not taking chemoprophylaxis were unpleasant side effects, complicated regimens, and incorrect information provided by tour operators, pharmacists, or doctors (Eurosurveillance Weekly, 2001).

## Belgium

Most of the cases of malaria imported every year into Belgium are *P. falciparum* acquired in Africa. The relatively severe problem of imported malaria in Belgium is due to its close ties with some countries of Africa. Van den Ende et al (2000) studied the epidemiology of imported malaria in Belgium. The number of reported imported malaria cases remained almost stable between 1988 and 1997, (249 cases in 1992, 320 cases in 1993). In 1997, there were more African patients, less infections from Central Africa, and 50% less in residents. Fewer patients reported use of malaria prophylaxis. The causative agent shifted from *P. falciparum* to other species. Subacute and atypical malaria became less frequent. In both years, there were no deaths, and severe malaria did not increase significantly. It was felt that the treatment of imported malaria cases was inadequate. In 2001, Kockaerts et al reviewed the clinical presentations of 101 imported cases at the Leuven University Hospital between 1 January 1990 and 31 December 1999. A serious finding was that in 48 of the patients (47%), malaria was not suspected by the referring physician. Only 13% of the malaria patients had taken correct chemoprophylaxis according to WHO recommendations. Eighty-three per cent of patients were admitted to a hospital, where they stayed for a median of four days

## Denmark

The number of malaria cases imported to Denmark has been increasing for some years. In 1999, there were 207 laboratory-notified cases of malaria in Denmark, a figure that is largely unchanged from 1998 (181), 1997 (213) and 1996 (191). There was nevertheless an increase in cases of *P. falciparum* in travelers from Africa (130 against 90 in 1998, 119 in 1997 and 97 in 1996). Concerned by the apparent low degree of compliance with prophylactic regimes by Danish travelers to malaria endemic areas, Christensen et al (1996) studied the contributing causes of malaria amongst the patients. They found that about 20% of those with *P. falciparum* had taken no chemoprophylaxis at all, while for many of the remainder, inadequate prophylaxis had been prescribed or the patients themselves had underdosed. The Statens Serum Institute and Copenhagen University Hospital carried out a survey of the side effects of malaria prophylaxis in about 4 500 travelers. The survey showed that about 60% of travelers using chloroquine + proguanil and 70% of those using mefloquine experienced no side effects. On the other hand, about 1% of chloroquine + proguanil users and about 3% of mefloquine users experienced unacceptable side effects. Over the course of journeys of less than three weeks, about 3%, 6% and 6% stopped taking chloroquine, chloroquine + proguanil and mefloquine respectively. On journeys of over three weeks, about 5%, 12% and 8% stopped the respective prophylactic regimens (Ronne, 2000).

## France

As in other countries of Europe, the number of cases of malaria imported into France shows an increasing trend, which is illustrated in Table 6. Epidemiological data from the French National Reference Center for Imported Diseases shows that the estimated number of cases of imported malaria in France increased from 5 940 in 1998 to 7 127 in 1999 and 8 056 in 2000. In 2001, the number of estimated cases fell back to 7 223. The regions from which cases originated were tropical Africa (95%), Asia (2.2%), and Latin America (2.7%). During the three-year period from 1998 to 2000, there were a total of 13 accidental autochthonous cases of malaria involving patients with no history of travel to tropical areas. Of all cases reported, 83% were due to *P. falciparum*, 6% to *P. vivax*, 6.5% to *P. ovale* and 1.3% *P. malariae*. Less than a tenth of the 45% of patients claiming use of prophylaxis complied with the correct regime. Many of the imported cases occurred amongst African migrants or African residents of France who returned from a visit to their countries of origin. As more than 20 deaths a year are due to imported malaria and the average length of hospital stay is a costly period of four days, the public health importance of imported malaria in France is considerable (Danis et al, 2002).

## Germany

Some three million Germans go on three- to four-week trips to malaria-endemic areas every year. Around 700 to 1 000 of them fall ill with malaria, two thirds of them with *P. falciparum*. Approximately 2% of patients succumb to the disease (Rieke and Fleischer 1993). A total of 931 imported cases of malaria were reported in Germany in 1999 (1998: 1 008 cases). Most of the infected patients were 24–45 years of age. However, studies on German travelers have shown that the percentage of travelers above the age of 60 is increasing, and the number of persons with severe malaria complications is also much higher among persons above this age. The duration of hospitalization increased with age from an average of five days for the group below 45 years to 21 days for those aged 60 years and above. These findings suggest a higher risk of a severe course of malaria in the elderly, and for this reason, extensive advice on the correct use of chemoprophylaxis to malaria and protection from exposure is especially important for travelers above the age of 60 (Stich et al, 2003). Eighty per cent of cases were acquired in Africa, 8.5 % in Asia, and 5% in Central and South America. *P. falciparum* accounted for the majority of cases (80%) followed by *P. vivax* (12%). In 1999, 60% of all imported malaria cases were among Germans. Most of them traveled for holidays or study purposes. Twenty deaths, all attributed to *P. falciparum*, were notified in 1999; most of them (19) were German citizens. In 1999, 61% of patients had not taken chemoprophylaxis at all while travelling abroad. Improving prophylactic measures is the only way to reduce the incidence of malaria cases in Germany (Schoneberg et al, 2001). Unfortunately, compliance and correct use of prophylactic drugs is regret-

tably low (not only among German travelers but among those of many countries); Harms et al (2002) found that among the patients at a travel medicine clinic in Berlin, only 34% of the returnees from malaria-endemic areas had taken chemoprophylaxis. In instances of travel to Africa and Asia, chemoprophylaxis corresponded to international standards in only 48 % and 23% of cases respectively, illustrating the reason for the large number of malaria cases among travelers.

In the years 2000–2001, 836 and 1 040 malaria cases respectively were reported as introduced into Germany. In both years, most of the patients were between 30 and 49 years old. Eighty-two percent of the infections had been acquired in Africa and 11 % in Asia. The predominant parasite species was *P. falciparum* (70 %), followed by *P. vivax* (12 % in 2000 and 16 % in 2001). The majority of infections occurred among tourists, while fewer cases were reported among immigrants or business travelers. About two-thirds of all patients had not taken any chemoprophylaxis, showing that compliance continued to be low. Mortality decreased from 18 deaths in 2000 to 8 in 2001 (Schoneberg et al, 2003).

## Italy

A total of 2 060 imported malaria cases were reported in Italy in 1999–2000. Epidemiological analysis of malaria cases reported in Italy from 1986 to 1996 shows that despite an increase in the number of people who traveled to malaria endemic areas (about 314 000 in 1989 compared to about 470 000 in 1996), the number of malaria cases in Italian travelers remained stable. Cases among immigrants are constantly increasing. The number of immigrants to Italy from malaria-endemic countries doubled from 1986 to 1992, and they are estimated to number about 1.3 million people. By 2002, migrants constituted 2.5% of Italy's population of 50 000 000. In 1997, 60% of the 875 malaria cases registered were among migrants, most of them from Africa. Eighty percent of these migrants failed to obtain pre-travel advice and to adopt malaria prevention measures when traveling back home, despite their relatively high level of knowledge about malaria. Many of the children of migrants born in Italy are taken to visit relatives in their parents' country of origin and have never previously been exposed to malaria (Scolari et al, 2002). Most of the malaria-infected travelers had taken inappropriate treatments or did not take prophylaxis at all. Reports from 1989 to 1996 show that half of Italian patients and only 7% of foreign citizens took chemoprophylaxis while traveling (Sabatinelli and Majori, 1998 *ibid*). Ninety-three per cent became infected in Africa, 4% in Asia, and 3% in Latin America. *P. falciparum* accounted for 84% of the cases, followed by *P. vivax* (8%), *P. ovale* (5%), and *P. malariae* (2%). Deaths corresponded to an annual case fatality rate of 0.3% in 1999 and 0.5% in 2000. In general, imported malaria cases reflect the number of Italian travelers who underestimate the infection risk in endemic countries and permanent residents of African origin who visit their relatives in their native countries (Romi et al, 2001). In the summer of 2000, 22 imported

malaria cases, of which 21 were caused by *P. falciparum*, were observed among illegal Chinese immigrants in northern Italy. The rate of severe disease was high because the patients were not immune and they sought health-care services late in their illness because of their clandestine status. Recognition of the outbreak was delayed because no regional alert system among infectious diseases hospitals was in place (Matteelli et al, 2001).

### **Netherlands**

As in other countries of Europe, the number of cases of malaria imported into the Netherlands has been increasing, especially among migrants (Makdoembaks and Kager, 2000). It is a matter of concern that the number of such cases appears to be seriously underreported. van Hest et al (2002) found that the number of cases of malaria diagnosed by laboratories in the Netherlands was much greater than the number of cases notified by physicians, and it is estimated that possibly as many as one-third of the cases of imported malaria may go unreported. Wetsteyn et al (1997) noted that the degree of compliance by Dutch travelers was actually decreasing; among migrants, especially those returning to Africa or Asia for visits, it was very poor.

### **Portugal**

In the decade 1985–1995, Portugal recorded 964 cases of imported malaria (Muentener et al, 1999 *ibid*); in a survey of 205 cases diagnosed as malaria in the Infectious Diseases Hospital in Lisbon during 1989–1995, 47% of cases originated from Angola, and 95% were due to *P. falciparum*. Nineteen percent of the patients developed severe complications, and six patients died (Proenca et al 1997). The number of imported cases has not exceeded 100 since 1991.

### **Romania**

Within this same decade, 1985–1995, only 146 cases of imported malaria were reported in Romania. In 1999, however, 32 cases of imported malaria were recorded, most of them *P. falciparum* imported from Africa. The remaining cases were *P. vivax* originating in Turkey. Of these cases, 65.6% were among sailors (Nicolaiuc et al, 1999). *An. atroparvovous* and *An. sacharovi* have disappeared from the previously endemic areas of malaria in the Danube Plain and Dobrudja, largely due to ecological changes. These include improved water management and changed agricultural practices such as an increase in mechanized farming, leading to reduced numbers of draught animals in the region. Bilbie et al (1978) considered the development of a new malaria epidemic in this area unlikely.

### **Spain**

Over the 10-year period between 1985 and 1995, Spain reported 1 927 cases of malaria (Muentener et al, 1999 *ibid*). Lopez et al (1999) observed that the number

of Spanish travelers visiting malaria-endemic areas, as well as the number of immigrants from malarial countries arriving in Spain is continuously increasing. A changing pattern of imported malaria in Madrid is presently emerging, however, as seen in the cases at a referral teaching hospital in that city. One-third of cases occur in immigrants, and two-thirds in nationals. It was noted that among 100 Spanish nationals, 44% did not follow any prophylaxis, 29% followed a correct prophylaxis, 27% were considered defaulters, and 39% took self-treatment without cure. In a hospital in Barcelona, 80% of the imported malaria cases seen were *P. falciparum*, and only 10% of the patients were found to have taken a correct course of chemoprophylaxis (Bartolome et al, 2002). Most of the imported cases of malaria originated from sub-Saharan Africa, a large proportion of these among immigrants from Equatorial Guinea.

### United Kingdom

The United Kingdom reports annually the greatest number of cases of imported malaria in Europe. In the decade between 1985 and 1995, 21 919 cases of malaria were imported into the United Kingdom (Muentener et al, 1999 *ibid*). In 1999, more than 2 045 cases of malaria were imported, with 14 deaths. The top ten source countries of malaria are shown in Table 7.

**Table 7. Source countries of malaria reported into the United Kingdom in 1999**

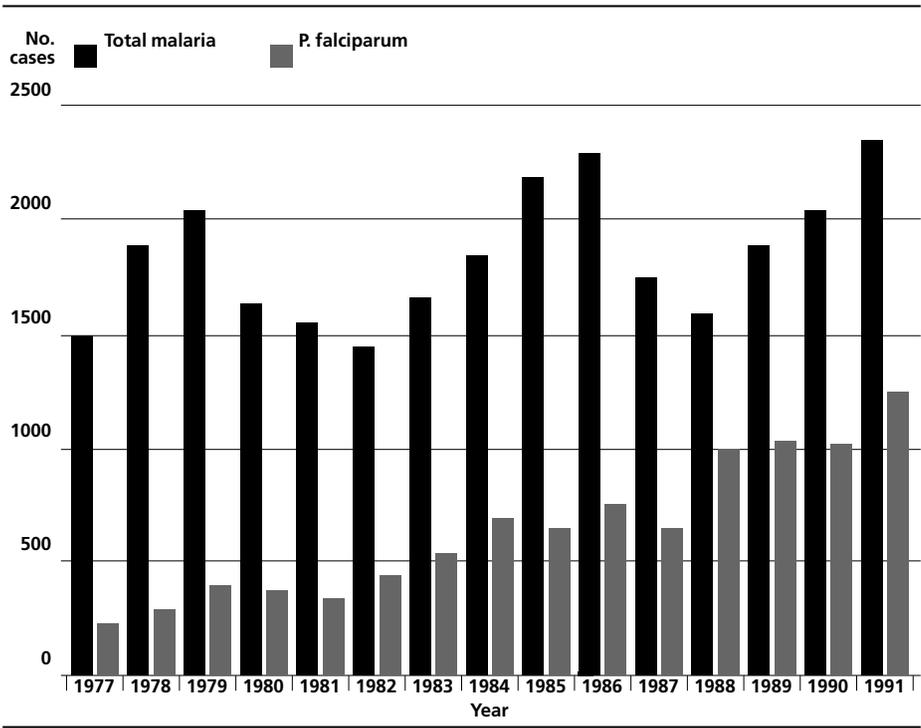
Country	Number of cases
1 Nigeria	444
2 Ghana	247
3 Pakistan	114
4 India	87 (one death)
5 Kenya	86
6 Gambia	74 (four deaths)
7 Overland travel through Africa	71
8 Uganda	62
9 Tanzania	42
10 Malawi	36

Behrens and Roberts (1994) made an economic appraisal of the benefits of chemoprophylaxis against malaria; the high incidence of imported malaria (0.70%) and low costs of providing chemoprophylaxis gave a cost-benefit ratio of 0.19 for chloroquine and proguanil and 0.57 for a regimen containing mefloquine. They concluded that the cost of treating malaria greatly exceeds the cost of chemoprophylaxis, and is highly cost-effective. However, a survey of 172 general practitioners in the West Yorkshire area of the United Kingdom who had traveled to South Asia showed that of the 145 (84%) responding to the survey, 50 (35%) took no che-

moprophylaxis, 28 (19%) did not complete the chemoprophylaxis course, and 67 (46%) were fully compliant. If medical professionals themselves do not keep to the guidelines, it is a matter of concern that they may not reinforce the importance of using chemoprophylaxis to their patients (Banerjee and Stanley, 2001).

While the number of cases of cases of autochthonous malaria in western Europe is relatively small, the number of cases of imported malaria is large enough to constitute both a public health and economic burden on the countries into which malaria is imported. The cost of treatment of malaria and the economic costs of deaths from imported malaria are considerable. Legros et al (1998) estimated that in France, the overall cost of an uncomplicated case of malaria (medical expenses and an average sick leave of two weeks) has been estimated at 6 400 Euros for inpatients and 1 400 Euros for outpatients. Thus, for the more than 8 000 cases of imported malaria in France in 2000, the total cost to the country would have between 10 to 20 million Euros. Pugliese et al (1997) reported that in 1995, 33 patients were hospitalized in Nice due to malaria. In 32 of these cases, malaria infection was due to the traveler having taken no or poor prophylactic measures. The cost of this poor prophylaxis was high in terms of human suffering and financial costs. Four patients had to be hospitalized in the intensive care unit, and one died during hospitalization. The cumulative cost for these 33 cases was evalu-

**Figure 1. Incidence of malaria imported into the United Kingdom**



ated at FF 660 000. Schlagenhauf et al (1995) observed that in Switzerland, the average cost of the treatment for a single case of malaria was SwFr. 44 000 or the equivalent of US \$32 000.

It is evident that more effort should be devoted to making travelers aware of the necessity of complying with a correct regime of chemoprophylaxis when traveling to countries where they will be exposed to malaria. In view of the growing problem of *P. falciparum* drug resistance, physicians and health clinics should have information about the most appropriate antimalarial drugs for chemoprophylaxis and treatment readily available. A large proportion of the cases of malaria introduced by travelers will be resistant to one or several of the antimalarial drugs, thus presenting a therapeutic challenge to health care professionals attempting to ensure effective treatment. Virtually every review of imported malaria in Europe emphasizes the low percentage of compliance with chemoprophylaxis among travelers to malaria-endemic countries, particularly amongst persons who have fallen ill with imported malaria on their return from travel.

Local transmission has also frequently occurred in Europe in the form of “airport malaria”. This refers to the transmission of malaria as a result of the inadvertent transport of live, malaria-infected mosquitoes aboard aircraft arriving from tropical malaria-endemic countries. Some 90 cases of airport malaria have been recorded, most of them in Europe. Most of the European cases have occurred in countries with the most frequent air transport connections with Africa, i.e. Belgium, France, Switzerland and the United Kingdom. In the Netherlands, *P. vivax* was reported in a woman who had never traveled to an endemic area, but lives near Schiphol airport in Amsterdam (Thang et al, 2002). Airport malaria poses a particular health risk as it can occur among people living near international airports who have had no travel exposure to malaria; consequently diagnosis is often delayed, which may result in prolonged illness and even death (Gratz et al, 2000). Many cases of airport malaria that occur where malaria transmission has long since been eradicated may go undiagnosed and unreported. The transport of mosquitoes and other vectors aboard aircraft has also resulted in the introduction of vector species into countries where they had not been found previously. Malaria may also be introduced as a result of mosquitoes imported most likely aboard seafaring vessels. *P. falciparum* occurred during summer 1993 in two inhabitants living close to Marseille harbour. History of blood transfusion and travel outside France were excluded, as was airport malaria. Entomological investigations confirmed the absence of *Anopheles* breeding sites in the port area. One hypothesis is a vectorial transmission following the introduction of one or several anopheles arriving on a ship from tropical Africa (Delmont et al, 1994). Indigenous malaria disappeared from Belgium in 1938, but indigenous malaria was detected in a patient living 3.5 km from the port of Ghent. An infected anopheles mosquito from a cargo load or baggage aboard an incoming vessel could have flown this distance (Peleman et al, 2000).

## SANDFLY-BORNE DISEASES – VIRUSES

The sandfly-transmitted viruses are all within the Bunyavirus group, the Phleboviruses; globally, some 45 viruses are associated with sandflies. Some Phleboviruses are transmitted by mosquitoes, e.g. Rift Valley fever, whereas others are transmitted by ticks. The sandfly-transmitted fevers identified in Europe include Arbia virus, Corfou virus, Naples virus, Radi virus, Sicilian virus and Toscana virus. Arbia virus has been isolated from sandflies in Italy and Corfou virus from *Phlebotomus major* on Corfou Island, Greece. Neither of these viruses appears to be of public health importance.

### SANDFLY FEVER

Naples and Sicilian viruses are largely responsible for the sandfly-borne diseases widely known as “pappataci fever” or sandfly fever. Both were isolated by Sabin during World War II, and are now known to be common throughout southern Europe and the Balkans, the eastern Mediterranean including Cyprus, and along the Black Sea coast and eastwards through Iraq, Iran and Pakistan into Afghanistan and India. The two infections frequently overlap. They were the cause of a very large number of illnesses among troops operating in the endemic area during both World Wars. After the Second World War and with the application of DDT residual sprays for the control of malaria vectors, Sicilian and Naples viruses virtually disappeared (Nicoletti et al, 1997). The incidence of these two viruses remains high in most of their endemic areas. In a survey conducted in the Adriatic littoral of Croatia, 23% of those examined were found positive for Naples virus (Borcic and Punda, 1987). Surveys carried out in Greece in 1981–1988 showed antibodies to Naples virus of 16.7% and to Sicilian virus of 2%. A survey in Cyprus revealed high antibodies prevalence rates of 57% and 32% to Naples and Sicilian viruses respectively, illustrating that sandfly fevers pose a significant public health problem in that country (Eitrem et al, 1991). Prevalence remains high in most other endemic countries. The importation of sandfly fevers by tourists and soldiers returning from endemic areas is a growing problem. Eitem et al (1991a, *ibid*) found that a number of Swedish tourists returning from Cyprus and Spain tested positive for antibodies; serum samples from a group of 95 tourists indicated that only 20% of the real number of sandfly fever infections had been correctly diagnosed by physicians.

Toscana virus was isolated from *Phlebotomus perniciosus* in Tuscany, Italy in 1971 (Nicoletti et al, 1996 *ibid*). It has been associated with acute neurologic disease, and clinical cases of aseptic meningitis or meningoencephalitis caused by

Toscana virus are observed annually in central Italy during the summer. Twenty percent of the antibodies collected from 479 normal people in Cyprus tested positive for Toscana virus (Eitem et al, 1991a, *ibid*). Acute meningitis is perhaps the most frequent among central nervous system infections in Tuscany, Italy. Valassina et al (2000) found that a high percentage of these cases were due to infections with Toscana virus, illustrating the public health importance of this infection. In Siena, Italy, Braitto et al (1998) reported that the virus is responsible for at least 80% of acute viral infections of CNS in children throughout the summertime. Clinical signs and symptoms range from aseptic meningitis to meningoencephalitis. Infected children had resided continuously or temporarily in rural or suburban areas of the Siena province, where ecological characteristics allow sandflies to be peridomestic in human settlements. They concluded that Toscana virus is the most common viral agent involved in acute infections of CNS in children in central Italy. Toscana virus is now known to be widely distributed in Italy, and has been reported from Portugal, Cyprus and Spain; in the latter, Mendoza-Montero et al (1998) studied 1 181 adults and 87 children from different regions of Spain and found prevalence rates of 26.2%, compared to 2.2% for Sicilian virus and 11.9% for Naples virus. The most common vector in Italy is *Phlebotomus perniciosus*.

Radi virus, a Vesiculovirus, has been isolated from *Phlebotomus perfiliewi* in Italy, but has not been associated with human disease.

In total, sandfly fevers may be the cause of hundreds of thousands of infections per year in southern Europe; only a moderate proportion of these human cases give rise to clinical illness and thus are not diagnosed or reported. It is likely that the real number of cases of this group of viruses is far higher than that reported.

## SANDFLY-BORNE DISEASES – LEISHMANIASIS

Leishmaniasis is a protozoan disease in which clinical manifestations are dependent both on the infecting species of *Leishmania* and the immune response of the host. Transmission of the disease occurs by the bite of a sandfly infected with *Leishmania* parasites. Infection may be restricted to the skin in cutaneous leishmaniasis, limited to the mucous membranes in mucosal leishmaniasis, or spread internally in visceral leishmaniasis or kala azar. Leishmaniasis is found in some 88 countries, mainly in tropical and sub-tropical areas, but, as will be seen, is also widespread in southern Europe. The overall prevalence of leishmaniasis is 12 million cases worldwide, and the annual global incidence of all clinical forms approaches 2 million new cases (World Health Organization WHO/LEISH/200.42, *Leishmania/HIV Co-Infection in Southwestern Europe 1990–98: Retrospective Analysis of 965 Cases*, 2000). In the last two decades, leishmaniasis, particularly visceral leishmaniasis, has been recognized as an opportunistic disease in the immuno-compromised, particularly in patients infected with human immunodeficiency virus (Choi and Lerner, 2001). In Mediterranean Europe, visceral leishmaniasis with splenomegaly, pallor, and fever was traditionally a childhood disease, whereas today the disease strikes immuno-compromised patients in atypical clinical expressions. In these atypical forms of visceral leishmaniasis, diagnosis and treatment are particularly difficult (Piarroux and Bardonne, 2001).

In Europe, visceral leishmaniasis (VL) is found in Albania, Bosnia, Croatia, Cyprus, France (southern regions: Nice, Marseille, Montpellier, Toulon, Avignon, Alpes-Martimes), Greece, Hungary, Macedonia, Malta, Montenegro, Portugal, Romania, Spain, Serbia and Montenegro, and Turkey. *L. (L.) donovani* and *L. (L.) infantum* are the causative organisms of visceral leishmaniasis (VL), or kala-azar, in the Old World.

Cutaneous leishmaniasis (CL) has been reported from Albania, Austria, Bosnia and Herzegovina, Bulgaria, Croatia, Cyprus, France, Greece, Italy, Malta, Monaco, Portugal (with the Azores and Madeira), Romania, Spain (including the Canary Islands), and Serbia and Montenegro. The causative organisms are *L. infantum*, *L. major* and *L. tropica*. The sandfly vectors are *P. perfiliewi* in Italy, *P. ariasi* in France and Spain, and *P. perniciosus* in France, Italy, Malta and Spain. In addition, Koehler et al (2002) reported a case of cutaneous leishmaniasis due to *L. infantum* in a horse in southern Germany. Since neither the infected horse nor its dam had ever left their rural area, autochthonous infection in Germany cannot be excluded.

Inasmuch as leishmaniasis is not a reportable disease in most countries of Europe, it is difficult to say just how many cases occur each year. Several countries, however, have reported an increasing trend in VL, CL and canine leishmaniasis. As early as 1988, Marty and LeFichoux (1988) noted that in the region of Marseille, the number of seropositive dogs had risen from 240 to 2 278 between 1976 and 1986, and between 40 and 50 cases of leishmaniasis were observed in the region every year, most of them visceral. *Leishmania*/HIV co-infection has been reported from 33 countries in the world, with most of these cases occurring in southwestern Europe. By 2001, 1 627 cases had been notified from Spain, France, Italy and Portugal (Desjeux et al, 2001, *ibid*). Catania province, Sicily, is an important focus for human visceral leishmaniasis. Current data indicate an annual average incidence of ten registered cases per year over the past three years. Of registered cases, more than 20% were among individuals who were also human immunodeficiency virus (HIV) positive (Orndorff et al, 2002). It has been estimated that 1% to 3% of AIDS patients in endemic areas suffer from visceral leishmaniasis (Nicolas et al, 1995).

In Malta, the reporting of leishmaniasis has been compulsorily notifiable since 1946; five cases of cutaneous infection were reported in 1997, and 23 cases of cutaneous and three of visceral infection were notified in the period of January–October 1998, but there may be considerable under-reporting of the disease. As dogs are the reservoirs of the infection, the incidence of canine leishmaniasis is an important indicator of the risk of leishmaniasis to the human population. In Malta, figures of between 18% and 47% have been reported for the prevalence of canine leishmaniasis. This large discrepancy between the prevalence in the dog reservoir and the number of cases in the human hosts suggests that the canine reservoir could be an increasingly serious threat. A survey for *L. donovani* by PCR showed that 62% out of a total of 60 dogs were seropositive (Headington, et al, 2002).

In the area of Athens, Greece, *L. infantum* is the causative agent of both human and canine visceral leishmaniasis (VL), and domestic dogs are the main reservoir of this parasite. Sideris et al (1999) surveyed 1 638 dogs in Athens; 366 (22.4%) had anti-*L. infantum* antibodies at a titre greater than or equal to 1/200, which is considered positive; many of the dogs were asymptomatic and constitute a serious danger for the spread of the disease. In later surveys carried out in Greece on healthy dogs using PCR as the means of detection, the percentage of positive dogs was even higher, with the prevalence and the incidence of *Leishmania* infection shown at 61.9% and 47.1%, respectively (Leontides et al, 2002). It is likely that earlier serological surveys may have underestimated the prevalence of *Leishmania* in dogs. In a 1993 survey of the greater Athens area, Chaniotis et al (1994) recorded seven species of sandflies taken in light and stick traps; there were small 'island' populations in residential districts and moderate or large populations in the quarries and corrals in the foothills of the mountains bordering the area and in the hills near the city centre. *Phlebotomus neglectus*, the putative vector of VL in

the area, was ubiquitous; it predominated in the quarries and was common in the sampled corrals and residential habitats.

In 1987, a regional reference centre for the active surveillance of VL was established in Sicily, where leishmaniasis is a notifiable disease. As it was suspected that the actual number of human cases was greater than that being reported, active surveillance of VL was established. Throughout 1995, a total of 284 cases were recorded, i.e. a mean of 31.5 cases/year and about four-fold more than had previously been reported. Of the 284 cases, 150 (53%) were found in children (< or = 14 years of age), and of the 134 adults, 39 (29%) were coinfecting with HIV (Casacio et al, 1997).

Clearly human (and canine) leishmaniasis is a serious problem in southern Europe, with infections showing a rising trend, especially cases of co-infection of HIV. Relatively neglected in the past, more attention must be given in the future to the control of the sandfly vectors; this is generally difficult, but Maroli et al (2002) demonstrated that the large-scale use of insecticide impregnated collars on dogs in the Mount Vesuvius area of the Campania region, Italy, where the vector is *Phlebotomus perniciosus*, could have an impact on the incidence of canine leishmaniasis, especially where transmission is high. Killick Kendrick et al (1997) carried out laboratory studies on the efficacy of deltamethrin-impregnated plastic collars in the south of France using *Phlebotomus perniciosus* females; for every 100 flies which fed on collarless dogs, only 4 fed on collared dogs, i.e. the collars protected dogs from 96% of the bites, and this activity was maintained for up to 34 weeks. During the same period, the percentage of recaptured female sandflies that had fed on collared dogs was 0–12%, compared to 55–95% on collarless dogs. The conclusion of the study was that, at least in the Mediterranean subregion, this insecticidal collar would protect a dog from the majority of sandfly bites and retain a killing effect for a complete sandfly season. Moreover, it seems likely that the use of collars on all dogs in a focus of *L. infantum* would reduce contact between sandfly vectors and canine reservoir hosts sufficiently to diminish the risk of infection for humans as well as dogs. Faced with the increased incidence of this serious disease, it would be prudent to encourage dog owners to make use of these cheap and effective insecticide-impregnated collars.

## CERATOPOGONIDAE – BITING MIDGE BORNE DISEASES

Members of this family of biting midges can be severe nuisances; they are also the vectors of two important animal diseases in Europe: bluetongue virus and African horse sickness. As regards human infections, there has only been a single isolation of Tahyna virus from *Culicoides* in Czechoslovakia (Halouzka et al, 1991). Therefore, the group has no apparent importance as vectors of human disease.

On the other hand, hemoglobins of the midge family Chironomidae, potent human allergens, have been identified as causative allergens in asthmatic patients. A study in Sweden (Eriksson et al, 1989) concluded that Chironomidae might be allergens of clinical importance in asthma and rhinitis, that cross-allergy exists between chironomids and shrimp, and that cross-allergy might also occur among chironomids, crustaceans and molluscs.

## FLEA-BORNE DISEASES

### PLAGUE

The best known of the human infections transmitted by fleas is plague, caused by the *Yersinia pestis* organism. The reservoirs are various species of rodents, and historically the black rat (*Rattus rattus*) was the main reservoir during the great epidemics that ravished Europe from the sixth century up until 1720, when the last major outbreak to occur in Europe took place in Marseille. The pandemics of plague from the thirteenth century onwards resulted in the deaths of tens of millions of people in Europe. Though plague remains endemic in many foci in Africa, Asia and the Americas, there are now no foci in Europe. There are, however, a number of other flea-borne human diseases endemic in Europe, some of which are emerging diseases little known to the public and even the medical profession, while others such as murine or endemic typhus are well known.

### FLEA-BORNE RICKETTSIAL DISEASES

#### Murine typhus

Murine typhus, whose causative agent is *Rickettsia typhi*, has a worldwide distribution. In Europe, the main reservoir is the rat *Rattus norvegicus* and the most common flea vector is the Oriental rat flea, *Xenopsylla cheopis*, and, less frequently, the cat flea *Ctenocephalides felis*. Transmission occurs by contamination with rickettsia-containing flea feces or tissue during or after blood feeding by the flea. Murine typhus is usually a benign, acute, febrile disease characterized by headache, rash and fever which persists for about 12 days. Mortality is low and more common in elderly patients. Misdiagnosis is frequent and the infection is probably much more common than reported (Azad et al, 1997). In Europe, murine typhus has been reported from Bosnia and Herzegovina, Croatia, the Czech Republic, France, Greece, Italy, Portugal, the Russian Federation, Serbia and Montenegro, Slovakia, Slovenia and Spain, and is likely to be present in most other countries as well. Surveys conducted in the northwestern part of Bosnia and Herzegovina in the early 1990s found that among the 231 sera tested, the rate for *R. typhi* was 61.5% (Punda Polic et al, 1995). In Evia Prefecture, Greece, 92% of the 53 rat sera tested by IFA were positive for anti-*R. typhi* antibodies (Tselentis et al, 1996), and human cases were common in the island's hospital. Daniel et al (2002 *ibid*) found that the prevalence of antibodies to *R. typhi* was 2% of 1,584 human sera in northern Greece, an area which had never before been surveyed for this infection. High antibody prevalence has also been found among rat populations in Spain and Portugal, and the death of an English tourist from murine

typhus was reported upon her return to the United Kingdom from the Costa del Sol in Spain (Pether et al, 1994). It appears that murine typhus is re-emerging in Portugal; the disease was fairly common there until the 1940s, when several cases were diagnosed in the Lisbon area. In 1993, antibodies against *R. typhi* were detected for the first time in serum from a patient in the Madeira Autonomous Region, an archipelago with two major islands: Madeira and Porto Santo. The patient was an HIV-positive woman with no clinical features of murine typhus. In November and December 1996, antibody titres against *R. typhi* exceeding 1:128 were detected in serum from several patients at Madeira Central Hospital; analysis showed the presence of antibodies to *R. typhi* in both humans and rats. The outbreak of 1996 was probably facilitated by ecological conditions extremely favorable to an increase of the rat population on the island during that year. A high level of rainfall allowed for the increase of vegetation, food and shelter, and hence, the rat population (Bacellar et al, 1998).

From 1975 to 1995, a long-term study was carried out in the south of Spain on 104 cases of patients with long lasting fevers. Murine typhus was the cause in 6.7% of 926 cases of fevers of intermediate duration (FID), characterized by a febrile syndrome lasting from seven to 28 days (Bernabeu Wittel et al, 1999). While most patients have a benign course of the disease, some may develop severe complications.

Northern Europe is largely free of murine typhus; Dirckx (1980), however, thought that there was historical basis to the 13th-century legend of the Pied Piper, who led away the rats from the town of Hamelin, Germany, and when refused payment for his services, led away 130 children and disappeared with them into the mountains. It is suggested that the children actually died in an outbreak of the disease and were buried in a common grave at the site of the legendary disappearance. The pied (mottled) coat of the piper suggests that the disease was murine typhus.

### **The ELB agent**

Although murine typhus has never been identified in Germany, another flea-borne disease, the “ELB agent” caused by *Rickettsia felis*, was reported in 2000. A couple in Düsseldorf showed symptoms of high fever and rash; PCR testing confirmed the presence of the ELB agent. This was the first report of this agent in Europe. This infection, first identified in the USA in 1990, is transmitted by the cat flea, *C. felis*. Studies have shown that cat fleas can maintain the infection for up to 12 generations by vertical transmission (Wedincamp and Foil, 1992). As regards the cases in Germany, the agent was probably contracted from fleas on the couple’s dog (Richter et al, 2002). The same infection has also been identified in a cat flea in southwestern Spain (Marquez et al, 2002). ELB agent was also identified in two patients with fever and rash in France (Raoult et al, 2001), and has also been isolated from the cat flea in that country (Rolain et al, 2003). In view of

the wide distribution of the cat flea throughout Europe, the infection will almost certainly be found in many more countries, and its diagnosis should be taken into account in patients showing a murine typhus-like disease with rash and fever following the bite of a flea.

### Cat scratch disease

The causative agent of cat scratch disease is *Bartonella henselae*. While the disease itself was first described in France in 1950, it was only in 1992 that the bacterial agent was described. Infection with this agent can give rise to bacillary angiomatosis in humans. Bacillary angiomatosis is a vascular proliferative disease most commonly associated with long-standing HIV infection or other significant immunosuppression. *B. henselae* has also been associated with bacillary peliosis, relapsing bacteraemia and endocarditis in humans. Cats are healthy carriers of *B. henselae*, and can be bacteraemic for months or years. Cat-to-cat transmission of the organism by the cat flea, with no direct contact transmission, has been demonstrated (Chomel, 2000).

*B. henselae* is now known to be widespread in Europe. About 10% of pet cats and 33% of stray cats harbour the bacterium in their blood. In immunocompetent patients, *B. henselae* is responsible for human cat scratch disease, characterized essentially by localized lymph node enlargement in the vicinity of the entry site of the bacteria (Piemont and Heller, 1998). Further studies have shown that cats may harbour three different *Bartonella* species, *B. henselae*, *B. clarridgeiae*, and *B. henselae* genotype/serotype Marseille (type II) which have been isolated from cats and cat fleas in France (La Scola et al, 2002). Despite the serious infections at times seen in infected patients, both *B. henselae* and *B. quintana* have been found in many otherwise healthy patients in an urban area of Greece; of 500 individuals in a healthy population, 99 (19.8%) and 75 (15%) were IgG seropositive to *B. henselae* and *B. quintana* respectively. A high percentage (12.4%) of cross-positivity between the two species was seen. The data show that the prevalence of both *Bartonella* species is high. Cat owners had significantly higher antibody titres only to *B. henselae* and not to *B. quintana* (Tea et al, 2003). In Europe, *B. henselae* and clinical cat scratch disease have now been reported from Croatia, Denmark, France, Germany, Greece, Italy, the Netherlands, Poland, Spain, Sweden, Switzerland and the United Kingdom, and it will no doubt be found in most other countries as well.

In Italy, *Bartonella* DNA was amplified and sequenced from four *Ixodes ricinus* ticks (1.48%) removed from humans in Belluno Province. This recent report (Sanogo et al, 2003) shows that the role of ticks in the transmission of *Bartonella* species should be further investigated.

## LOUSE-BORNE DISEASES

### LOUSE-BORNE RICKETTSIAL DISEASES

#### Epidemic or louse-borne typhus

Epidemic typhus or louse-borne typhus due to *Rickettsia prowazekii* is transmitted by the human body louse, *Pediculus humanus*. Until World War II, the disease was responsible for an enormous number of cases and a great many deaths, especially among armies, refugees and inmates of camps of all types. The Russian Federation suffered heavily from epidemic typhus during the Second World War, with as many as 20 million cases (Rydkina et al, 1999). In 1943 an outbreak of typhus in Naples, Italy, was controlled by mass dusting with DDT powder. There were outbreaks of louse-borne typhus in Bosnia and Herzegovina between 1946 and 1949, but these were also successfully controlled by DDT. Although scattered cases occurred up until the 1960s, no important outbreak was registered in Europe until 1997, when an outbreak occurred in a hospital in Lipetsk, Russian Federation. A total of 23 patients and 6 members of the staff suffered symptoms of typhus, with 22 shown to be seropositive for *R. prowazekii*. The clothes of the patients were infested with body lice, and these tested positive for typhus. It is thought that poor public health practices following a breakdown in a heating system led to body louse infestations (Tarasevich et al, 1998). This outbreak demonstrates that epidemic typhus has the potential for recrudescence even in areas where it has been absent for a number of years. In view of the recrudescence of body louse populations in several countries of Europe, (Gratz, 1997, Rydkina, *ibid*, 1999) the risk of the recrudescence of louse-borne infections such as louse-borne typhus and trench fever is increasing.

In areas where louse-borne typhus was once epidemic, Brill-Zinsser's disease may occur; this disease is a recrudescence of an earlier infection with epidemic typhus, and it may occur many years after the initial illness. It affects people years after they have completely recovered from epidemic typhus. It may be due to a weakening of their immune system through aging, surgery, illness, or other factors. The illness tends to be extremely mild, and there is no mortality from it. However, as the disease arises from *Rickettsia* retained in the body, lice that feed on patients may acquire the infection and transmit the agent. *R. prowazekii* may be isolated from the blood by animal inoculation. The disease is sporadic, occurring at any season and in the absence of infected lice. There have been recent reports of the disease in France (Stein et al, 1999) in three patients, all of whom had a history of body louse infestations at one time. Cases are also reported in eastern Europe, generally among older persons with a history of louse-borne typhus. In

populations infested with body lice, a person falling ill with this disease may thus initiate a recrudescence of epidemic or louse-borne typhus. This possibility is another reason why the control of body-lice infestations is important.

### **Trench fever**

Trench fever, whose causative organism is *Bartonella quintana*, (previously *Rochalimaea Quintana*) affected perhaps a million soldiers during World War I, then disappeared in 1918 when the war ended; it reappeared to infect smaller yet substantial numbers of soldiers and camp inmates during World War II. Like epidemic typhus, it is transmitted to persons through the contaminated feces of the human body louse. Infection gives rise to fever, cutaneous bacillary angiomatosis, and endocarditis. Mortality is rare, but the disease may be the cause of prolonged disability. As was the case following the First World War, the disease seemed to disappear after the Second World War; however, in the early 1980s, trench fever reappeared, generally among homeless, often HIV-infected men, in Europe and North America (Foucault, et al, 2002). The disease has since been reported in Australia, Burundi, France, Germany, Mexico, Peru, Portugal, the Russian Federation, and the United Kingdom, as well as in the United States. Infections with this agent are associated with poor personal sanitation and the presence of lice, and *B. quintana* has been isolated from lice on some of the patients (Roux and Raoult, 1999, La Scola et al, 2001). The current epidemiology of this infection is not well understood, other than that the disease appears to mainly affect the homeless. Drancourt et al (1995) searched for this organism in three alcoholic homeless men with endocarditis in France. *B. quintana* was isolated from one patient in the blood-agar culture and from the other two patients in the endothelial-cell culture. In Seattle, 20% of the patients in a downtown clinic serving an indigent and homeless population had a greater than 1:64 microimmunofluorescence titre to *B. quintana*, although most of these patients did not have symptoms of *B. quintana* infection (Jackson et al, 1996).

### **Louse-borne relapsing fever**

The aetiological agent of louse-borne relapsing fever, otherwise known as epidemic relapsing fever, is *Borrelia recurrentis*. The vector is the human body louse, *P. humanus*. At one time the infection was widespread in Europe, but following the outbreaks during and immediately after the Second World War, the disease has disappeared from Europe, although it remains common in Africa and has recently caused epidemics in Burundi and Ethiopia.

### **Head lice**

Head lice, *Pediculus capitis*, are not vectors of any disease. Infestations with this species are extremely common, especially among school children, amongst which lice are rapidly passed from one child to another. Infestation rates of 10% to

20% or even higher are frequently seen, particularly of children within the same class in school. Large sums of money are expended for the control of this ubiquitous pest, and in most countries of Europe, hundreds of thousands of insecticide preparations are purchased annually for head lice control (Gratz, 1997, *ibid*). The widespread occurrence of insecticide resistance to malathion, carbaryl and the pyrethroids impedes control.

### **Body lice**

The body louse, *P. humanus*, is, as noted above, the vector of epidemic typhus, epidemic relapsing fever and trench fever. Until shortly after the Second World War, body lice infestations were very common in Europe. With the advent of DDT and other modern insecticides, body louse infestations and diseases associated with the species virtually disappeared. The presence of homeless persons with meager levels of personal sanitation in many large cities has resulted in a certain degree of recrudescence of body lice infestations, as seen in France, the Netherlands, and the Russian Federation, and this is associated with the reappearance of trench fever.

### **Pubic lice**

As is the case with head lice, pubic lice or “crab lice”, *Pthirus pubis*, are not vectors of disease. Accurate information on the prevalence of this species of human louse is, understandably, difficult to obtain, but infestations are quite common. Pubic lice are usually found on the hairs of the pubic region and transmission takes place, for the most part, through sexual contact. Infestations may cause irritation. Physicians finding pubic lice should consider the possible presence of other STDs, as there is a high degree of correlation between the presence of *P. pubis* and other venereal infections. Opaneye et al (1993) found that 37% of the patients at a clinic in Coventry, England testing positive for *P. pubis* had another STD as well.

## TICK-BORNE DISEASES – VIRUSES

### TICK-BORNE VIRUSES

By 1972, some 68 different viruses had been recorded from more than 80 tick species, some 20 of which were believed to cause disease in man or domestic animals (Hoogstraal, 1973). Since the publication of Hoogstraal's review, many other viruses have been isolated from ticks, although their role as causative agents of human or animal disease is often unknown or uncertain. Many areas of Europe remain poorly surveyed, and more viruses will certainly be found in further studies.

### TICK-BORNE ENCEPHALITIS

Tick-borne encephalitis (TBE) is the most important and widespread of the arboviruses transmitted by ticks in Europe. It is a member of the family Flaviviridae. Tick-borne encephalitis should be considered a general term encompassing at least three diseases caused by similar flaviviruses, whose range spans an area from the British Isles (Louping ill), across Europe (central European tick-borne encephalitis), and to the Far East of Russia (Russian spring-summer encephalitis). These three diseases differ in degree, with Louping ill the mildest and Russian spring-summer encephalitis the most severe. Man is infected by the bite of infected ticks and, much more rarely, by the ingestion of new milk from infected domestic animals (Dumpis et al, 1999). TBE is often the cause of a serious acute central nervous system (CNS) disease which may result in death or long-term neurological sequelae for a considerable period after recovery from the initial infection. The disease may take the forms of meningitis, meningoencephalitis, meningoencephalomyelitis, or meningoencephalomyelitis. About 40% of infected patients are left with a residual post-encephalitic syndrome. The course of the disease is more severe in the elderly than in young people. The mortality of the central European form of TBE is 0.7–2% (Ozdemir et al, 1999); this may be even higher in severe cases of infections. In regards to the Far Eastern form of the disease, the mortality rate may be as high as 25% to 30%. No specific treatment is available. An effective vaccine is available for prevention of infection, and its use is recommended for persons that are at particular risk, such as foresters. Until the early 1980s, TBE was a frequent cause of central nervous system infectious disease in Austria. From 1981, vaccination was encouraged by intensive media campaigns, but it was voluntary rather than compulsory. As a result, the number of hospitalized cases due to TBE declined significantly from 1981 to 1990, with important savings in health care costs (Schwarz, 1993). A study of the rate of vaccination among school children in Austria revealed that the prevalence of at least

one TBE vaccination was 91.4% for 7-year-olds, 97.3% for 10-year-olds, and 97.1% for 13-year-olds. The prevalence of basic TBE immunization was 84.0%, 91.7% and 92.3% respectively. The lowest vaccination rates were found in families with four or more children and in children with mothers of the lowest educational level (Stronegger et al, 1998).

The virus is endemic in most of western Europe, with foci in Alsace, France, Scandinavia, and across the Russian Federation to the Pacific. The Far-Eastern form appears to be genetically distinct from that of western Europe. The eastern strain is more virulent than that of western Europe. The tick is both a vector and reservoir of the virus; it remains infected all through its life and through its metamorphoses, and it transmits the virus to its progeny. Small rodents (field-mice, voles) are the prime vertebrate hosts. There are indications of an increasing trend in the incidence of the disease, and it appears to be spreading to geographical areas in which it has not been found previously. TBE infection has been known to occur in dogs for nearly 30 years, and the number of canine TBE cases is increasing. In addition to fever, cerebrocortical, thalamic, and brainstem symptoms occur simultaneously. Not all TBE infections in dogs lead to clinical signs, but peracute/lethal as well as subacute and chronic courses have been reported. TBE is a seasonal disease dependent on climate-related tick activity. Infected ticks are spreading the virus over central Europe with a tendency to expand to new endemic areas in western Europe (Leschnik et al, 2002). Infection rates in ticks can be very high in TBE-endemic high-risk areas; Danielova et al (2002), examined the Rate of TBE infections in ticks in two districts of the South-Bohemian region of the Czech Republic. TBE virus was found in 17 of 187 pooled samples, consisting of a total of 2 968 *I. ricinus* ticks. The mean minimum infection rate was 0.6% for all tick stages combined. Infection rates in nymphs collected in different locations varied between 0.2 and 1.3% and between 5.9 and 11.1% in adult ticks.

The distribution of TBE in Switzerland was determined by a study carried out on the sera of foresters, who are particularly exposed to TBE, restricting serum collection to the plateau between the Lake of Constance and the Lake of Geneva. Virus isolations were performed on 8 600 ticks (*I. ricinus*) collected all over the country. In four regions, natural foci of varying size were detected: (1) in the northern parts of the Canton of Zurich, in conjunction with the southern parts of the Canton of Schaffhausen, (2) in the region of Horgen on the Lake of Zurich, (3) in the region of Thoune, and (4) in the marshy region situated between the Lakes of Neuchatel, Bienne and Morat. The morbidity rate in foresters varied from 0–5%, and rose to 12–16% in regions with a known concentration of natural foci. The infection rates in ticks average 0.1%, but, depending on the regions in which ticks were collected, maximum rates of 1% were attained (Matile et al, 1981). All in all, 271 cases of TBE were reported to the government of Switzerland between 1984 and 1992; a survey of 1 700 human sera and 6 539 ticks captured in 13 zones of probable endemicity in nature revealed only 9 (0.1%) ticks as

positive. On the basis of these studies, the author determined that there are 16 foci of TBE in Switzerland, with another possible focus near Lugano, and recommended vaccinating only those prone to exposure (Marvazi F de, 1995). Shortly thereafter, a review was made of TBE in Switzerland (Baumberger et al, 1996). Between 26 and 97 cases of TBE have occurred in Switzerland in recent years. The largest endemic areas were reported in Canton of Schaffhausen, the northern part of the Canton of Zurich, and the northwest of Canton of Thurgau. Another endemic area is known in the region of Thun in Canton of Berne, while a possible endemic area is known in the Zurich Oberland around Elgg, 7 km from Aadorf in Thurgau. Diessenhofen in the northwest of Thurgau was the only known possible endemic area. In 1994 and 1995, the authors of the review observed an accumulation of TBE infections in western Thurgau, and therefore studied the TBE cases to be registered there between 1990 and 1995 from data derived from the reports of cantonal health authorities. Clinical data were taken from the case histories of the two cantonal hospitals along with data from family doctors and patients. Between 1990 and 1995, 30 TBE infections (1990: 1, 1991: 4, 1992: 3, 1993: 1, 1994: 4 certain, 3 uncertain, 1995: 14) were observed. TBE infections appeared between May and October (mostly in May). Fourteen patients remembered a bite by a tick several weeks before onset of the illness. Seven bites occurred in the area of Frauenfeld/Aadorf. Only one bite occurred in Diessenhofen. Two patients were infected in well-known endemic areas in the Canton of Zurich, a region in the west of Thurgau. In 1995, the incidence of TBE in Thurgau was 5.4/100 000 population. In nine of the 14 patients recalling a bite by a tick (64.4%), the bites occurred near their domiciles. No bites were seen east of a line between Steckborn and Weinfeld. The incidence of TBE in Thurgau in 1995 was clearly higher than the average in Switzerland in recent years (0.46/100 000), and higher than in the well-known endemic areas in the vicinity (Schaffhausen 3.95, Zurich 1.31). Based on this data, the region Frauenfeld/Aadorf is considered a new endemic area for TBE. It is likely that the well-known endemic area in the Zurich Oberland in the vicinity of Elgg has spread eastward. Persons who are often in the forests of this region should be advised to be vaccinated.

In neighboring Liechtenstein, only been a few cases of TBE have been observed in the last 20 years. A survey was carried out to determine whether a vaccination campaign was warranted in the country. The mean seroprevalence found was 3.6%, and this percentage was not higher even in persons who were active in professional forestry. The antibodies measured in all groups derived mainly from previous vaccination and in only 2 cases (0.6%) from natural infection. It is concluded that the risk of TBE infection in Liechtenstein is very low. Therefore, a reduction in cases would probably be achieved only by mass vaccination (Krech, 1992).

The recent increases in TBE cases in central Europe and the Baltic States may have arisen largely from changes in human behaviour that have brought more

people into contact with infected ticks (Randolph, 2001). Randolph (2000) believes that global warming will drive TBE into the higher-latitude and higher-altitude regions of Scandinavia and possibly decrease its incidence in southern regions as tick seasonal dynamics are disrupted by climate change. This has to some extent been confirmed by findings in the Czech Republic, where the tick vector *I. ricinus* is now found at higher altitudes than before. The incidence of the infection is increasing in the country, with cases having been contracted at heights of 900m (Daniel et al, 2003). As will be discussed below, the incidence of tick-borne encephalitis (TBE) in Sweden has substantially increased since the mid-1980s, and the distribution and abundance of *I. ricinus* has also increased. While this may be due to climatic changes, other factors that may have influenced TBE incidence include a greater number of people in endemic locations as well as increases in host animal populations, factors that are partly climate related. Access to TBE vaccination in Sweden since 1986 and increased awareness of ticks might have caused an underestimation of the links found. The findings by Lindgren and Gustafson (2001) also suggest that the incidence of other tick-borne zoonoses might have been affected by the milder climate. The marked increase in the incidence of tick-borne encephalitis in most parts of Europe since 1993 may be also be due to non-biological causes such as political and sociological changes.

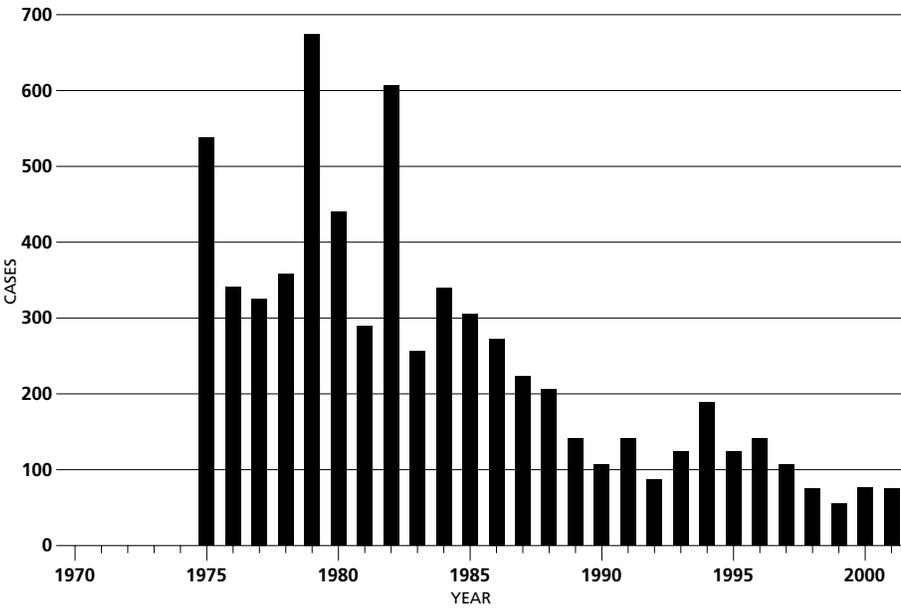
The vector in western Europe is the tick *I. ricinus*, while in eastern Europe the principal vector is *I. persulcatus*. The distribution of the latter species extends from the Baltic to the Far East.

Overall, 3 000–4 000 TBE cases are reported annually from the European countries including the Baltic States. An additional 6 000–8 000 cases are reported each year from the Russian Federation. The quality of reporting varies from country to country, depending on the availability of laboratory diagnostic facilities and the surveillance system in place. Nevertheless, there is an increasing trend of TBE cases in Europe, and this can be seen graphically in Figure 2 and by the list in Table 8.

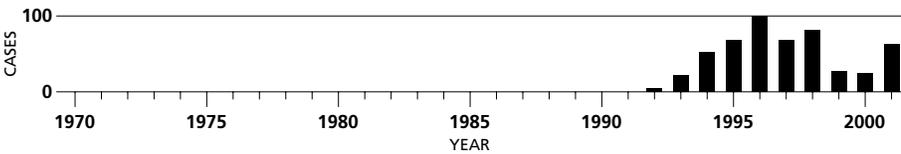
As can be seen from Table 8, there is an overall trend of increase in the incidence of TBE as well as an increase in its geographical distribution. This may be due in part to improved diagnosis or, more likely, to ecological changes that have led to increases in vector tick populations. There also appears to be an urbanization of both vector species of TBE; tick populations may be established and persist both in peripheral park-forests and within suitable ecological areas such as parks within cities (Korenberg et al, 1984). The decline in incidence in Austria is marked and is certainly due to the active vaccination programme in that country; since the introduction of the mass vaccination programme, an estimated 18 million TBE vaccinations have been given in the country, with some persons having received up to 8 vaccinations (Hofmann, 1995), and an active educational programme encourages vaccination in young people (Stronegger et al, 1998, *ibid*). While a decline may be noted in Hungary, few diagnostic tests are

**Figure 2. Annual case numbers of Tick-Borne Encephalitis in European Countries, 1970–2001. NB – the data for Russia are expressed as incidence / 1000 population.**

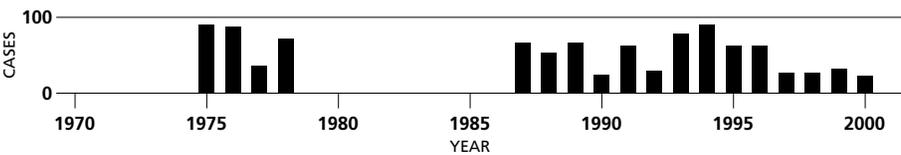
**Austria**



**Belarus**

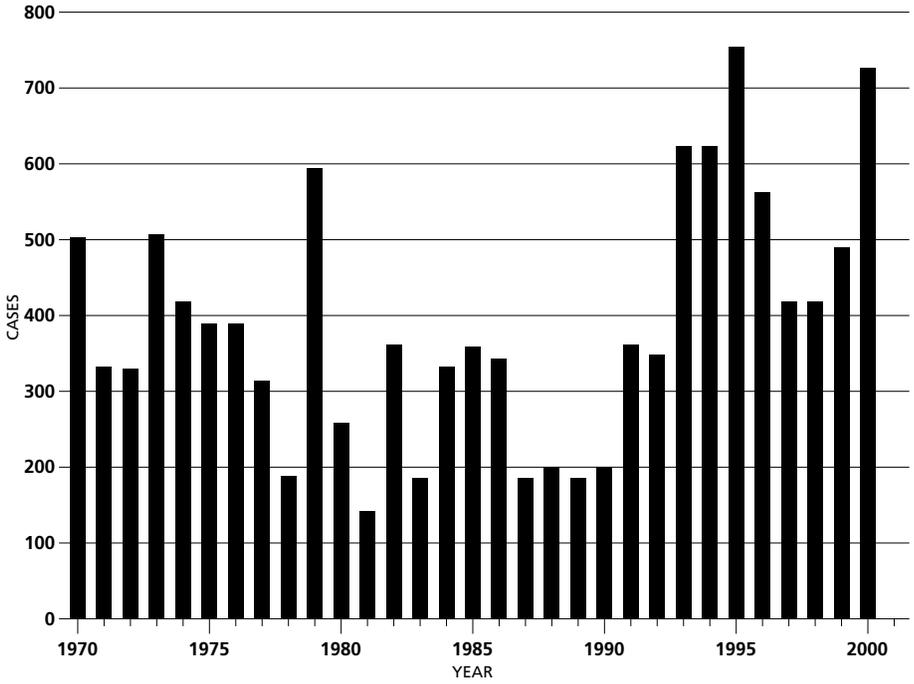


**Croatia**

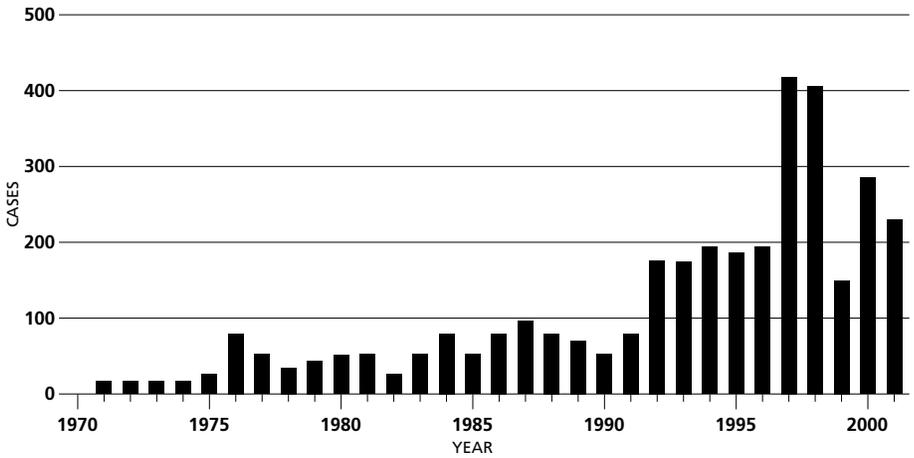


From Randolph, S. (2002) The changing incidence of tick borne encephalitis in Europe. *Eurosurveillance Weekly*: 6 June 2002. Volume 6, Issue 23

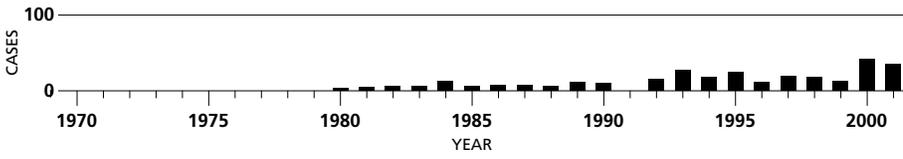
**Czech Republic**



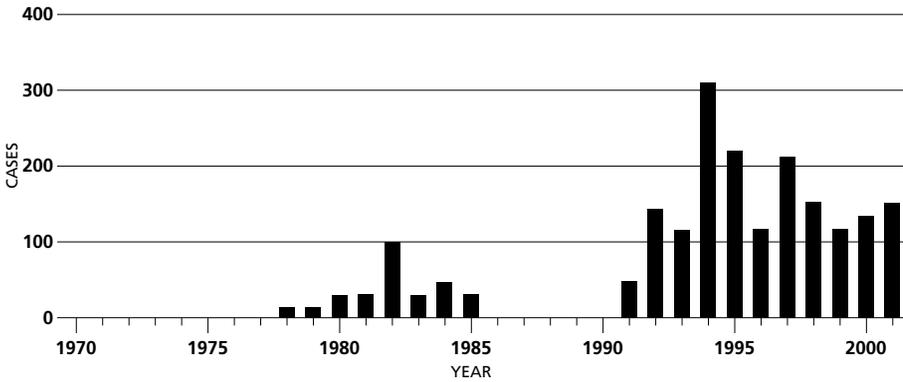
**Estonia**



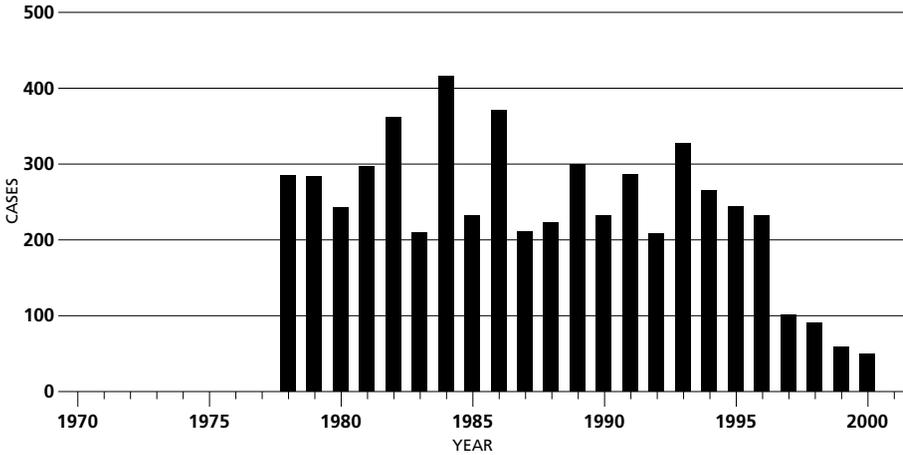
**Finland**



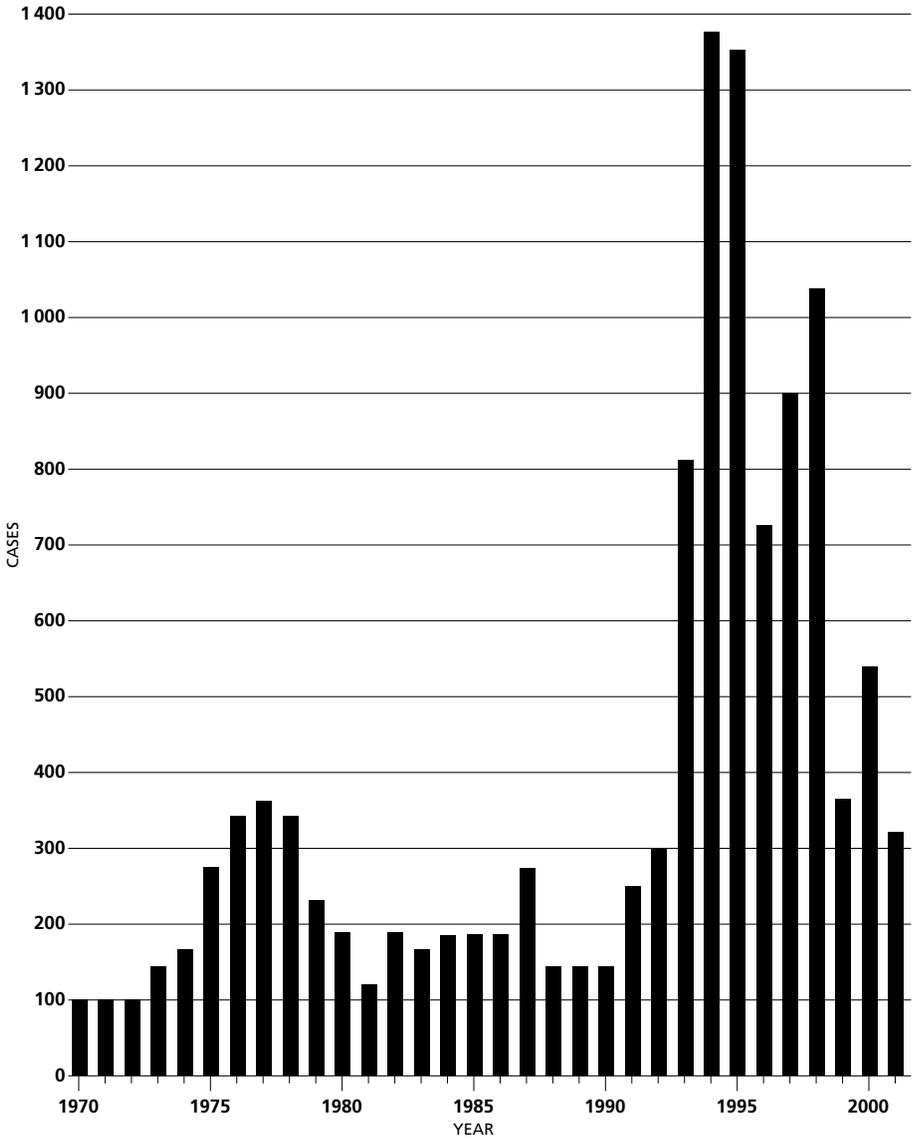
**Germany**



**Hungary**

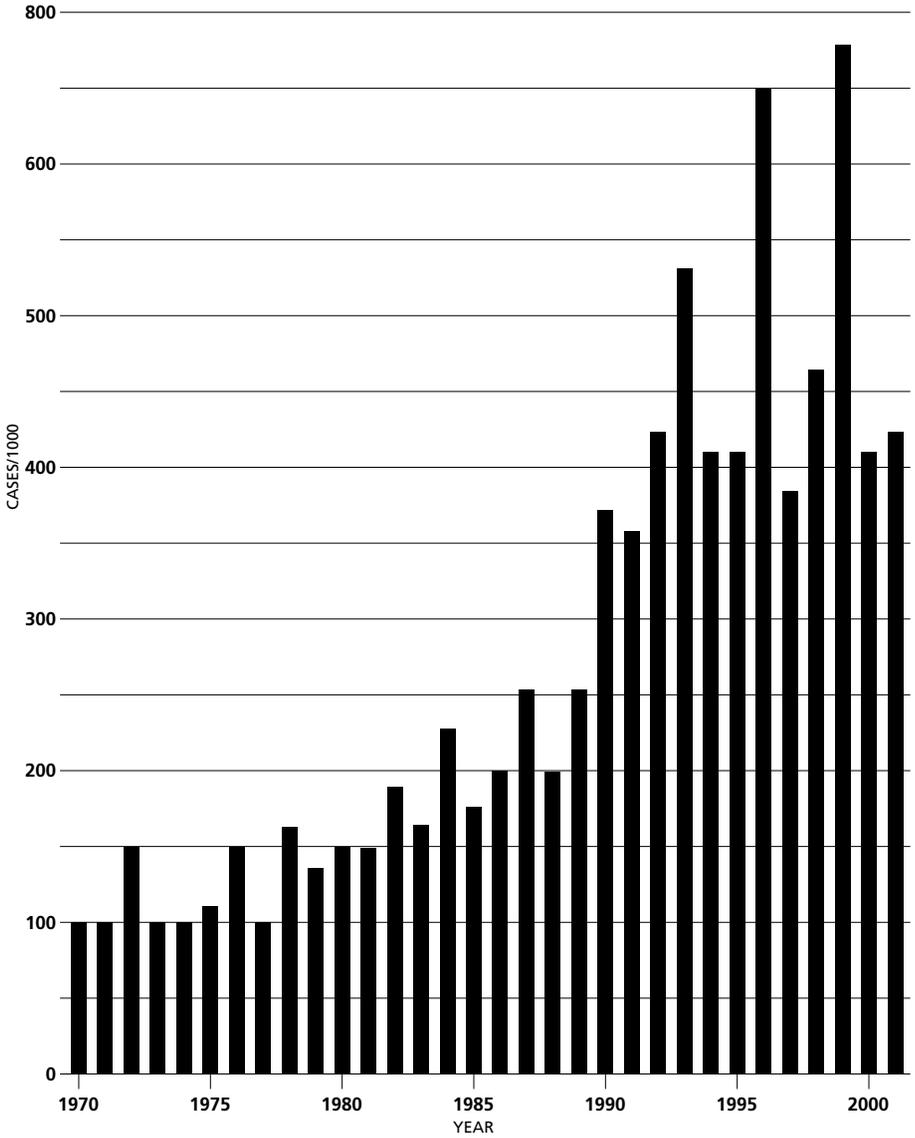


Latvia

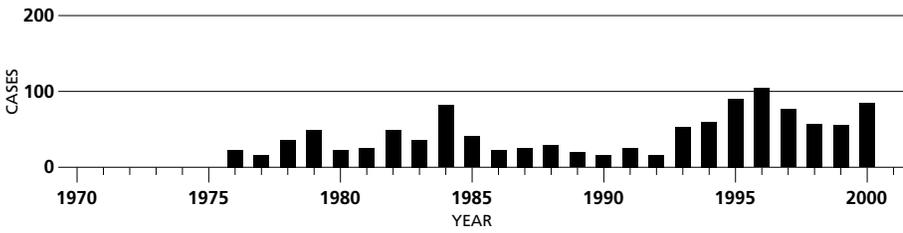




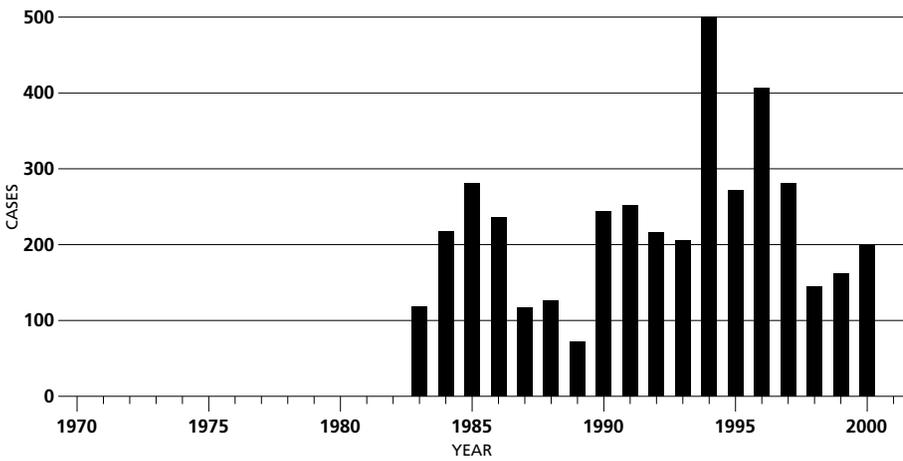
Russian Federation (incidence per 1000)



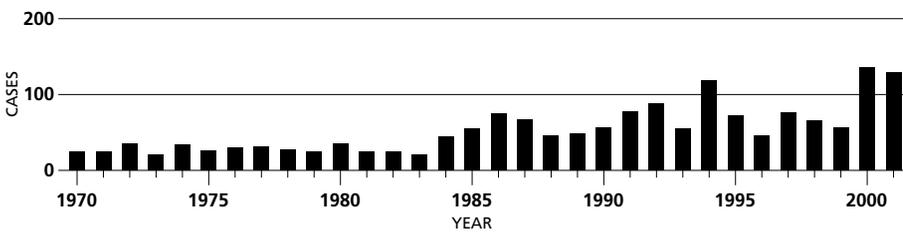
**Slovakia**



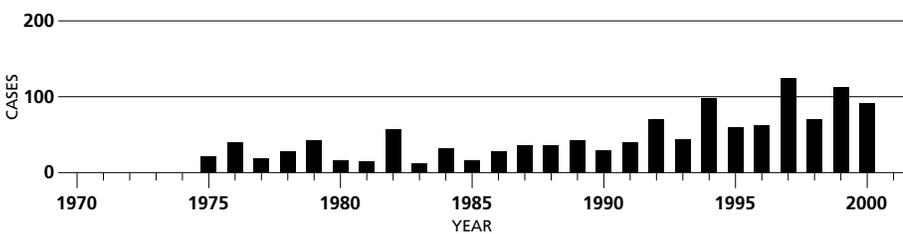
**Slovenia**



**Sweden**



**Switzerland**



**Table 8. Number of TBE cases reported in various European countries (data on file)**

Country	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986
Albania								10	7	3	9
Austria	346	318	351	677	438	294	612	242	336	300	258
Croatia	84	34	69								
Czech Republic	374	309	175	598	246	139	348	172	320	350	333
Denmark											
Estonia	64	40	26	35	47	43	16	47	69	37	65
Finland					2	3	4	4	11	5	5
France										1	1
Germany			8	11	32	30	97	29	50	26	
Hungary			287	281	245	295	351	207	406	226	372
Italy				1	1		3	1			1
Latvia	322	347	318	220	184	103	166	133	179	152	184
Lithuania	65	70	30	41	32	13	16	18	21	10	12
Poland	40	54	36	35	25	17	9	20	25	14	10
Russian Federation							1365	2912			
Slovak Republic	22	15	34	49	20	25	48	34	78	36	21
Slovenia								111	209	274	226
Sweden	27	29	25	23	30	22	22	17	41	52	70
Switzerland	39	20	31	41	13	15	57	10	32	15	27

From the International Scientific Working Group on Tick-Borne Encephalitis. TBE cases, 2000

carried out in some endemic areas of the country, and therefore a large number of patients remain undetected. Only 3–5% of the Hungarian population has been vaccinated (Lakos et al, 1996). While Randolph (2001 *ibid*) believes that there will be an eventual decline in the distribution and incidence of TBE due to global climatic changes, for the time being, both geographical distribution and incidence of the infection are increasing, and there is a continuing need for vaccination programmes in many endemic areas, as well as greater attention to the prevention of tick bites. Uspensky (1996) observed that tick control measures were the leading strategies for TBE prevention in the Russian Federation from about 1950 to the end of the 1970s, but concern about environmental safety makes the large-scale application of insecticides for tick control impossible. Newer, more biodegradable compounds, selectively applied, may effectively and safely reduce tick populations, especially in peri-urban areas (Schulze et al, 2001). Control of vector tick populations is relatively feasible in areas around homes, but difficult and probably in sylvatic areas.

### **Crimean Congo Haemorrhagic Fever**

Crimean Congo Haemorrhagic Fever (CCHF) is caused by a Nairovirus, a group of related viruses forming one of the five genera in the Bunyaviridae family of

1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000*
12	8	25	8										
215	201	131	89	128	84	102	178	109	128	99	62	41	60
63	49	62	23	60	27	76	87	59	57	25	24	26	
178	191	166	193	356	338	629	613	744	571	415	422	490	719
											1	4	3
91	68		37	68	163	166	177	175	177	404	387	185	272
6	7	10	9		14	25	16	23	10	19	17	12	41
	2	3	2	1	2	5	4	6	1	1	2	5	
				44	142	118	306	226	114	211	148	115	133
208	218	295	222	288	206	329	258	234	224	99	84	51	45
1						3	2	5	3	6	6	10	10
246	119	117	122	227	287	791	1366	1341	716	874	1029	350	544
9	17	8	9	14	17	198	284	426	309	645	548	171	419
24	15	6	8	4	8	249	181	267	257	201	209	101	142
			5486	5225	6301	7893	5593	5982	9548	6539	6987	9427	
24	29	18	14	24	16	51	60	89	101	76	54	57	79
107	114	65	235	245	210	194	492	260	406	274	136	150	190
65	43	38	54	75	83	51	116	68	44	76	64	53	133
34	34	43	26	37	66	44	97	60	62	122	71	108	90

\*partly preliminary data

viruses. All of the 32 members of the Nairovirus genus are transmitted by argasid or ixodid ticks, but only three have been implicated as causes of human disease: the Dugbe and Nairobi sheep viruses, and CCHF, which is the most important human pathogen amongst them. Crimean Congo Haemorrhagic Fever was first observed in 1944 and 1945 in the Crimea by Russian scientists. At that time it was established by studies in human volunteers that the aetiological agent was filtrable and that the disease in man was associated with the bite of the tick *Hyalomma marginatum*. The agent was detected in the larvae and in adult ticks, as well as in the blood of patients during the fever. This agent, presumably a virus, was not maintained in the laboratory and was lost. Congo virus was first isolated in Africa from the blood of a febrile patient in Zaire in 1956 and later shown to be identical to the infection detected in the Crimea.

In Europe, CCHF has been reported in Albania, Bulgaria, Greece, Hungary, Kosovo, The former Yugoslav Republic of Macedonia, Portugal, the Russian Federation, Turkey and Ukraine, either by the occurrence of human cases, by isolations from ticks, or by serological surveys. The most recent outbreaks in Europe concerned eight cases in a family cluster in Albania in 2002 (Papa et al, 2002), and in Kosovo in 2001, from where the World Health Organization reported 69 suspected cases, with six patient deaths (WHO, 2001). From 8 May to 28 July

2002, 12 confirmed cases of CCHF were registered in Kosovo, of which three cases ended fatally (WHO, 2002b). On 26 July, 1999, the Ministry of Health of the Russian Federation reported that Crimean Congo Haemorrhagic Fever in the Stavropol Region, an area between the Black and Caspian Seas, had been confirmed by laboratory tests. A total of 65 cases were reported, with six deaths to follow, three of them among children. The outbreak appeared to be tick-transmitted.

The CCHF virus may infect a wide range of domestic and wild animals. Many birds are resistant to infection, but ostriches are susceptible and may show a high prevalence of infection in endemic areas. Animals become infected with CCHF from the bite of infected ticks. A number of tick genera are capable of becoming infected with CCHF virus, but the most efficient and common vectors for CCHF appear to be members of the *Hyalomma* genus. Transovarial and venereal transmission have been demonstrated amongst some vector species, indicating one mechanism which may contribute to maintaining the circulation of the virus in nature. However, the most important source of acquisition of the virus by ticks is believed to be infected small vertebrates upon which immature *Hyalomma* ticks feed. Once infected, the tick remains infected throughout its developmental stages, and the mature tick may transmit the infection to large vertebrates such as livestock. Domestic ruminant animals such as cattle, sheep and goats are viraemic (virus circulating in the bloodstream) for about one week after becoming infected. Humans who become infected with CCHF acquire the virus from direct contact with blood or other infected tissues of livestock during this time, or they may become infected from a tick bite. The majority of cases have occurred in those connected with the livestock industry, such as agricultural workers, slaughterhouse workers and veterinarians (WHO, 1998).

CCHF is a severe disease in humans, with a mortality of approximately 30% or more. There is no specific treatment and general supportive therapy is the mainstay of patient management of the disease. When patients with CCHF are admitted to the hospital, there is a serious risk of the nosocomial spread of infection, and a number of outbreaks have occurred in this way; it is thus imperative that adequate infection control measures be observed to prevent this disastrous outcome. Patients with suspected or confirmed CCHF should be isolated and cared for using barrier nursing techniques.

Where outbreaks have been caused by transmission by ticks, the most common vectors are *Hyalomma* species. In western Europe and the Middle East, the most frequent vector is *H. marginatum*. In the Republic of Moldova, CCHF has been isolated from *I. ricinus*, *Dermacentor marginatus* and *Haemaphysalis punctata* (Chumakov et al, 1974, *ibid*), but their importance as vectors is uncertain. CCHF has been isolated from *Rhipicephalus bursa* in Greece (Papadopoulos and Koptopoulos, 1978).

### **Bhanja virus**

A Bunyavirus and member of the Bhanja antigen group, the virus is distributed mainly in southern Europe and the Balkans, as well as in Africa and Asia. Its northernmost appearance in Europe was in the form of an isolation from *Dermacentor marginatum* in the Czech Republic (Hubalek et al, 1988). Antibodies to the virus have been isolated in Romania in 1986 in *Dermacentor* ticks, humans and domestic animals (Ungureanu et al, 1990); the first report of human illness due to infection with Bhanja virus was in Dalmatia, Croatia in 1977, where an antibody rate of 31% was found on the island of Brac (Vesenjsek et al, 1991), and the virus was isolated from *Haemaphysalis punctata*. Antibodies have also been detected either in animals or humans or isolations made from ticks in Bulgaria, Italy, Kosovo, Portugal, Slovakia, and Spain. Hubalek (1987) reviewed the distribution, isolations and antibody findings of Bhanja virus and reported that it has been isolated in 15 countries of Asia, Africa and Europe, and antibodies against it have been detected in 15 additional countries. Its vector range includes *Ixodid* ticks, and species of 6 genera (*Haemaphysalis*, *Dermacentor*, *Hyalomma*, *Amblyomma*, *Rhipicephalus* and *Boophilus*) have yielded the virus. Bhanja virus has only rarely been isolated from vertebrates (*Atelerix*, *Xerus*, *Ovis*, *Bos*, and possibly bats), although antibodies have been detected frequently in a wide range of mammals, mainly ruminants, in several species of birds (Passeriformes, Galliformes), and even in reptiles (*Ophisaurus apodus*). Natural foci of the Bhanja virus infections are closely associated with pastures of domestic ruminants infested by ticks in the regions of tropical, subtropical and partly temperate climatic zones. Dobler (1996 *ibid*) classifies Bhanja virus among those infections likely to cause neurological disorders. The high incidence of this virus in animals implies that the risk of human exposure is also high, although its overall public health importance is at present small.

### **Thogoto virus**

Thogoto virus is a tick-borne virus, a member of the family Orthomyxoviridae; it is widely distributed in Africa, and in Europe it has been found in Italy (Sicily) and Portugal. Antibodies were found in human sera in Portugal (Filipe et al, 1985), and it has been isolated from *Rhipicephalus bursa* in Sicily (Albanese et al, 1972). Dobler (1996, *ibid*) also classes this virus among those that are known to cause neurological disorders, although overall it does not appear to be of public health importance in Europe.

### **Dhori virus**

Also a member of the Orthomyxoviridae, both Thogoto and Dhori viruses share structural and genetic properties with the influenza viruses. Dhori virus has been isolated from *Hyalomma marginatum* in Portugal (Filipe and Casals, 1979); antibodies were also found in humans in Portugal (Filipe et al, 1985 *ibid*), and isola-

tions were made from ticks in Portugal (Filipe et al, 1990). Four strains of Dhori virus were isolated from ticks, *H. marginatum*, and from a hare found in the middle zone of the delta of the Volga River, Astrakhan Region, in 2001, which represented the first isolation of Thogotovirus genus virus from wild vertebrates (L'vov et al, 2002). The potential clinical importance of infection by this virus was shown when five laboratory workers were accidentally infected during the preparation of cultural agents. Clinically, Dhori infection was characterized by an acute course with marked general toxicity and a febrile period of two to four days. Two out of five patients had changes on the part of the nervous system of the type of encephalitic reaction, predominantly with subcortical symptoms and mild involvement of the pyramidal system, or in the form of encephalopolyradiculoneuritis, with paresthesia and sensitivity disorders (Butenko et al, 1987). As in the case of Thogoto virus, this agent does not appear to be of public health significance in Europe at present. Dhori virus is closely related to Batken virus (Frese et al, 1997), and may in fact be identical to it.

### **Tribec virus**

Tribec virus, an Orbivirus, was first isolated from *I. ricinus* in Slovakia and has been reported from Belarus, Estonia, France, the Czech Republic, Hungary, Italy, Norway, the Republic of Moldova, Romania, the Russian Federation and Ukraine (Hubalek and Halouzka, 1996 *ibid*), either by isolation or through antibody surveys. In the Tribec mountains, the virus circulates among rodents, goats and different stages of *I. ricinus*. Although some 20 patients with CNS infection in Czechoslovakia had antibodies to Tribec (Libikova et al, 1978), its overall public health importance is limited.

### **Tettngang virus**

Three strains of this virus were isolated from *I. ricinus* ticks in the former Czechoslovakia, and the isolates of the virus were lethal for suckling mice (Kozuch et al, 1978). In the same country, yet another virus, identified as Tettngang virus, was isolated from the cerebrospinal fluid (CSF) of an 18-month-old child with pharyngitis, accompanied by an encephalitic reaction (Malkova, 1980). Although the agent may have been the cause of disease, its restricted known distribution and the few reports of illness appear to limit its public health importance.

### **Eyach virus**

This Coltivirus virus is closely related to the American Colorado tick fever virus. It has been isolated from *I. ricinus* in Baden-Wurttemberg, Germany (Rehse Krüpper et al, 1976), and from *I. ricinus* and *I. ventralloii* ticks in France (Chastel et al, 1984). Chastel (1998) observes that Eyach virus and Erve virus, which were also isolated in western France in 1981–1982, are able to infect human beings and are responsible for severe neurological disorders. Eyach virus has also been

found in the Netherlands and the Czech Republic. The virus is widespread in hare populations, and probably in rodents as well.

There are a number of other viruses that have been isolated from ticks in various parts of Europe whose importance as causative agents of disease is unknown or uncertain. Further research will undoubtedly find other viruses, as many areas of the continent remain unstudied. As noted above, ecological changes have resulted in the increase of some of the tick-borne viruses, and surveillance must be maintained on the group.

## TICK-BORNE BACTERIAL INFECTIONS

Since the identification of *Borrelia burgdorferi* as the agent of Lyme disease in 1982, 11 tick-borne human bacterial pathogens have been described throughout Europe. These include five spotted fever rickettsiae, the agent of human granulocytic ehrlichiosis, four species of the *B. burgdorferi* complex, and a new relapsing fever borrelia (Parola and Raoult, 2001).

### TICK-BORNE RELAPSING FEVER

Several spirochete species are the causative agents of Tick-borne relapsing fever (TBRF) in Europe. Globally TBRF can be caused by some 15 different *Borrelia* species, and these should be distinguished from louse-borne relapsing fever caused by *Borrelia recurrentis*, which is generally associated with a higher mortality. Tick-borne relapsing fever is a serious disease; however, if appropriately treated in a timely fashion, it has a mortality rate of less than 5%. If acquired during pregnancy, tick-borne relapsing fever poses a high (up to 50%) risk of fetal loss. The illness is characterized by periods of fever, chills, headaches, body aches, muscle aches, and cough, alternating with periods when the fever subsides. The *Borrelia* agents of tick-borne relapsing fever are transmitted by the soft ticks of the family Argasidae, primarily those of the genus *Ornithodoros*. The infection is widespread in Africa, where *Ornithodoros moubata* and *O. erraticus* are the vectors of *B. duttonii* and *B. crocidurae*. The wild hosts of the infectious agents are usually rodents. In Europe, *Borrelia hispanica* is the causative agent of relapsing fever in Spain, although the disease caused by this agent is now rarely detected in patients (Anda et al, 1996). Sanchez Yerba et al (1997) consider that the incidence of this disease is underestimated. In Portugal, there have been no cases of tick-borne relapsing fever since the 1960s (Sofia Nuncio, personal communication). This species has also been reported in Portugal, Greece and Cyprus (Goubau, 1984). The vector in Europe is *Ornithodoros erraticus*. A new *Borrelia*, closely related to other tick-borne agents of relapsing fever in Europe and Africa, has been isolated from *Ornithodoros erraticus* and humans in Spain (Anda et al, 1996, *ibid*) and Portugal (Estrada-Pena and Jongejan, 1999). It can be concluded that tick-borne relapsing fever is now of very minor public health importance in Europe, and it is most often seen as an imported disease; however, a survey near the Rhein valley of Germany has shown that relapsing fever-like spirochetes infected 3.5% of the questing vector *I. ricinus* ticks collected. These spirochetes differed genetically from their American and Asian analogs, and their public health importance remains unknown. No co-infections with *B. burgdorferi* were found in the ticks (Richter et al, 2003).

## Lyme disease

Lyme borreliosis, or Lyme disease (LD), is the most commonly reported tick-borne infection in Europe and North America, and, indeed, the most commonly reported vector-borne disease. The disease is a multi-system disorder that can affect a complex range of tissues including the skin, heart, nervous system, and, to a lesser extent, the eyes, kidneys and liver. Its incidence is increasing in many parts of Europe.

The first record of a clinical condition associated with Lyme disease was recorded in Breslau, Germany in 1883, when a physician named Alfred Buchwald described a degenerative skin disorder now known as acrodermatitis chronica atrophicans (ACA). In a 1909 meeting of the Swedish Society of Dermatology, a Swedish physician, Arvid Afzelius, presented his research on an expanding, ring-like lesion he had observed, although his observations of it were published 12 years later (Afzelius, 1921). Afzelius speculated that the rash came from the bite of an *Ixodes* tick. The condition known as erythema chronicum migrans, or more commonly, erythema migrans (EM), was known to occur widely in Europe, and was often found associated in *I. ricinus*, although the causative agent remained unknown, and for some time it was thought that EM might be due to infection by TBE. Putkonen et al (1962) compared the pathology of TBE and EM and were able to conclude that EM was not caused by TBE.

In 1972, an outbreak of a disease occurred in the town of Lyme, Connecticut, USA in what appeared as an epidemic form of arthritis. Steere et al (1977) described the infection and observed that "Lyme arthritis" was a previously unrecognized clinical entity, the epidemiology of which suggested transmission by an arthropod vector. Shortly thereafter, it was noted that the disorder had been found in other areas as well, and that it might have been transmitted by ticks (Steere et al, 1978a). They hypothesized that the infection had been transmitted specifically by *I. scapularis* (Steere et al, 1978b). Burgdorfer (1983) later determined that a spirochete was the causative agent of Erythema chronicum migrans, and the name *Borrelia burgdorferi* was given to the spirochete. Soon thereafter, in Germany, Ackermann (1983) demonstrated the presence of antibodies to *Rickettsia duttoni* in six patients with erythema chronicum migrans and eight patients with tick-borne meningopolyneuritis, a disease was similar to the newly described Lyme diseases in the USA, and furthermore, that *I. ricinus* had served as the vector.

By the year 2000, Lyme disease had become the most common tick-borne disease in the USA, with distribution throughout almost all of the country. In 2000, 17 730 cases of LD were reported to the Center for Disease Control (CDC, 2002). LD is not only the most common tick-borne disease in the USA, but also the most common vector-borne disease in the northern hemisphere.

To date, *B. burgdorferi* can be divided into at least ten species (*B. burgdorferi* sensu stricto, present in Europe and in the USA but absent from Asia, *B. garinii*,

*B. afzelii* and the genospecies *B. valaisiana* and *B. lusitaniae* in Eurasia, *B. japonica*, *B. tanukii* and *B. turdae*, restricted to Japan, and *B. andersonii* and *B. bissettii* in the USA). Other borrelia transmitted by hard ticks have been identified in the USA (*B. lonestari*) and Japan (*B. miyamotoi*).

Of the ten different species, only *Borrelia burgdorferi* sensu stricto, *B. garinii*, and *B. afzelii* are undoubtedly involved in clinical cases of LD. There is evidence resulting from isolation from patients, PCR, and serological data that the division of *B. burgdorferi* sensu lato into genospecies has clinical relevance. Thus, *B. burgdorferi* sensu stricto is most often associated with arthritis, particularly in North America, where it is the only known cause of Lyme disease. *B. garinii* is associated with neurological symptoms, and *B. afzelii* is implicated in a chronic skin condition known as acrodermatitis chronica atrophicans (ACA). Overlap between species in relation to clinical manifestations occurs, and all cause the pathognomic symptom erythema migrans (EM), although there is evidence in Europe that this early sign occurs more frequently in *B. afzelii* infections than in those caused by *B. garinii*. *B. valaisiana* could be associated with pathologic features, although no strain has yet been isolated from a human sample. *B. valaisiana* has so far only been associated with EM. The least amount of information is available for *B. bissettii*, a species encountered mostly in California, USA. No strain belonging to this species has been isolated from a human patient in the USA, although rare cases of human disease due to it have been reported in Europe.

In Europe, the *Borrelia burgdorferi* sensu lato complex is represented by five distinct genospecies: *Borrelia burgdorferi* sensu stricto, *Borrelia afzelii*, *Borrelia garinii*, *Borrelia valaisiana*, and *Borrelia lusitaniae*. These taxonomic entities are known to differ in their specific associations with vertebrate hosts and to provoke distinct clinical manifestations in human patients (Derdakova et al, 2003). Lyme borreliosis (LB) occurs throughout Europe and is particularly prevalent in the east. In a small proportion of untreated cases, serious sequelae may occur, but Lyme borreliosis alone does not cause death. Clinical and serological diagnosis remains problematic, and the various genomospecies may cause different disease manifestations.

### **The incidence of Lyme disease in Europe**

Very few countries have made LB a compulsorily notifiable disease and therefore, case rates give only an approximate estimation of LB incidence in Europe. In most countries, reporting is mainly conducted through diagnostic laboratories reporting available details of patients with positive tests. There are several drawbacks involved in using such systems for the estimation of LB incidence in Europe, including under-reporting of EM, varying patterns of test referrals, varying serodiagnostic criteria, and seropositivity linked to past exposure.

Prospective clinically based studies yield the most accurate information on incidence. However, these are more costly in time and resources than indirect

methods, which may represent the only means to carry out surveys in some areas. Indirect methods may include the measurement of the abundance of *I. ricinus* ticks, the prevalence of *B. burgdorferi*-infected ticks and seroprevalence studies. All of these indirect measures have weaknesses as indicators of Lyme borreliosis, but at present human seroprevalence studies probably represent the best method for obtaining epidemiological data throughout Europe. From data presented at a WHO workshop, and taking the limitations of seroprevalence methods into account, it is clear that LB shows a gradient of increasing incidence from west to east, with the highest incidences in central-eastern Europe (Table 9). A gradient of decreasing incidence from south to north in Scandinavia and north to south in Italy, Spain and Greece has also been noted.

**Table 9. Estimated Lyme borreliosis annual incidence in selected European countries\***

Country	Incidence per 100,000 population	Annual number of cases
United Kingdom*	0.3	200
Ireland	0.6	30
France	16.0	7 200
Germany**	25.0	20 000
Switzerland**	30.4	2 000
Czech Republic*	39.0	3 500
Bulgaria	55.0	3 500
Sweden (south)	69.0	7 120
Slovenia	120.0	2 000
Austria	130.0	14 000

\*based on Report of WHO workshop on Lyme Borreliosis Diagnosis and Surveillance, Warsaw, Poland, 20–22 June 1995, WHO/CDS/PH/95. (1996) 141-1.)

\*\* No published figures available

O'Connell et al (1998), in a review of the epidemiology of European Lyme borreliosis, emphasized that few countries have official reporting systems for Lyme borreliosis, and most figures on incidence are extrapolated from serodiagnosis data and seroprevalence studies. Geographical variations in incidence seem to correlate with the prevalence of infected ticks, which are mainly associated with varied deciduous forest.

Although the clinical entity EM has been known in Europe since the early part of the last century, the incidence of infection appeared to be relatively stable during most of the century. In the last decades, however, there has been an increasing trend in the incidence of the disease in most of the areas in which it is endemic. Korenberg (1998) contends that the observed increase was due to improved diagnosis, but it is generally believed that the increase is a real one; Barbour (1998) noted that LD infections were most often acquired in suburban residential and recreational areas, and, consequently, the rise in cases of LD and the other *Ixodes*

tick-borne infections is, in part, the consequence of reforestation and the increase in deer populations in developed countries. Increasing human recreational activities in these same areas also greatly increase the chance of being bitten by deer tick vectors of LD. George and Chastel (2002) observed that the number of persons suffering from tick-borne diseases has notably increased in the French region of Lorraine since the mid 1990s, and that greater awareness of the pathology is insufficient to explain such an increase in incidence. Instead, the proliferation of ticks is a major factor in the increased incidence of cases, and is mainly due to a modification of the ecosystem. The human impact on the environment has increased both the habitat and wildlife hosts of ticks, and has allowed tick populations to multiply significantly. This probably accounts for a genuine emergence of Lyme borreliosis, with its high potential transmission rate, in both the USA and Europe, although the rate of emergence has been somewhat exaggerated by improved surveillance and diagnosis (Randolph 2001, *ibid*).

In Austria, tick vector densities are high and, the incidence of Lyme disease is the highest in Europe, around 120 per 100 000 population with about 14 000 new cases per year.

Eldoen et al (2001) found that the annual incidence of LD in the area of More and Romsdal, Norway, had almost doubled in 1998 from the average of the previous decade, and thought that this might reflect a changing prevalence of the tick vector along the Norwegian coastline.

Lyme disease has been mandatorily reportable in Slovenia since the late 1980s. It is now the most common tick-borne disease, and it is spread throughout the country. Its incidence has been increasing, and by 1997, it had reached 155/100 000 cases, with the incidence substantially higher in some regions. The disease affects both sexes (but as a rule more often women than men) and all age groups. The incidence is the highest in persons 30–50 years of age, followed by children aged 6–15 years. Erythema migrans is by far the most common recorded manifestation (Strle, 1999).

Increases in the incidence of LD have also been reported from France (George and Chastel, 2000 *ibid*), Germany (Trieb et al, 1998), Italy (Grazioli, 1996), Poland (Dziubek, 1995 Ellert Zygadłowska et al, 1996), and the Russian Federation (Lesnyak et al, 1998). Santino et al (1997) reviewed the geographical distribution of LD in Europe, with special reference to Italy. Data on the seroprevalence of the diseases was established in European patients or at-risk populations and in blood donors or control subjects. In northern Europe, the seroprevalence of antibodies to *B. burgdorferi* in patients or in at-risk subjects is higher in Sweden (19%) and lower in Estonia (2.7%). However, recent unpublished studies in Sweden indicate that in some areas, a real increase in cases may have occurred over the last few years, apparently related to the greater abundance of ticks. In central Europe, the incidence of antibodies to *B. burgdorferi* in patients or in at-risk subjects is higher in the Netherlands (28%) and Switzerland (about 26%)

and lower in Poland (15%). The range of antibodies to *B. burgdorferi* in blood donors or control subjects shows the highest spikes in Ireland (15%) and the lowest in Austria (7.7%) and Germany (5.5%). In southern Europe, the highest incidence is seen in Croatia (43%) and the lowest in Greece (1.1%). In Italy, the seroprevalence of antibodies to *B. burgdorferi* in patients or in at-risk subjects varies: in northern Italy, the lowest incidence is in Lombardia (3.2%) and the highest in Friuli (22.3%); in central Italy, the lowest incidence is in Emilia (Parma) (0.2%), and the highest in Tuscany (18.3%). The range of antibodies to *B. burgdorferi* in blood donors or control subjects shows the lowest spikes in Lazio (1.5%), while the highest are in Sicily (10.9%). Although the number of works on infection diffusion by *B. burgdorferi* is increasing, statistical evaluations, comparisons, and the drawing of acceptable conclusions continue to be difficult. In fact, data obtained from various European laboratories are often not directly comparable, due to the use of different serological tests used to detect antibodies to *B. burgdorferi*.

Lyme borreliosis is widespread in the Russian Federation; foci are widely distributed over the forest zone from the Baltic region to the Far East and to the south of Sakhalin Island (Dekonenko et al, 1988). *Borrelia garinii* and *Borrelia afzelii* are the most common species. With improved diagnosis, the number of cases in the Russian Federation may reach from 10 000 to 12 000/year (Korenberg, 1998, *ibid*). In a survey in Krasnodar Territory not far from Sochi, the classical causative agent of Lyme borreliosis (*B. burgdorferi* sensu stricto) was detected for the first time in the Russian Federation, along with *Borrelia* species found earlier in the country (*B. garinii*, *B. afzelii*, *B. valaisiana* and *B. lusitaniae*) (Gorelova et al, 2001).

There has also been an increase in the incidence of Lyme disease in the United Kingdom, but this appears to be due to greater awareness on the part of physicians and thus the more accurate diagnosis of cases; the increase is less than that on the continent, and no more than some 200 cases per year are reported. However, Smith et al (2000) reported that Lyme borreliosis in the United Kingdom has increased from 0.06/100 000 from 1986–1992 to 0.32/100 000 in 1996. Erythema migrans was reported in 41% of patients, arthritis in 4%, musculoskeletal symptoms in 18%, and neuroborreliosis in 15%. The degree of exposure appears to vary considerably from one area to another. Thomas et al (1999) noted that prevalence of antibodies to *B. burgdorferi* was only 0.2% among 606 farmers and their families studied in three different areas of the United Kingdom.

In studies in southern England, Kurtenbach et al (1998) found three genospecies of *B. burgdorferi* in questing ticks, with the highest prevalences found for *B. garinii* and *B. valaisiana*. *B. burgdorferi* sensu stricto was rare (< 1%) in all tick stages. *Borrelia afzelii* was not detected in any of the samples. More than 50% of engorged nymphs collected from pheasants were infected with borreliae, mainly *B. garinii* and/or *B. valaisiana*. Nineteen percent of the rodent samples harboured *B. burgdorferi* sensu stricto and/or *B. garinii* in their internal organs. Recent find-

ings in Scotland show that both *B. burgdorferi* and *B. afzelii* are present (Ling, 2002). In Ireland, Robertson et al (1998) considered that the low overall seroprevalence of 3.4% in Ireland correlates with the rarity of clinical cases as compared with continental European countries, and is due in part to the scarcity of high-risk Lyme borreliosis habitat in the country. Stanford et al (1990) found antibodies to *B. burgdorferi* in 14.3% of the members of a group of randomly selected farmers in Northern Ireland who represented a more exposed group than the rangers studied by Robertson.

The co-infections of humans, ticks and small mammal reservoirs with more than one tick-borne infection pose a growing diagnostic and clinical problem. Co-infections with Lyme disease, ehrlichiosis, babesiosis and tick-borne encephalitis are being reported with increasing frequency, due to both more reliable diagnostic techniques and actual increases in the incidence of the tick-borne diseases. The co-infections of more than one species of *Borrelia* in a Prague park have already been described. In Lyon, France, 12.1% of the *I. ricinus* collected were infected by a combination of *Borrelia valaisiana* and *Borrelia garinii*. No tick was infected with more than two borrelial species (Quessada et al, 2003). In a survey in the Pomerania province, northern Poland, Stanczak et al (2000) found that as many as 21/424 ticks (5%) contained both the *Ehrlichia* HGE agent and *B. burgdorferi* s. l. which perpetuate in the same foci and frequently co-infect the same tick vector, thereby increasing the risk of humans acquiring mixed infection. Inasmuch as *I. ricinus* is the vector of Lyme disease, TBE, ehrlichiosis and bartonellosis, the risk of acquiring more than one disease, or more than one serospecies of *Borrelia*, is great. In another survey of infections of *I. Ricinus* in Poland, Skotarczak et al (2003) found that of 533 processed ticks, 16.7% were positive for *B. burgdorferi* s. l., 13.3% for *B. microti*, and 4.5% for the HGE agent. Twenty ticks were coinfecting with two or three of the pathogens. Naumov and Vasil'eva (2002) raised the question as to whether mixed infections of more than one disease agent in ticks were an exception or a rule. They suggested that the natural tolerance of ticks to pathogens due to primary infection may be reduced; a review of the literature available on this topic, however, revealed that the actual number of ticks with mixed infections was higher than might be anticipated.

### Tick vectors of Lyme disease

*I. persulcatus* and *I. ricinus* are the main vectors of the *Borrelia burgdorferi* sensu lato in Eurasia. The distribution of the *I. persulcatus* tick in the west of the Russian Federation is limited. The range of *I. ricinus* covers most of the western part of Europe. A broad zone in which these vectors are widely sympatric exists in eastern Europe. Korenberg et al (2000) studied the two vector tick species in the area in which they are sympatric in the northwestern area of the Russian Federation in order to determine the influence of the vector species on the *Borrelia* species isolated in them. *B. afzelii* and *B. garinii* were found only in *I. persulcatus*. *Borrelia*

prevalence in this species is almost always higher than in *I. ricinus*. In some areas, the incidence of infection in tick populations is extremely high; Golubic and Zember (2001) describe an area in Croatia where 45% of the ticks are infected with *B. burgdorferi*. Infection prevalence in *I. ricinus* is almost identical in forests with the distinct predominance of *I. persulcatus*. In natural foci, closer interaction exists between the *Borrelia* and *I. persulcatus* tick than between the pathogens and *I. ricinus*. Seven hundred and seventy nine *I. ricinus* were collected from an urban park in Prague, Czech Republic; the incidence of *Borrelia burgdorferi sensu lato* was 9.2% in 1995, 3.4% in 1996, 4.5% in 1997 and 2.8% in 1998. The *Borrelia garinii* to *Borrelia afzelii* ratio was 1.4:1 and it did not differ significantly throughout the study period. *Borrelia burgdorferi sensu stricto* was not detected. *Borrelia garinii/Borrelia afzelii* coinfection was found in 5.7% of positive ticks. The results indicate it is possible for an urban population to come into contact with the causative agent of Lyme disease in an urban park (Basta et al, 1999). In investigations carried out in the St. Petersburg and Kaliningrad Baltic regions of the Russian Federation, *B. afzelii* and *B. garinii* were found both separately and together in ticks. A significant difference existed between levels of infection in *I. ricinus* and *I. persulcatus*, with all three types of *Borrelia* infection observed twice as often in *I. persulcatus* than in *I. ricinus*, and dual infection occurred in *I. persulcatus* 3.7 times more often. It appeared that *I. persulcatus* is a much more effective or dangerous vector of tick-borne borrelioses than *I. ricinus* (Alekseev et al, 1998). In Sweden, the replies to a questionnaire completed by 1 200 people indicated that *I. ricinus* ticks are more widespread today than in the early 1980s in many regions of the country, and the proportion of the population being exposed to ticks is significantly increasing (Talleklint and Jaenson, 1998).

Many investigations have been made to ascertain whether other arthropod vectors of the causative agent of Lyme disease in Europe exist. *B. burgdorferi* has been isolated from several other tick and insect species in Europe, but, in most cases, their role as vectors of the infection to man appears to be minor.

Angelov et al (1996) sampled *Dermaentor marginatus* and *Haemaphysalis punctata* in Bulgaria; three (7.9%) of the adult *H. punctata* and two (3.57%) of the adult *D. marginatus* were infected with *B. burgdorferi*, and the authors believed that, in some ecosystems, *D. marginatus* could be a secondary vector.

Hubalek et al (1998) investigated haematophagous arthropods for borreliae in the South Moravia region of the Czech Republic; borreliae were detected in 6.1% of larval and 10.3% of nymphal *I. ricinus* and in one larval *Haemaphysalis concinna*. Among 3 464 female mosquitoes of six species, 4.1% contained spirochaetes: 1.4% of *Ae. vexans*, 1.3% of *Ae. cantans*, 2.2% of *Ae. sticticus*, 2.2% of *Cx. pipiens pipiens* and 5.9% of *Cx. pipiens molestus*. Borreliae were also detected in 8.4% of 142 fleas, mainly *Ctenophthalmus agyrtus* and *Hystrichopsylla talpae* collected from small mammals. Twelve isolates of *B. burgdorferi sensu lato* were identified to genospecies: six strains from *I. ricinus* (four *Borrelia garinii*, one *B. afzelii* and one

*B. lusitaniae*), one strain from *A. vexans* (*B. afzelii*), two strains from *C. agyrtus* (*B. afzelii*), and three strains from host rodents (*B. afzelii*).

Kahl et al (1992) collected and individually examined for spirochetes three species of ticks from two sites in Saxony, Germany: *I. ricinus*, (n 414), *Dermacentor reticulatus* (n 116) and *Haemaphysalis concinna* (n 96). The prevalence of *Borrelia* (probably *B. burgdorferi*) in *I. ricinus* varied from 12.1% to 21.0%. No borreliæ were found in *H. concinna*. Of the examined *D. reticulatus* from one site (n = 97), 11.3% contained either *B. burgdorferi* or a related *Borrelia*, and the authors thought that this might represent the first finding of *Borrelia* in a Eurasian *Dermacentor* species.

In Spain, two other *Ixodes* species were found infected with borrelia in various areas; both *I. canisuga* and *I. hexagonus* had high rates of *B. burgdorferi* prevalence (30 and 28%, respectively) in an area where *I. ricinus* was absent. Immatures of *I. frontalis* were found to be carriers of the spirochete only in those zones where *I. ricinus* is present, suggesting evidence for reservoir competence in a tick-bird cycle (Estrada Pena et al, 1995). Pichot et al (1997) also mention that *I. hexagonus* was found naturally infected by *B. burgdorferi* in surveys in and around Lyon, France.

A survey was carried out in Switzerland of hedgehogs and their tick ectoparasites in suburban areas where both *I. ricinus* and *I. hexagonus* were present, as well as in an urban area where *I. ricinus* was not present. The European hedgehog, *Erinaceus europaeus*, is a common host of both *I. ricinus* and *I. hexagonus*. Both species were found on all hedgehogs from the suburban area; however, in the urban area, only *I. hexagonus* infested the hedgehogs. A total of 12/13 hedgehogs harboured *B. burgdorferi* infected ticks. DNA of *B. burgdorferi* sensu stricto, *B. garinii* and *B. afzelii* was detected in culture from ear biopsy and needle aspiration material and characterized by using a genospecies-specific PCR assay. One hedgehog presented a mixed infection of the skin with *B. burgdorferi* sensu stricto and *B. garinii*. This study also identifies an enzootic transmission cycle in an urban area involving *E. europaeus* and *I. hexagonus*. The close association of *I. hexagonus* with the burrows of its hosts means that the risks of contact between *I. hexagonus* and humans may be low (Gern et al, 1997).

In Germany, Beichel et al (1996) identified 434 nymphal and adult ticks on animals presented to a veterinary clinic in north Baden over a period of one year. The ticks found consisted of *I. ricinus* (385), *I. hexagonus* (48), and *I. ventralloi* (one). The polymerase chain reaction was used to examine 132 *I. ricinus* and 21 *I. hexagonus* for the presence of *B. burgdorferi*. Twenty-two per cent of adult *I. ricinus* were infected, as were one female and one larval *I. hexagonus*.

In the United Kingdom, an unusual study was made of alcohol-preserved specimens from the British Museum of eight species of ticks known to attack humans: *I. ricinus*, *I. hexagonus*, *I. uriae*, *I. trianguliceps*, *Dermacentor reticulatus*, *Haemaphysalis punctata*, *Rhipicephalus sanguineus* and *Argas vespertilionis*.

The sample comprised all life stages and originated from a wide range of host species with collection dates from 1896 to 1994 and representing geographical localities in England, Scotland and Wales. *Borrelia burgdorferi* s.l. DNA, detected by a PCR that targeted the outer surface protein A gene, was found in all eight species. The overall proportion of PCR-positive specimens ranged from 7.8% for *I. hexagonus* (mostly from mustelids and hedgehogs) to 98.3% for *I. uriae* (mostly from seabirds). *Borrelia burgdorferi* s.l. DNA was found for the first time in the bat parasite *A. vespertilionis* (85.3%). The spirochete is newly recorded in British populations of *I. trianguliceps* (97.4%), mostly from voles, mice and shrews, *D. reticulatus* (12.5% from dog and man) and *R. sanguineus* (30% from dogs and human dwellings). Of the four tick species with larvae available for testing, examples of *I. ricinus*, *I. uriae* and *A. vespertilionis* were PCR positive, as were significantly more nymphs than adults of *I. ricinus*, *I. hexagonus* and *A. vespertilionis*. Analyses showed that *B. burgdorferi* s.l. has been consistently present in British tick populations since at least 1897. Ticks testing positive for *B. burgdorferi* s.l. DNA were collected in every month of the year from throughout Britain and taken from a wide range of mammal and bird species. PCR positivity does not prove vector or reservoir competence, but the use of archived material has demonstrated an extensive range of host-tick relationships involving *B. burgdorferi* s.l. in Britain for > 100 years (Hubbard et al, 1998).

A similar study carried out on archived ticks in Germany showed that *Borrelia* could be detected in ticks stored for about 100 years. Spirochetal DNA was detected by PCR in six ticks preserved for up to a century or more, the oldest of which was collected in 1884. *Borrelia garinii*, which predominates in modern ticks in the region, infected three of these older ticks, while the presently infrequent *B. burgdorferi* sensu stricto infected two. These data indicate that residents of Europe have been exposed to diverse Lyme disease spirochetes since at least 1884, concurrent with the oldest record of apparent human infection (Matuschka et al, 1996).

### **Animal and bird reservoirs of *Borrelia***

Small rodents are the most common reservoirs of *Borrelia*, while larger animals serve as hosts for ticks. Insectivores, hares and birds may also serve as reservoirs.

Gern et al (1998) reviewed existing information concerning the bird and mammal reservoirs of *Borrelia* in Europe of *B. burgdorferi* s.l. At the time of writing, nine small mammals, seven medium-sized mammals and 16 bird species, including passerines, sea birds and pheasants, appeared to be capable of transmitting spirochaetes to ticks and thus participating in the natural circulation of *B. burgdorferi* s.l. in Europe. The house mouse, *Mus musculus* is strongly suspected of being a competent reservoir, and many other small rodent species, particularly in eastern Europe and the Russian Federation, have been implicated. Ungulates are not thought to play a major role as reservoir hosts, although co-feeding trans-

mission may permit some tick infection. As shown in the tables below, additional reservoir species are being found in the process of further studies.

A study was made to determine the involvement of birds in the Lyme disease cycle in a LD-endemic area of Swiss woodlands. Thirteen passerine species were found to be parasitized by *I. ricinus* subadults, particularly *Turdus merula*, *T. philomelos* and *Erithacus rubecula*. *B. burgdorferi*-infected ticks were removed from five species of passerines and mainly three species of Turdidae (*T. merula*, *T. philomelos* and *E. rubecula*). Infection rates of larvae and nymphs by spirochetes averaged 16.3% and 21.7% respectively, and Turdidae may serve as amplifying hosts for spirochetes in the focus (Humair et al, 1993). Confirmation was made of the reservoir status of blackbirds, *T. merula* and one song thrush (*T. philomelos*) in Switzerland when they were found infected by *B. garinii* and by *Borrelia* from group VS116; blackbirds are therefore implicated as reservoirs for these two genomic groups of *Borrelia*, and it was shown that in a laboratory they can transmit living borreliae to ticks. An association seems to exist between birds and *Borrelia* VS116, and, to a lesser extent, *B. garinii*, similar to the association existing between small rodents and *B. afzelii* (Humair et al, 1998). Humair (2002) concluded that *B. burgdorferi* s.l. circulates not only in terrestrial environments involving *I. ricinus* and undergrowth-frequenting birds but also in marine environ-

**Table 10. Bird species found positive for antibodies or by isolations of one or more genospecies of *B. burgdorferi* s.l. in Europe**

<i>Acrocephalus scirpaceus</i> , nightingale	Kaiser et al, 2002
<i>Alca torda</i> , razorbill	Olsen et al, 1995a
<i>Anthus trivialis</i> , tree pipit	Olsen et al, 1995b
<i>Coccothraustes coccothraustes</i> , hawfinch	Olsen et al, 1995b; Humair et al, 1993
<i>Erithacus rubecula</i> , robin	Olsen et al, 1995b; Humair et al, 1993
<i>Fringilla coelebs</i> , chaffinch	Olsen et al, 1995b; Humair et al, 1993
<i>Fratercula artica</i> , puffins	Gylfe et al, 1999
<i>Luscinia luscinia</i> , thrush nightingale	Olsen et al, 1995b
<i>Luscinia megarhynchos</i> nightingale	Kaiser et al, 2002
<i>Luscinia svecica</i> , bluethroat	Olsen et al, 1995b
<i>Parus major</i> , great tit	Humair et al, 1993
<i>Phasianus colchicus</i> , pheasant	Kurtenbach et al, 1998a; Crain et al, 1997
<i>Phoenicurus phoenicurus</i> , redstart	Olsen et al, 1995b
<i>Prunella modularis</i>	Kaiser et al, 2002
<i>Psylloscopus collybita</i> , chiffchaff	Olsen et al, 1995b; Kaiser et al, 2002
<i>Sylvia atricapilla</i> , blackcap	Olsen et al, 1995b
<i>Sylvia communis</i> , whitethroat	Olsen et al, 1995b; Humair et al, 1993
<i>Troglodytes troglodytes</i> , wren	Olsen et al, 1995b
<i>Turdus merula</i> , blackbird	Olsen et al, 1995b; Humair et al, 1993 1998
<i>Turdus philomelos</i> , song thrush	Olsen et al, 1995b; Humair et al, 1993

ments involving *I. uriae* and seabirds. Migrating birds contribute to the spread of *B. burgdorferi* and infected tick vectors along migration routes. Spirochetes identified as *B. burgdorferi* were found in ticks, *I. uriae*, and seabirds on the island of Bonden 12 km from the mainland of Sweden. As there are no mammals present on the island, the authors (Olsen et al, 1993) have suggested that the birds play a role in the maintenance of the infection and mammals may not be necessary. Clearly, further research is necessary regarding the bird and animal reservoirs of the various species of *Borrelia* in Europe. Some of the records available are shown in Table 10, while records of animals found positive for *B. burgdorferi* are shown in Table 11.

### Infections in other animal species

Many species of large animals have been found positive for one or more *Borrelia* species. As the infectious agents are not passed on to ticks, these animal infections have little epidemiological significance, and the large animals are therefore “dead-end hosts” rather than true reservoirs. Nevertheless, as hosts for vector ticks, they are important in the epidemiology of the infection. Clinical signs of Lyme disease are recognized in dogs, horses and cattle. Deer are not affected by infection with *Borrelia*. In dogs, signs of Lyme disease may develop within weeks to months after

**Table 11. Mammal species found positive for antibodies or by isolations of one or more genospecies of *B. burgdorferi* s.l. in Europe**

<b>Rodents and shrews</b>	
<i>Apodemus sylvaticus</i> , wood mouse	Frandsen et al, 1995
<i>Apodemus flavicollis</i> , yellow-necked field mouse	Hovmark et al, 1998
<i>Apodemus agrarius</i> , black striped mouse	Matuschka et al, 1991
<i>Clethrionomys glareolus</i> , bank vole	Gern et al, 1994
<i>Glis glis</i> , edible dormouse	Matuschka et al, 1994
<i>Microtus agrestis</i> , meadow vole	Frandsen et al, 1995
<i>Microtus arvalis</i> , vole	Pawelczyk Sinski, 2000
<i>Neomys fodiens</i> , water shrew	Talleklint Jaenson, 1994
<i>Rattus norvegicus</i> , brown rat	Matuschka et al, 1993 1996
<i>Rattus rattus</i> , black rat	Matuschka et al, 1997
<i>Sorex minutus</i> , pigmy shrew	Talleklint Jaenson, 1994
<i>Sorex araneus</i> , common shrew	Talleklint Jaenson, 1993
<b>Other mammals</b>	
<i>Erinaceus europaeus</i> , hedgehog	Gern, 1997 Gray, 1994
<i>Lepus timidus</i> , varying hare	Talleklint Jaenson, 1993
<i>Lepus europaeus</i> , brown hare	Sykora et al, 1990
<i>Sciurus carolinensis</i> , grey squirrel	Craine et al, 1997
<i>Sciurus vulgaris</i> , red squirrel	Humair Gern, 1998

exposure to the spirochete. Symptoms include episodes of lameness, arthritis in any joint, and swollen lymph nodes. Abortion, laminitis and chronic weight loss resulting from Lyme disease have been identified in cattle and horses. In horses, neurological signs (head tilt, difficulty in swallowing, aimless wandering) and blindness have been reported due to infection and inflammation in the central nervous system (encephalitis) or eyes (panuveitis). Fatal impairment of kidney or heart function has occurred in dogs as a sequela to Lyme disease. Colts born to infected mares have displayed birth defects. Many horses may be infected with the spirochete but display no symptoms.

### **Lyme disease summary**

Lyme disease is the most common vector-borne disease in Europe; its incidence is clearly increasing, and new species of *Borrelia* are continuously being found. While in some areas the reported increases may be due to greater awareness of the infections and improved diagnosis, on the whole it must be concluded that the increase is real. Among the reasons for this increase are ecological changes that favour greater densities of tick vector populations and increased exposure of persons to tick bites when visiting endemic areas.

## TICK-BORNE RICKETTSIAL INFECTIONS

The tick-borne rickettsial diseases endemic to or reported in Europe include the spotted fevers or Boutonneuse fever, more than one species of ehrlichiosis, rickettsial pox, and Q fever.

### **BOUTONNEUSE FEVER OR MEDITERRANEAN SPOTTED FEVER**

Boutonneuse fever is also known as tick typhus, Mediterranean spotted fever, South African tick bite fever, tache noir, Kenya tick typhus, and Indian tick typhus; the causative agent of the disease is *Rickettsia conorii*. The vector of *R. conorii* in Europe is the “brown dog tick” *Rhipicephalus sanguineus*, although other species of ticks may occasionally be found infected as well. The infection is endemic throughout many parts of Africa and Asia, as well as in the Mediterranean area of Europe. Patients usually present with fever, malaise, generalized maculopapulous rash and a typical black spot or “Tache Noir”. While the disease is usually mild, serious forms, including encephalitis, while infrequent, do occur, and they are associated with a high mortality rate (Para et al, 2002). Raoult et al (1986), in a review of 199 serologically confirmed cases, reported a mortality rate of 2.5%. Some 10% of cases have complications that may include neurological syndromes (Ezpeleta et al, 1999). Mediterranean spotted fever and African tick bite fever are different illnesses in the same geographic area. African tick bite fever differs from Mediterranean spotted fever in having local adenopathy and multiple eschars, but the causative organism is the same. Brouqui et al (1988) reviewed the status of boutonneuse fever in the Mediterranean area at the time, and they observed that more malignant forms had recently been found, and that with the growth of dog populations, the incidence of the disease and its distribution is increasing as well, as will be seen in other studies referred to below.

### **The distribution of *Rickettsia conorii* and its tick vectors**

*R. conorii* is widely endemic in southern Europe and throughout most of the countries bordering on the Mediterranean, including Bosnia and Herzegovina, Croatia, Greece, France, Portugal, Slovenia, Spain and Turkey; the countries bordering the Black Sea; as well as in Algeria, Morocco, Tunisia, and Egypt in North Africa, and Israel in the Middle East. *R. conorii* has also been isolated from ticks on birds in Cyprus (Kaiser et al, 1974). *R. conorii* has been detected in *Rhipicephalus bursa* and *Dermacentor marginatus* in Croatia (Radulovic et al, 1994) and from *D. marginatus* in the Crimea (Balayeva et al, 1993). *R. turanicus* is suspected as a possible secondary vector in France (Gilot et al, 1990); *R. conorii* has been

isolated from this species in Israel (Guberman et al, 1996). Dogs which have been taken to southern Europe frequently return to countries of northern Europe infested with *R. sanguineus*. *R. conorii* has also been detected in dogs returning to Germany after having been taken to either Italy or Greece (Gothe, 1999). Although there have been occasional isolations from other species, *R. sanguineus* is the primary vector of *R. conorii* in Europe.

### **The role of dogs in the epidemiology of *R. conorii* and MSF**

*R. sanguineus* is both the vector and reservoir of *R. conorii*; nevertheless, the role of the dog in the epidemiology of the agent is of much importance, as it serves as the primary host for the tick. In both urban and rural areas where dog populations are dense and no effort is made to control their tick ectoparasites, population densities of *R. sanguineus* are also likely to be high, permitting the ready transmission of *R. conorii*. Although the preferred host of *R. sanguineus* is the dog, they will also feed on humans, and, if infected, will transmit the disease agent. Uspensky and Ioffe Uspensky (2002) studied populations of *R. sanguineus* in relation to dogs in Israel. Abundant micropopulations of ticks were formed in small yards or gardens near the dwellings where dogs lived in kennels. A huge field population of *R. sanguineus* was observed on a farm where watchdogs constantly patrolled the farm perimeter. Tick abundance near the kennels and in the permanent resting sites of the dogs reached more than 30 adults per 10 minutes of collecting, while the number of adults on a dog reached 100. They observed that conglomerations of *R. sanguineus* of such size create a great risk to humans, who can be attacked by infected ticks in and around their homes, even in large towns, and thought that this type of situation most likely exists not only in Israel but in other countries as well.

Evidence that the main role of dogs is not more than serving as favourable hosts for vector/reservoir ticks and thus ensuring that tick population densities remain high was demonstrated by a study carried out by Espejo et al (1993) in Spain in 1988. Eight dogs in Barcelona that had showed serum positivity to *R. conorii* when tested in the spring-summer of 1989 were tested again during the next winter, 4–10 months later. The serum titre became negative in six dogs, persisted high in one of them, and fell from 1:640 to 1:40 in another. This suggests a short persistence of antibodies in dogs after contact with *R. conorii* in the Mediterranean area, making their role as true reservoirs of the causative agent unlikely.

A study in Spain showed that seroprevalences were significantly different between the different provinces of origin of the animals. Seroprevalence was below 30% in almost all the provinces studied with the exception of Salamanca province, where the percentage of seropositive dogs was much greater (93.3%). Potential risk factors (presence of ticks on the animals, age, sex, use, habitat, and season) relating to the presence of Mediterranean spotted fever, or Boutonneuse

fever, were evaluated. Animals used for guard or pasture activities and those living in rural areas (these factors are closely linked), together with those suffering from tick infestation, had significantly higher seroprevalences. The frequency of seropositive dogs increased during the summer months, and this coincided with the period of greatest activity by the vector (Delgado and Carmenes, 1995).

### The Public Health Importance of Mediterranean Spotted Fever

It is estimated that the incidence of Mediterranean spotted fever (MSF) or Boutonneuse fever throughout the Mediterranean region is some 50 cases/100 000 inhabitants per year. Asymptomatic cases are quite common, and in serological surveys such cases are more frequently detected than those with clinical symptoms. The incidence of infection may be quite high in endemic areas where *R. sanguineus* is present, and isolated cases can occur in locations where the tick has been introduced, even if only temporarily; local transmission of *R. conorii* has occurred in the Netherlands (Bodegraven and van Sindram, 1991), a non-endemic area of northern France (Senneville et al, 1991), and Switzerland (Chamot et al, 1987, Morier and Ruffieux, 1989, Peter et al, 1984) via infected

**Table 12. Surveys of the incidence of *R. conorii* infection/antibodies in Europe, human and canine populations**

Country	Host	Results	Reference
Croatia	dogs	62.4%–69.9%	Punda Polic et al, 1991
France - Corsica	human	48/100 000	Raoult et al, 1985
France	human	18% of 325	Raoult et al, 1987
France – Marseille	human	24.2/100 000	Raoult et al, 1993
Greece	human	18.1% of 337	Gourgouli et al, 1992
Greece	human	7.9% of 1584	Daniel et al, 2002
Italy	dogs	85% of 55	Mansueto et al, 1984
Italy	horses	42%	Rosa et al, 1987
Italy	human	10.4% of 241	Federico et al, 1989
Italy	dogs	35.5% of 163	Masoero et al, 1991
Portugal	dogs	85.6% of 104	Bacellar et al, 1995a
Portugal	human	1 000 cases/year	Oliveira et al, 1999
Slovenia	human	20% of 315	Novakovic et al, 1991
Spain	human	73.5% to 82%	Herrero et al, 1989
Spain	dogs	93% overall	Herrero et al, 1989
Spain	human	11.6% of 200	Espejo Arenas et al, 1990
Spain	dogs	36.8% of 103	Espejo Arenas et al, 1990
Spain	human	73.5% of 400	Ruiz Beltran et al, 1990
Spain	dogs	58.6% of 58	Herrero et al, 1992
Spain	human	8% of 150	Segura Porta et al, 1998
Spain	dogs	26.1% of 138	Segura Porta et al, 1998

*R. sanguineus* attached to dogs brought back from endemic countries. Within the endemic areas, the incidence of *R. conorii* or Mediterranean spotted fever may vary considerably from one area to another, depending on factors such as the distribution and density of dog populations and, consequently, of the dog tick vectors.

The importance of MSF in Europe is determined mainly through retrospective surveys of the prevalence of antibodies in man and dogs in various areas of the continent, as well as by clinical reports of individual cases.

Inasmuch as the reporting of cases of MSF is not obligatory in all countries of Europe, information on the overall occurrence and incidence of the infection is largely dependent on a review of scientific literature reporting the results of surveys. As a result, public health services may not necessarily be aware of the burden of the disease in their countries and, consequently, funds and efforts devoted to the control of the tick vectors or their dog hosts may be inadequate. Table 12 provides a partial review of the incidence of infections/antibodies found in surveys carried out in Europe:

The surveys listed in the above table are not exhaustive, presenting only examples of selections of surveys from endemic countries. Nevertheless, it can be seen that the serological prevalence rates in most surveys of humans and dogs indicate that the incidence of infection is quite high, although this may be due to surveys being carried out in areas that are at high risk of transmission, or among human populations that are particularly at risk to MSF, such as agricultural workers. Overall, the infection is widespread in southern Europe and is almost certainly underdiagnosed, due to the lack of familiarity of physicians with the disease or the difficulties encountered in carrying out serological surveys. The disease clearly represents an important public health burden whose magnitude is greater than the attention currently being given to its prevention and control. Furthermore, ecological changes are causing an increase in endemic areas, and climate change may favor an increase in the range of the infection. Companion dog populations are growing in many cities of Europe, and this has resulted in an increase in the incidence of urban MSF. In rural areas, dogs are common on farms, and human association with them and consequently their tick ectoparasites is close, thus resulting in the frequent transmission of MSF in endemic areas. In the late 1970s, some regions of Italy (Lazio, Liguria, Sicily, Sardinia) registered what was considered an extraordinary epidemiological event, the endemoepidemic expansion of Boutonneuse fever, of which only about thirty cases a year had been seen previously. By 1981, the infection was showing an increase; 864 cases were notified in 1979, although it was considered that the real incidence of the disease was much greater. It does not appear that this phenomenon has previously occurred in the Mediterranean. The author (Scaffidi, 1981) presumed that ecological changes involving carrier ticks were the reason for the increase. Although previously thought to be a relatively benign infection, serious forms of the disease, including encephala-

litis, do occur. While such cases are infrequent, they are associated with a high mortality rate when they do occur (Parra et al, 2002). When treatment is delayed as a result of a failure to make a timely diagnosis, or when there are underlying risk factors in the patient, the disease can be quite severe (Chaumentin et al, 1997).

In the former Soviet Union, an outbreak of Mediterranean spotted fever due to infection with *R. conorii* occurred in Crimea from 1947 to 1957. Only sporadic cases of the disease were reported until 1995, when the incidence of Mediterranean spotted fever increased in central Crimea, with 40 cases in 1996 and more than 70 in 1997. Most cases occurred in the summer, when the *Rh. sanguineus* nymphs were active. A survey showed that 8% of the *Rh. sanguineus* studied contained *R. conorii* DNA, providing further evidence that a Mediterranean spotted fever outbreak had occurred in the region (Rydkina et al, 1999). This report considerably extends the area in which the infection may be endemic, and further surveys in the region should be carried out concerning endemicity in the countries that have reported clinical cases, especially among persons (and their dogs) who have not traveled to endemic areas.

### **Other spotted fever rickettsiae**

With the availability of improved diagnostic techniques and immunological methods, other tick-borne rickettsial agents are being detected and identified in Europe in humans, ticks and mites. Several new rickettsioses have been described in Europe in the last decade, the species described below amongst them.

#### ***Rickettsia aeschlimannii***

*Rickettsia aeschlimannii* was first isolated from *Hyalomma marginatum marginatum* ticks collected in Morocco. Identical PCR-RFLP profiles have, however, been found in *H. marginatum marginatum* from Portugal and *H. marginatum rufipes* from Zimbabwe, suggesting that the distribution of this rickettsia reaches from the Mediterranean to southern Africa (Beati et al, 1997). Although one case was imported into France from Morocco, no autochthonous cases have been reported in Europe.

#### ***Rickettsia helvetica***

*Rickettsia helvetica* was first isolated from *I. ricinus* in Switzerland in 1979; at that time it was recognized as a new and hitherto undescribed spotted fever agent and called the "Swiss agent" (Burgdorfer et al, 1979). This agent was later identified as a new member of the spotted fever group of rickettsiae and given the name *R. helvetica* (Beati et al, 1993). This new species of rickettsia was later isolated from *I. ricinus* in Puy-de-Dome, an area in central France where a high prevalence of non-specific rickettsia antibodies had already been found (Parola et al, 1998). The species has also been isolated from *I. ricinus* in different regions of Switzerland (Beati et al, 1994).

In a serological survey in Sweden which examined 748 *I. ricinus* collected in the southern and central part of the country, 13 (1.7%) of these ticks tested positive for rickettsia; no species of the genus *Rickettsia* had previously been found in Scandinavian ticks, nor has any case of rickettsial infection in humans or animals been previously reported. Sequencing showed that isolations were apparently identical to *R. helvetica*, (Nilsson et al, 1997) and that the species was now endemic in the country. The species was not at first linked with human disease, but an investigation was made of two young Swedish men who died of sudden cardiac failure during exercise; they both showed signs of perimyocarditis similar to those described in rickettsial disease. The examination showed chronic interstitial inflammation and the presence of rickettsia-like organisms predominantly located in the endothelium. As *R. helvetica* transmitted by *I. ricinus* ticks is the only non-imported rickettsia found in Sweden, it may, therefore, be an important pathogen in the aetiology of perimyocarditis, and it may result in sudden unexpected cardiac death in young people (Nilsson et al, 1999b). The identification of the causative agent in the cases described above was confirmed as *R. helvetica* in a DNA study of the rickettsiae isolated from a large number of *I. ricinus* ticks in the country (Nilsson, 1999a). In August 1997, a 37-year-old man living in eastern France was found to have seroconverted to *R. helvetica* four weeks after the onset of an unexplained febrile illness. Results of a serosurvey of forest workers from the area where the patient lived showed a 9.2% seroprevalence against *R. helvetica* (Fournier et al, 2000) amongst them. Studies were also carried out in Italy in view of the abundant populations of *I. ricinus* attacking man in that country. Beninati et al (2002) studied 109 *I. ricinus* ticks collected in north and central Italy; PCR examinations were performed and nine ticks positive for rickettsia were found. Among them, no less than three different spotted fever groups of rickettsiae were revealed, including *R. helvetica*. These results raise the possibility that species other than *R. conorii* are involved in rickettsial diseases in Italy, and they demonstrate that tick species other than *R. sanguineus* may be involved as vectors.

The studies reviewed above indicate that *R. helvetica* is widespread throughout Europe and may be the cause of more clinical disease and even mortality than currently recognized. In view of the serious illness that may be associated with *R. helvetica* infections, the fact that the infection is being found in an increasing number of countries is a matter of concern.

### ***Rickettsia massiliae***

In 1990, 17 adult *Rhipicephalus turanicus* ticks were collected in the south of France. Two spotted fever group rickettsiae, Mtu1 and Mtu5, were isolated from the hemolymphs of two of these ticks (Beati et al, 1992); these isolations were later recognized as a new species of the spotted fever group and were given the name *Rickettsia massiliae*. PCR analysis showed the stains to be distinct from all previously recognized spotted fever group rickettsiae (Beati and Raoult, 1993).

*R. massiliae* was later isolated from *R. sanguineus* in Greece (Babalís et al, 1994) and from the same species in Catalonia, Spain (Beati et al, 1996) and Portugal (Bacellar et al, 1995c). It has most recently been isolated from a few *R. sanguineus* in the Canton of Ticino in the south of Switzerland (Bernasconi et al, 2002). It can thus be stated that *R. massiliae* is widely distributed in Europe, but for the time being, its pathogenicity and public health importance remain unknown.

### ***Rickettsia slovaca***

*Rickettsia slovaca* was first isolated from *Dermacentor marginatus* ticks in Slovakia in 1968, and it has been implicated in human febrile illness (Sekeyova et al, 1998). *R. slovaca* has been reported in Armenia, Austria, the former Czechoslovakia, France, Germany, Hungary, Italy, Kazakhstan, Lithuania, Portugal, the Russian Federation, Spain and Switzerland. It was isolated in France from *Dermacentor marginatus* ticks in the south of the country in 1991 (Beati et al, 1993). Fifty-one partially engorged *Dermacentor marginatus* females were collected in March–April 1975 in southern Germany; four strains of rickettsiae were isolated from the ticks, and the authors concluded that the isolated strains are similar to and almost undistinguishable from *R. slovaca* (Rehacek et al, 1977). A rickettsia identical to *R. slovaca* was isolated from the ticks *Argas persicus* and *Dermacentor marginatus* collected in Oktemberyan in the Armenian S.S.R. in 1974 (Rehacek et al, 1977), and its presence in that country was later confirmed by PCR analysis (Balayeva et al, 1994). Antibodies to *R. slovaca* have been reported in *R. sanguineus* collected on the outskirts of Rome, Italy (Cacciapuoti et al, 1985). *R. slovaca* was isolated from 18 of 632 adult *D. marginatus* (Bacellar et al, 1995b) in Portugal and Hungary. It is likely that the rickettsia isolated from 7.2% of *Dermacentor marginatus* and 4.7% of *D. reticulatus* ticks in Hungary were of this newly recognized species as well, and the isolation represented the first rickettsiae of the spotted fever group found in that country (Rehacek et al, 1979). It has also been detected in man and isolated from *D. marginatus* in Austria (Bazlikova et al, 1977), as well as in *I. ricinus* in Lithuania (Tarasevich et al, 1981). The finding of *R. slovaca* in *Dermacentor* ticks in the Russian Federation and Kazakhstan has considerably extended the known distribution of this species eastward (Shpynov et al, 2001).

The pathogenic role of *R. slovaca* was first noted in 1997 in a patient with a single inoculation lesion of the scalp and enlarged cervical lymph nodes who had been bitten by a *Dermacentor* tick. The authors (Raoult et al, 2002) subsequently evaluated the occurrence of *R. slovaca* infections among patients living in France and Hungary who had presented with these symptoms. *R. slovaca* infections were confirmed by polymerase chain reaction (PCR) in 17 of 67 patients. Infections were most likely to occur in patients aged <10 years and in patients who had been bitten during the colder months of the year. The median duration of incubation for the disease was seven days. Fever was present in only two patients, and only one patient developed a rash. Sequelae included persistent asthenia (3 cases) and

localized alopecia (4 cases). Immunofluorescence and antibodies were detected in 50% of tested patients. *R. slovaca* was detected by PCR in three *Dermacentor* ticks obtained from patients. In 1996, a woman who had visited the Pyrenees mountains fell ill a week later with fever, arthralgia and fatigue. Before becoming ill, she found and removed a tick (*Dermacentor marginatus*) from her hair. She complained of severe headache and, on examination, was found to have a necrotic eschar on the occiput surrounded by a reddish halo, and four enlarged occipital lymph nodes. Direct evidence was found of *R. slovaca* in skin biopsy, and seroconversion was demonstrated to be specific for *R. slovaca* by Western blotting. *R. slovaca* was isolated from the tick removed from her scalp (Raoult et al, 1997). The patient appeared to have been infected by tick bite in Burgundy. The isolation of *R. slovaca* from an ill patient in France provides further evidence of its role as a human pathogen. *R. slovaca* was demonstrated both in the tick and in a biopsy from the patient by PCR. Clinical signs of infection consist of a skin lesion at the site of a tick bite on the scalp (often a dermacentor tick) and regional lymphadenopathy that may be painful. Fever and rash subsequently develop, and the acute stage of the disease can be followed by fatigue and residual alopecia at the site of the bite (Cazorla et al, 2003). A detailed study was made in Hungary from 1996 through 2000; data was collected on 86 patients with similar symptoms following a tick bite. Most patients showed enlarged regional lymph nodes and/or vesicular-ulcerative local reactions at the site of the tick bite, which was located on or near the scalp in 96% of instances. The time from the recognition of the tick bite to the first symptom varied between 0 and 55 (mean nine) days. A characteristic local reaction (eschar) was seen in 70 (82%) patients. The eschar may be surrounded by a circular erythema (18 cases, 21%). Other main symptoms include enlarged and sometimes painful lymph nodes in the region of the tick bite, characteristically in the occipital region and/or behind the sternocleidomastoideal muscle. The most frequent general symptoms were low-grade fever, fatigue, dizziness, headache, sweat, myalgia, arthralgia, and loss of appetite. Without treatment, the symptoms were seen to persist for as long as 18 months. One of the patients reported symptoms suggestive of encephalitis. The infection occurs most commonly in young children (age range: 2–57 years, mean: 12.6 years, 63% less than 10 years of age). A predominance of females was registered (50/36). Doxycycline treatment can shorten the usually benign illness. *R. slovaca* PCR gave positive results from skin or lymph node biopsy samples in 10/13 (77%) patients (Lakos, 2002).

*R. slovaca* is widely distributed in Europe, and the number of infections and illnesses is probably much greater than reported in the literature reviewed above. As is the case with the other rickettsial infections reviewed here, correct diagnosis by a physician requires a degree of suspicion that a tick-borne rickettsial infection is a probable cause of infection, yet widespread awareness of the rickettsial infections is absent.

***Rickettsia monacensis***

*Rickettsia monacensis* was isolated from a specimen of *I. ricinus* collected in the English Garden Park in Munich, Germany. Analysis demonstrated that the isolate was of a spotted fever group (SFG) rickettsia closely related to several yet-to-be-cultivated rickettsiae associated with *I. ricinus*. *R. monacensis* joins a growing list of SFG rickettsiae that colonize ticks but whose infectivity and pathogenicity for vertebrates are unknown (Simser et al, 2002). There have been no other reports of this species to date.

***Rickettsia mongolotimonae***

*Rickettsia mongolotimonae* was first isolated from *Hyalomma asiaticum* collected in Inner Mongolia in 1991 and described and named in 1996. The first case reported in France was initially suspected to be imported (Raoult et al, 1996). However, when a second case due to the same agent occurred in Marseille, France, it appeared that the disease might be more common than previously presumed around the city, and that it may represent a new clinical entity with a broader geographic distribution than previously documented (Fournier et al, 2000). The identity of the vector in southern France remains unknown.

An agent given the name Israeli Spotted Fever belonging to the *R. conorii* complex and transmitted by *R. sanguineus* (Wolach et al, 1989) was isolated from ticks and humans in Israel. It was first suspected that its distribution was limited to that country (Goldwasser et al, 1974). However, the finding of three cases of this disease in Portugal and its isolation from *R. sanguineus* in Sicily, Italy, (Giovanni et al, 2003) indicates that the geographic distribution of Israeli spotted fever is wider than originally thought and includes the Iberian Peninsula. Because initial signs and symptoms of the disease are particularly uncharacteristic of the spotted fevers, and appropriate treatment may be delayed by a failure of timely diagnosis, this rickettsia can cause life-threatening disease; two of the three cases reported in Portugal led to death after hospitalization despite intensive treatment (Bacellar et al, 1999). The clinical course of Israeli spotted fever is more severe than that of boutonneuse fever, from which it differs in having a very low proportion of cases with eschar at the site of the tick-inoculation (Walker et al 1995). In view of the deaths associated with this infection in Israel (Shaked et al, 1994) and Portugal, the appearance of this strain in Europe is a matter of concern.

**Spotted fever summary**

Spotted fever group infections in Europe are widespread, and there is evidence that the incidence of these infections is increasing. This rise is due, in part, to ecological changes that encourage greater man-tick contact. The growing dog population in Europe, both pet and feral, has resulted in higher densities of the dog-tick vectors and hence, the increased transmission of MSF. The recognition of new species and new strains of spotted fevers further increases the public health

importance of this group. It is possible to prevent infections of MSF by the control of dog ticks. To ensure timely diagnosis and treatment, physicians must be aware of the possibility of illnesses arising from a member of this group. For those species in which infections may be the cause of mortality, timely and adequate treatment is clearly more urgent.

## EHRlichiosis

Ehrlichioses are diseases caused by rickettsia-like organisms, which are extremely small, intracellular bacteria belonging to the family Rickettsiaceae, genus *Ehrlichia*. Ehrlichiosis was first described in Algerian dogs in 1935. Human ehrlichiosis is a recently recognized disease. The first diagnosed case occurred in the USA in 1986 in a 51 year-old man from Detroit, Michigan who had been exposed to ticks in a rural area of Arkansas. In 1990, the agent of human ehrlichiosis was isolated from the blood of a U.S. Army reservist at Fort Chaffee, Arkansas (Dawson et al, 1991). The newly recognized organism was named *E. chaffeensis* (Anderson et al, 1991). The two recognized ehrlichial diseases are human monocytic ehrlichiosis (HME) and human granulocytic ehrlichiosis (HGE). The causative agent of HGE in man is *E. equi*, first reported in the USA in 1994 and now reported from North America, Europe and the Middle East.

The number of species in the genus *Ehrlichia* is growing. Prior to the discovery of *E. chaffeensis*, *E. sennetsu* was the only species known to infect humans. *E. sennetsu* causes Sennetsu fever, a mononucleosis-type illness first described in 1954 and occurring primarily in Japan. Sennetsu fever is very rare, and is usually benign, with no fatalities reported to date. The other species of *Ehrlichia* cause veterinary disease and include *E. canis* (canine ehrlichiosis), *E. ewingii* (canine granulocytic ehrlichiosis), *E. risticii* (Potomac Horse Fever), *E. equi* (disease in horses), *E. phagocytophila* (disease in sheep and cattle), as well as a few others (Rikihisa 1991).

Symptoms of human ehrlichiosis appear within 1-21 (average 7) days following infection and resemble those of Rocky Mountain spotted fever (RMSF). The spectrum of disease may range from a mild or asymptomatic illness to a severe, life-threatening condition. The characteristic clinical features are high fever and headache, but may also include malaise, myalgias, nausea, vomiting, and anorexia. A rash is more rarely seen (present in only about 20% of cases). Since *E. chaffeensis* invades white blood cells, the body's immune system is adversely affected. This lessens the body's ability to fight other infections. In those patients with severe complications, acute renal or respiratory failure is most common. There have been a small number of fatalities in the USA (Dawson et al, 2002; Eng et al, 1988), and a number of fatal cases have been described in Europe (Hulinska et al, 2002).

The first human case of ehrlichiosis in Europe was reported in Portugal (Morais, 1991). As shown in Table 13, various species of *Ehrlichia* have now been reported from many countries in Europe; the listing does not include all detec-

tions of *Ehrlichia* species in Europe, but presents a review of the countries, hosts and vectors that have been identified as the infectious agents.

### **The public health importance of ehrlichiosis**

Ehrlichiosis is recognized as widespread in Europe, and, as with another tick-borne infection, Lyme disease, its incidence appears to be increasing and spreading geographically. In several instances, ticks have been found infected with both agents. While the increased incidence of ehrlichial infections may be due in part to improved recognition and diagnosis of the disease, changing ecological conditions that favor increased human-tick contact must be considered a major factor. As with the other infections which have been discussed, awareness of the potential for infections by these agents is important, as delays in diagnosis and treatment can lead to adverse outcomes, including mortality. A greater awareness of the potential severity of ehrlichiosis is needed by physicians to ensure that proper treatment is initiated early in the course of the disease. Surveillance of human and animal cases can provide guidance as to areas where the risk of infection is high and where tick control measures are necessary. As has been seen above, coinfections of *Ehrlichia* species and Lyme disease are common and represent a diagnostic challenge.

### **Q Fever**

Q Fever is a worldwide zoonoses caused by *Coxiella burnetii* which is an obligate intracellular parasite. As with all rickettsiae, humans are dead-end hosts for *C. burnetii* and play no part in the maintenance of the organism in nature. Q fever was first identified as a separate syndrome in 1937 in Australia. The disease usually takes the form of an acute atypical lung pneumonia disease, but subclinical or non-typical forms are also known. It is usually associated with a high fever of 40°, which may persist for one to three weeks or more. Unlike other rickettsial diseases, no cutaneous exanthema is seen. About 1/3 of the patients with protracted Q fever develop hepatitis, while endocarditis is more serious but uncommon. Q fever is rarely fatal, with a mortality rate of about 1% in untreated patients and even lower amongst treated patients. Most of the literature published on Q fever deals with its prevalence in animal populations rather than in humans. The quality of surveillance and its reporting varies greatly from country to country, depending on local physicians' awareness of the possible occurrence of the disease, as well as the degree to which they are familiar with the diverse clinical presentations of a Q fever infection. There are considerable variations in the clinical presentations of the infection in humans from one country to another, perhaps due to strain differences. Only some 50 cases a year of Q fever are reported in Portugal (Oliveira and Corte Real, 1999 *ibid*), although antibodies to *C. burnetii* in dogs may be quite high in some locations. In the United Kingdom and Ireland, between 100 and 200 cases of human Q fever are encountered annually. The majority of cases are sporadic, but occasionally large outbreaks occur. Direct con-

Table 13. Reports on the presence of ehrlichiosis in Europe

Country	Species	Host	Reference
Belgium	<i>Ehrlichia chaffeensis</i>	humans	Guillaume et al, 2002
Bulgaria	<i>Ehrlichia</i> sp	humans	Christova, Dumler, 1999
Bulgaria	<i>E. phagocytophila</i> *	ticks	Christova et al, 2001
Czech Rep.	<i>E. chaffeensis</i>	humans	Hulinska et al, 2001
Czech Rep	<i>E. phagocytophila</i>	humans	
Czech Rep.	<i>E. phagocytophila</i>	humans	Zeman et al, 2002
Czech Rep.	<i>E. phagocytophila</i>	humans, deer, boar, birds	Hulinska et al, 2002
Denmark	<i>E. chaffeensis</i>	humans	Lebech et al, 1998
Denmark	<i>E. equi</i>	dogs	Ostergard, 2000
Denmark	<i>E. chaffeensis</i>	humans	Skarphedinsson et al 2001
France	<i>E. equi</i> <i>E. phagocytophila</i>	<i>I. ricinus</i> <i>I. ricinus</i>	Parola et al, 1998
Germany	<i>E. canis</i>	dogs	Reider & Gothe, 1993
Germany	<i>E. canis</i>	dogs	Gothe, 1999 ibid
Germany	<i>E. Phagocytophila</i>	humans	Fingerle et al, 1997, 1999
Germany	<i>E. Phagocytophila</i>	<i>I. ricinus</i>	Baumgarten et al, 1999
Germany	<i>Ehrlichia</i> sp	humans	Hunfeld & Brade, 1999
Germany	<i>A. phagocytophila</i> *	<i>I. ricinus</i>	Hildebrandt et al, 2003
Greece	<i>E. chaffeensis</i>	humans	Daniel et al, 2002
Ireland	<i>E. phagocytophila</i>	cows	Purnell et al, 1978
Italy	<i>E. canis</i>	dogs	Buonavoglia et al, 1995
Italy	<i>E. phagocytophila</i>	humans	Nuti et al, 1998
Italy	<i>E. chaffeensis</i>	humans	Santino et al, 1998
Italy	<i>E. phagocytophila</i>	<i>I. ricinus</i>	Cinco et al, 1998
Netherlands	<i>Ehrlichia</i> sp	<i>I. ricinus</i>	Schouls et al, 1999
Netherlands	<i>E. phagocytophila</i>	cows	Siebinga & Jongejan, 2000

Norway	<i>E. phagocytophila</i>	moose, <i>I. ricinus</i>	Jenkins et al, 1998
Norway	<i>E. spp</i>	humans	Bakken et al, 1996
Norway	<i>Anaplasma phagocytophila</i> *	sheep	Stuen et al, 2002
Poland	<i>Ehrlichia</i> sp	<i>Microtus arvalis</i>	Bajer et al, 1999
Poland	<i>E. phagocytophila</i>	<i>I. ricinus</i>	Grzeszczuk et al, 2002
Portugal	<i>E. canis</i>	humans	Morais et al, 1991 ibid
Portugal	<i>E. canis</i>	dogs	Bacellar et al, 1995a ibid
Russian Federation	<i>E. phagocytophila</i>	<i>I. ricinus</i>	Alekseev et al, 2001
Russian Federation	<i>E. phagocytophila</i>	voles	Telford et al, 2002
Slovenia	<i>E. equi</i>	humans	Lotric-Furlan et al, 1998
Slovenia	<i>Ehrlichia</i> sp	humans	Cizman et al, 2000
Slovenia	<i>E. phagocytophila</i>	humans	Lotric-Furlan et al, 2001
Spain	<i>E. phagocytophila</i>	<i>I. ricinus</i>	Oteo et al, 2000
Spain	<i>E. phagocytophila</i>	humans	Oteo et al, 2001
Sweden	<i>E. chafeensis</i>	humans	Bjoersdorff et al, 1999a
Sweden	<i>E. equi</i>	humans	Bjoersdorff et al, 1999b
Sweden	<i>E. equi</i>	<i>I. ricinus</i>	Gustafson & Artursson, 1999
Sweden	<i>E. equi</i>	horses	Artursson et al, 1999
Switzerland	<i>E. phagocytophila</i>	cows	Pusterla et al, 1997
Switzerland	<i>E. canis</i>	dogs	Pusterla et al, 1998a
Switzerland	<i>E. phagocytophila</i>	dogs	Pusterla et al, 1998a
Switzerland	<i>E. phagocytophila</i>	humans	Pusterla et al, 1998b
Switzerland	<i>E. equi</i>	<i>I. ricinus</i>	Liz et al, 2000
Switzerland	<i>E. phagocytophila</i>	rodents	Liz et al, 2000
United Kingdom	<i>E. phagocytophila</i>	cows	Purnell & Brocklesby, 1978
United Kingdom	<i>E. phagocytophila</i>	humans	Sumption et al, 1995
United Kingdom	<i>E. phagocytophila</i>	<i>I. ricinus</i>	Ogden et al, 1998
United Kingdom	<i>E. Phagocytophila</i> <i>I. trianguliceps</i>	roe deer	Alberdi et al, 2000

\* formerly Ehrlichia phagocytophila

tact with farm livestock or other animals cannot always be established (Aitken, 1987). In Germany, the average annual Q fever incidence nationwide from 1979 to 1989 was 0.8 per million, whereas from 1990 to 1999, 1.4 per million. The mean annual incidence from 1979 to 1999 ranged from a minimum of 0.1 per million in several northern states to 3.1 per million in Baden-Württemberg in the south. Forty outbreaks have been documented since 1947, 24 in which sheep were implicated as the source of transmission. The seasonality of community outbreaks has shifted from predominantly winter-spring to spring-summer, possibly because of changes in sheep husbandry. The location of recent outbreaks suggests that urbanization of rural areas may be contributing to an increase in Q fever (Hellenbrand et al, (2001).

Q fever is a zoonoses. The most important sources of infection are cattle, sheep and goats; transmission to man may occur by vectors (ticks), but more often it is passed on by carriers such as aerosols, non-pasteurized milk and dairy products. A large proportion of cases occur among farm and abattoir workers. The infective agent is transmitted among domestic animals either by tick bites or by contact with infected excreta (Aitken et al, 1987). In many endemic situations in Europe and elsewhere, the role of ticks in the transmission of human, and especially animal, infections of *C. burnetii* must be taken into account. It is, however, difficult to determine with any accuracy the extent to which ticks play a role in the transmission of Q fever in Europe, as compared to the extent to which the reported cases are due to exposure to sheep and cattle. Ticks may play a role in the silent maintenance of the rickettsiae, transmitting the agent from one animal to another (Walker and Fishbein, 1991). Many large and small mammals and birds have been found infected, and they may also play a role in the maintenance of the infection. The seroprevalence of *C. burnetii* in a population of wild rats, *Rattus norvegicus*, ranged from 7 to 53% in four Oxfordshire and nine Somerset farmsteads in the UK (Webster et al, 1995). On the other hand, in an area of southern Bavaria in Germany, where 12% of 1095 cattle tested seropositive for *C. burnetii*, neither rodents nor ticks in the same area were positive, and the authors assumed that an independent natural cycle involving only cattle maintained the infective agent (Rehacek et al, 1993). Further studies on the role of animal reservoirs in maintaining Q fever are thus important.

### **Tick vectors of Q fever**

Ticks play a role not only of vectors but reservoirs of *C. burnetii*. Much has yet to be ascertained as to their role in transmission of the infection from one animal to another, as well as their role in transmitting the disease to humans. Nevertheless, many surveys concerning the degree to which ticks carry *C. burnetii* in Europe have been carried out, the most important of which will be reviewed below. In a survey in Slovakia in which almost 7,000 ticks were examined, six strains of *C. burnetii* were recovered from *I. ricinus*, the remaining ones from single pools

of *D. reticulatus*, *D. marginatus*, *H. concinna* and *H. inermis*. In addition to the previous recovery of *C. burnetii* from *H. punctata*, the agent was isolated from all important ticks living in Slovakia. The agent was found in tick habitats throughout the entire country, regardless of the latitude and altitude (Rehacek et al, 1991). Despite the number of tick species found positive, the incidence of Q fever in the country was low. In surveys in Bulgaria, antibodies to *C. burnetii* were found in *Ixodes ricinus*, *D. marginatus*, *Rhipicephalus bursa* and *Hyalomma plumbeum* (Aleksandrov et al, 1994). PCR surveys in Cyprus found *C. burnetii* in *R. sanguineus* and *Hyalomma* spp collected on the island (Spyridaki et al, 2002). Liebisch and Rahman (1976) reviewed the importance of *D. reticulatus* and *D. marginatus* in Germany, and they concluded that *D. marginatus* has a role in the epidemiology of Q fever. In Lithuania, Tarasevich et al (1981, *ibid*) reported finding *C. burnetii* in *I. ricinus*.

It is suspected that *R. sanguineus* was introduced into Switzerland in the 1990s; in a survey carried out in the southern part of the country (Canton Ticino), Bernasconi et al (2002 *ibid*) identified the presence of *Coxiella* spp. (probably *C. burnetii*) both in *R. sanguineus* and *Rhipicephalus turanicus*. *R. sanguineus* in the same area were also infected by *Rickettsia massiliae*. The authors observed that due to climatic changes which may occur as a result of global warming, imported tick species may adapt to new area, and they might be considered as epidemiological markers for a number of infectious agents transmitted by them. It must be added that the finding of *C. burnetii* in a given tick population does not necessarily indicate the vectorial importance of the species, nor its role in transmission as compared to direct contact with animals.

### The public health importance of Q fever

The overall public health importance of Q fever in Europe is no longer great. Its incidence is low in most countries, and mortality is quite uncommon. Improved working conditions on farms have tended to reduce exposure to the infectious agent. Yet the infectious agent remains widely endemic in Europe, and the putative vectors of *C. burnetii* are widespread both in rural and urban areas. Raoult et al (2000), who carried out in France what is perhaps the largest series of examinations of both Q fever patients and of sera (1 383 patients hospitalized in France for acute or chronic Q fever), in an analysis based on 74 702 sera in their reference center, concluded that Q fever is a protean disease and that it is grossly underestimated. They noted that some of the clinical manifestations have only recently been reported, such as those of Q fever during pregnancy, chronic vascular infection, osteomyelitis, pericarditis, and myocarditis. Their data confirmed that chronic Q fever is mainly determined by host factors and demonstrated for the first time that host factors may also play a role in the clinical expression of acute Q fever. Because *C. burnetii* can survive for long periods in the environment, it poses a continuing health hazard once it is disseminated. Q fever usually occurs

sporadically, but large outbreaks are frequently observed throughout the world and with a certain degree of mortality (Sawyer et al, 1987). Finally, the increasing trend in the incidence of other tick-borne diseases such as TBE and Lyme disease have resulted, in part, from ecological changes that have favored increases in tick population densities. Inasmuch as some of the vectors of these two diseases are also vectors/reservoirs of *C. burnetii*, close surveillance must be maintained on the trends of infection with Q fever in Europe in order to note any similarities.

## Babesiosis

Human babesiosis is an emerging tick-borne zoonotic disease which now occurs in significant numbers in Europe. It is an intraerythrocytic parasitic infection caused by protozoa of the genus *Babesia* and transmitted through the bite of an *Ixodes* tick. The disease most severely affects elderly patients, those who are immunocompromised, or those who have undergone splenectomy. Babesiosis is usually an asymptomatic infection in healthy individuals. Babesial parasites (and those of the closely related genus *Theileria*) are some of the most ubiquitous and widespread blood parasites in the world, second only to the trypanosomes, and consequently, they have considerable worldwide economic, medical, and veterinary impact (Homer et al, 2000).

The first published case of babesiosis occurred in Europe. Babesiosis as a disease was first described in Romanian cattle in 1888, and the first human infection caused by *Babesia* was described in the former Yugoslavia in 1957 from an asplenic farmer. Many species of *Babesia* have now been reported from Europe (Gorenflot et al, 1998). Many hundreds of cases have been reported in the United States, most of them caused by *Babesia microti*. Human babesiosis in Europe is caused by a different species of *Babesia* than in North America, *i.e.* *Babesia divergens*, and is frequently the cause of a much more serious disease, particularly in asplenic persons. In the USA, mild to severe disease resulting from *Babesia* infections has also been reported from non-splenectomised patients. Human babesiosis is relatively rare in Europe, but cases have been reported from the former Yugoslavia, Ireland, France, Portugal, the Russian Federation, Switzerland and the United Kingdom. Most of the human cases have occurred in France, Ireland and the United Kingdom, and antibodies to the infection have been detected in Turkey. In Europe, it is symptomatic in a large proportion of the infections, and may often be fatal (Rowin, 1984). Disease manifestations range from asymptomatic infection in healthy individuals to severe illness and death in those who are asplenic, elderly, or immunocompromised. Splenectomy was the main risk factor, found in 86% of patients. Clinically, babesial infections appear suddenly with a non-periodic high fever, shaking, chills, sweat, headache, myalgia and jaundice induced by intravascular hemolysis. The mortality rate was higher than 50% (Brasseur and Gorenflot, 1996), and, unfortunately, the effect of treatment is poor in splenectomized patients, especially if treatment is delayed (Hohenschield,

1999). All of the cases which have involved bovine *Babesia*, *B. divergens*, have occurred in individuals who were splenectomized. Canine babesiosis is caused by *B. canis* and *B. gibsoni*; *B. motasi* is found in sheep, and *B. bigemina* and *B. divergens* are cattle parasites.

### Tick vectors of babesiosis

The tick vectors of babesiosis in Europe include both the *Ixodes* and *Dermacentor* species. In Western Europe, the most frequent vector species are *I. ricinus* and *D. marginatus*. In the Russian Federation, *I. trianguliceps* has been found infected with *B. microti* (Telford et al, 2002 *ibid*). In Germany and France, the ticks *Dermacentor reticulatus* and *D. marginatus* are vectors of *Babesia canis* (Zahler et al, 1996). In Germany, France, Ireland, and the United Kingdom, *I. ricinus* is the primary vector. In Spain, *I. hexagonus* is thought to be the vector of *B. microti*-like infections in dogs, a parasite which has now been identified as *Theileria annae* (Camacho et al, 2003). Sixl et al (1989) provided evidence in Austria of the presence of *C. burnetii* in hedgehogs (*Erinaceus europaeus*), and the role of *I. hexagonus* and *I. ricinus* as vectors of the causative agent. In Switzerland, *B. microti* DNA has been detected in *I. ricinus* in the eastern part of the country; 1.5% of 396 human residents in the region had antibodies to *B. microti*. These observations constitute the first report demonstrating *B. microti* in a human-biting vector, associated with evidence of human exposure to this agent in a European site (Foppa et al, 2002). In Poland, however, a high infection rate of DNA of *B. divergens* and *B. microti* has also been found in *I. ricinus* (Skotarczak and Cichocka, 2001). Experimental studies have shown that strains of *B. microti* from the USA would infect and be readily transmitted by *I. ricinus* from one gerbil to another. This suggests that European *B. microti* strains are probably infective for *I. ricinus*, supporting the view that infection of humans with European *B. microti* may be a regular occurrence (Gray et al, 2002). Studies in Slovenia examined questing *I. ricinus* adult and nymphal ticks collected in various parts of the country; when tested for the presence of babesial parasites with a PCR assay; thirteen of 135 ticks were found to contain babesial DNA. Sequence determination and analysis of amplified portions of nss-rDNA revealed their identity with *Babesia microti* and a high degree of homology with *Babesia odocoilei* and *B. divergens*. The authors considered that the results of this study represent the first genetic evidence of *B. microti* and *B. divergens*-like parasites in *I. ricinus* ticks in Europe (Duh et al, 2002).

*Babesia* species have also been isolated from a number of small, wild mammals in Europe, as listed in Table 14

### The public health importance of babesiosis

The importance of Babesiosis in Europe lies not so much in the relatively small number of clinical cases which have so far been diagnosed and reported but in the

**Table 14. Small mammals found positive for Babesia species in Europe**

Country	Host species	Parasite species	Reference
Austria	<i>Pitymys subterraneus</i> , <i>M. agrestis</i> , <i>Clethrionomys glareolus</i> , <i>M. arvalis</i> , <i>A. flavicollis</i>	<i>B. microti</i>	Sebek et al, 1980
Czech Rep.	<i>Myotis emarginatus</i> , <i>Myotis myotis</i> , <i>C. glareolus</i> , <i>Microtus arvalis</i> , <i>Microtus agrestis</i>	<i>B. microti</i>	Sebek, Z., 1975
Germany	<i>M. agrestis</i>	<i>B. microti</i>	Walter & Liebisch, 1980
Poland	<i>C. glareolus</i>	<i>B. microti</i>	Karbowiak & Sinski, 1996
Poland	<i>M. agrestis</i> , <i>M. oeconomus</i>	<i>B. microti</i>	Karbowiak et al, 1999
Russian Federation	<i>C. glareolus</i>	<i>B. microti</i>	Telford et al, 2002 ibid
Switzerland	<i>Apodemus sylvaticus</i> , <i>A. flavicollis</i> , <i>C. glareolus</i>	<i>Babesia spp</i>	Aeschlimann et al, 1975
United Kingdom	<i>C. glareolus</i>	<i>B. microti</i>	Randolph, S. E., 1995

severity of the disease which often develops in infected persons. The surveys cited above show that emerging babesial infections in both man and animals are widespread throughout the European continent. Spielman (1994), in considering the emergence and spread of Lyme disease and babesiosis in the USA and Europe, believed that the emergence derives from the recent proliferation of deer populations, with the abundance of deer deriving in turn from the process of reforestation now taking place throughout the North Temperate Zone of the world. Residential development seems to favour small tree-enclosed meadows interspersed with strips of woodland, a “patchiness” prized by deer, mice, and humans. As a result, increasingly large numbers of people live where the risk of Lyme disease and babesiosis is intense. The agents of these infections that once were transmitted enzootically by an exclusively rodent-feeding vector have become zoonotic. It is thus possible that the incidence of babesiosis in Europe may increase, as has been the case with other tick-borne diseases. Surveillance must be maintained in endemic areas to rapidly identify any increased incidence as a basis for control. As in other emerging diseases, physician awareness of the possible occurrence of babesiosis is important so as to enable rapid diagnosis and effective treatment.

## Tularemia

Tularemia is an infectious disease caused by the gram-negative pleomorphic bacterium *Francisella tularensis*. The name of the diseases relates to the description in 1911 of a plague-like illness in ground squirrels in Tulare County, California, and the subsequent work performed by Dr Edward Francis on its epidemiology. *F. tularensis* occurs worldwide in more than 100 species of wild animals, birds,

and insects. It produces an acute febrile illness in humans. The route of transmission and factors relating to the host and organism influences the presentation. Humans can become infected through diverse environmental exposures: bites by infected arthropods, handling infectious animal tissues or fluids, direct contact with or ingestion of contaminated food, water, or soil, and inhalation of infective aerosols. Untreated, tularemia has a mortality rate of 5–15%; this rate is even higher with the typhoidal form. Appropriate antibiotics lower this rate to about 1%.

A few hundred cases of tularemia are reported annually in the United States, although the majority of cases are likely unreported or misdiagnosed. In the United States, the frequency of tularemia has markedly decreased over the last 50 years, and a shift from its occurrence as a winter disease (usually from rabbits) to a summer disease (more likely from ticks) has been observed.

In Europe, a large outbreak of tularemia occurred in Kosovo in the early post-war period of 1999–2000. Epidemiological and environmental investigations were conducted to identify sources of infection, modes of transmission, and household risk factors. Case and control status was verified by enzyme-linked immunosorbent assay, Western blot, and microagglutination assay. A total of 327 serologically confirmed cases of tularemia pharyngitis and cervical lymphadenitis were identified in 21 of 29 Kosovo municipalities. Matched analysis of 46 case households and 76 control households suggested that infection was transmitted through contaminated food or water and that the source of infection was rodents. Environmental circumstances in war-torn Kosovo led to epizootic rodent tularemia and its spread to resettled rural populations living under circumstances of substandard housing, hygiene, and sanitation (Reintjes et al, 2002). By 5 February 2002, the Institute of Public Health in Pristina had reported 715 cases of tularemia since the onset of the outbreak on 1 November 2001. No deaths were reported.

According to the statistics of the International Animal Disease Office, (Office International des Epizooties, OIE), tularemia was diagnosed in 917 and 468 individuals in Finland and Sweden respectively in the year 2000. This infectious disease has been known to be endemic in both of these countries, particularly in hares and other small mammals, for some time. An extensive epidemic of tularemia with 529 cases, 400 of which were confirmed by laboratory tests, occurred in the northern part of central Sweden during the summer of 1981. The outbreak was of short duration and was restricted to certain communities within a narrow geographical area. It began in the middle of July and progressed during that month and August, with only sporadic cases seen in September and October. Over the two years preceding the outbreak, only three and seven cases respectively had been reported annually in Sweden. The infection was reported as being transmitted mainly by mosquitoes and most cases were ulceroglandular. The later cases reported in September and October were infections caught by contact

with hares or rodents. All age groups were affected, with a slight predominance of women and the 30–60 year age groups (Christenson, 1984). More cases of infection are being observed in eastern Europe, particularly Bulgaria, Hungary, the Russian Federation, and, to some extent, The former Yugoslav Republic of Macedonia and Slovakia. However, isolated cases are reported sporadically from other European countries. *F. tularensis* is said to be a potential pathogen for use in bio-terrorism and has qualities which make it suitable for use as a biological weapon: the human dose is relatively low, the pathogen is quite resistant in the environment, and diagnosis is difficult.

### Tick vectors of tularemia

In central and western Europe, *I. ricinus* is probably the most important vector, while *Dermacentor nuttalli* may be a vector in the Russian Federation. In a study on tick vectors of tularemia in the Czech Republic, 26 478 ticks were collected and examined in 935 pools, from which three strains of *Francisella tularensis* were isolated (one each from *I. ricinus* and *D. reticulatus* males in southern Moravia, and one from *D. marginatus*-engorged females collected from sheep in eastern Slovakia). *D. marginatus* and *D. reticulatus* represented new vector species for the former Czechoslovakia (Hubalek et al, 1990). A survey conducted from 1984 to 1993 in the region of Bratislava, the capital of Slovakia, collected 6 033 ticks, mostly adults of *D. reticulatus* (4 994) and *I. ricinus* (1 004), and 35 *Haemaphysalis concinna* nymphs. Out of 4 542 starving ticks, 34 *F. tularensis* strains were isolated from *D. reticulatus* (30), *I. ricinus* (3) and *H. concinna* (1). Natural infection with *F. tularensis* was further shown in 27 of 1 491 adult *D. reticulatus* fed on laboratory animals, rabbits and white mice (Gurycova et al, 1995).

Other arthropods are also involved in the transmission of tularemia organisms, although not to the same extent as ticks. Some species of deer and horse flies are proven vectors. In the original study of tularemia in the United States, transmission by the deer fly, *Chrysops discalis*, was demonstrated. Mosquitoes may be involved in transmission, at least in Scandinavia, as there have been several reports from Sweden of mosquitoes as vectors during outbreaks (Christenson, 1984 *ibid*, Eliasson et al, 2002).

### THE PUBLIC HEALTH IMPORTANCE OF TULAREMIA

The annual number of cases of tularemia is fairly high and the infection is widespread. It frequently appears as epidemic outbreaks, although these are usually not due to tick transmission. Due to the virulence of the infection and its broad geographical distribution, physician awareness of the disease and a good surveillance system are necessary. Although the disease is not of broad public health importance at this time, it may periodically take on considerable focal importance. Because of its facile transmission and relatively high mortality, tularemia is considered a potential weapon of bio-warfare.

## FILARIASIS INFECTIONS

### DIROFILARIASIS

The only filarial parasite in Europe that is occasionally transmitted to and infects man is canine dirofilariasis, caused by the zoonotic filarial species, *Dirofilaria immitis* and *D. repens*. *Dirofilaria* are becoming increasingly recognized worldwide as inadvertent human pathogens. The usual hosts of these infective nematodes are domestic and wild carnivores, including dogs, cats and foxes, whereas the nematode is transmitted by mosquitoes. In their canine and feline hosts, they are commonly known as dog heartworm.

Bancroftian filariasis is caused by the nematode parasite *Wuchereria bancrofti*, the most common human filarial infection throughout the world. In Europe, however, this is seen only as an imported disease. The last record of it within an area near continental Europe comes from Turkey in 1966 as the result of a survey carried out in Alanya, a port on the Mediterranean coast. In this survey, 0.6% of the surveyed inhabitants were parasite-positive, with *Culex molestus* as the vector. The antimalarial house sprayings being carried out at the time were reducing indoor resting mosquito densities (Ozdem, 1975), and there have been no further reports from Turkey or Europe of the presence of Bancroftian filariasis.

Canine subcutaneous and cardiopulmonary dirofilarioses have been found to be widely extended through the southern countries of the continent, whereas they are much less frequent or completely absent toward the north. Most of the epidemiological information gathered from studies on dogs and cats is tainted by methodological biases. In many of the studies, the samples were analyzed in veterinary clinics from big cities, and they are not representative of the global population. Moreover, in some cases, the methods applied did not detect microfilaremic infections. In Italy, Spain, France, Portugal and Greece, epidemiological studies have demonstrated the presence of both *D. immitis* and *D. repens* in domestic (dogs and cats) and wild carnivores (mainly foxes). The European country in which *Dirofilaria* spp. are most frequently found is Italy, and the northern limit in which these species have been reported is the area of Cherbourg, France (Doby et al, 1986). The diagnosis of dirofilariasis has been made in several countries of northern Europe, but in each case, these have resulted from infections received during stays in the southern endemic countries. The distribution of *Dirofilaria* worms is not homogeneous, since the highest prevalences occur in the valleys of rivers and in humid zones, where the environmental conditions are more favorable for the breeding of vectors. At present there is clear evidence that *Dirofilaria* infections are spreading in animal populations (Rossi et al, 1996). Mosquito den-

sity and a large number of microfilaremic dogs are the most important risk factors for the human population.

Human infection manifests with either subcutaneous nodules or lung parenchymal disease that may be asymptomatic. The significance of infection in humans is that pulmonary and some subcutaneous lesions are commonly labeled as malignant tumors requiring invasive investigation and surgery before a correct diagnosis is made. The pathology of the condition is associated with aberrant localization of immature worms that do not reach adulthood; therefore, microfilariae are almost always absent in the blood. The most commonly reported manifestation of human dirofilariasis worldwide is subcutaneous nodular disease, caused by *D. repens*, with more than 400 case reports in medical literature. Endemic foci for *D. repens* are found in southern and eastern Europe, Asia Minor, central Asia, and Sri Lanka.

Italy has the highest prevalence of human dirofilariasis in Europe (66% of total cases), followed by France (22%), Greece (8%), and Spain (4%). Cases of canine and human disease have been described in northern European countries, but these have all been the result of patient exposure during a southern European visit. Human dirofilariasis due to *D. immitis* appears to be less common in Europe than *D. repens*-induced subcutaneous disease. Dirofilariasis appears to be endemic in canine populations in several other areas of Europe from which human cases have also been reported, including Hungary, Portugal, Serbia, and southern Switzerland (Bucklar et al, 1998). The true prevalence of human exposure to and disease with *D. immitis* is underestimated because canine infection is widespread throughout the world and most infected people are asymptomatic.

A seroprevalence study of humans in Spain, where 33% of dogs are infected with *D. immitis*, revealed that 22% of the human population had developed antibodies of immunoglobulin G (IgG), 5.8%; immunoglobulin M (IgM), 3.5%; or immunoglobulin E (IgE), 12.6% isotypes. IgG seroconversion was most prevalent in people older than 60 years, while IgM seropositivity was most commonly observed in those younger than 19 years. The level of IgE also decreased with age. The authors concluded that repeated contact with *D. immitis* in this endemic population was common and began at an early age (Nissen and Charles, 2002).

*D. immitis* infection is usually associated with pulmonary lesions or radiologic coin lesions of the lung. There are isolated reports of *D. immitis* or *D. immitis*-like worms causing cutaneous or abdominal nodular disease and conjunctival disease.

*D. repens* infection is the most frequent and widespread dirofilariasis globally. The most common localization is a subcutaneous or submucosal nodule. Ophthalmic involvement is also described, and direct visualization of the worm can be made in the bulbar conjunctiva. Breast nodules due to *D. repens* are also commonly misdiagnosed as potential tumorous masses and are observed in hyperendemic areas for the parasite, particularly Italy and Sri Lanka. Imported cases

of breast *D. repens* have been reported in the United States, Canada, Japan, and Australia. Pulmonary and abdominal lesions due to *D. repens* have also been reported in endemic areas of Italy, France, and Greece.

### **Mosquito vectors of *Dirofilaria***

Mosquitoes of the genera *Aedes*, *Anopheles* and *Culex* are among the vectors of *Dirofilaria* in Europe. In the Piedmont region of Italy, four species (*Ae. caspius*, *An. maculipennis s.l.*, *Cx. modestus* and *Cx. pipiens*) play a major role in the transmission of canine filariasis in Piedmont. (Pollono et al, 1998). In the Ticino region of southern Switzerland, dirofilariasis was found to be quite common among dogs; of blood samples taken from 308 local dogs, 10.7% were circulating microfilariae for *D. immitis* and 5.5% for *D. repens*. Infective stages of *D. immitis* were observed in local strains of *Ae. geniculatus* and *Cx. pipiens*, following engorgement on a microfilaraemic dog. *Ae. vexans* was the most abundant mosquito species in the area (Petruschke et al, 2001).

### **The public health importance of dirofilariasis**

No fatality directly due to dirofilariasis has been recorded in medical literature. Infection is symptomatic in 38–45% of cases. The primary significance of infection in adults is the confusion and invariable radiologic misdiagnosis of a primary or metastatic lung tumor, which usually leads to thoracotomy with open lung biopsy or wedge resection of the lung to obtain the correct diagnosis. Infections can remain unidentified due to poor knowledge of the parasite on the part of physicians. As has been noted above, the parasite is widespread in carnivorous animals in Europe, and the number of human cases is probably considerably underestimated, especially when the high rates of seropositivity found in serological surveys for the parasites are considered, and in fact indicate that the contact of humans with these parasites is more frequent than it is shown by the number of clinical cases documented. As most individuals fail to develop symptoms, they are not diagnosed.

## MITE INFECTIONS AND INFESTATIONS

### SCABIES

Scabies is an intensely pruritic and highly contagious infestation of the skin caused by the mite *Sarcoptes scabiei*. It lives its entire life on the human host. A variant of scabies is canine scabies, in which humans become infected from pets, particularly dogs. Canine scabies (i.e., mange) causes patchy loss of hair and itching in affected pets. The scabies infection and the mite that causes it are extremely contagious. A highly contagious form of scabies, known as Norwegian or crusted scabies, is increasingly found in individuals who are immunocompromised, aged, physically debilitated, or mentally impaired. Extensive widespread crusted lesions appear with thick hyperkeratotic scales over the elbows, knees, palms, and soles. Extensive proliferation occurs in immunocompromised patients. It is readily spread by close contact within families, in institutions, and by sexual contact, and its global prevalence is estimated at 300 million cases (Walker and Johnstone, 2000).

Although the sarcoptic mite does not transmit disease, it is the cause of a disease condition; its presence, especially in younger persons who have been infested through sexual contact, should lend a high degree of suspicion to the possible presence of another sexually transmitted disease. Nevertheless, scabies is not primarily a sexually transmitted disease; scabies spreads in households and neighborhoods in which there is a high frequency of intimate personal contact or sharing of inanimate objects; fomite transmission is a major factor in household and nosocomial passage of scabies (Fujimoto, 1994, Burkhart et al, 2000). Scabies is becoming a serious problem in institutions such as hospitals and other health care institutions, especially homes for the aged. In 1998, van Vliet et al, after reviewing literature in the Netherlands and elsewhere, identified six important factors contributing to the transmission and return of scabies in health care institutions: (a) among residents, a considerable number of persons are, once infested, at risk of developing crusted scabies, (b) the exposure of many people through close contact, (c) generally long delay in diagnosis (d) insufficient survey of the epidemiological problem, (e) treatment failures and (f) incomplete post-intervention monitoring.

Particular attention must be given to the prevention of scabies, especially crusted or Norwegian scabies, in institutions such as hospices for AIDS patients. Corbett et al (1996) described a nosocomial outbreak of scabies in a HIV-unit in London, England which resulted from a patient admitted with crusted scabies. Treatment of his infection with scabicides (malathion) alone failed and

he remained infectious for several weeks. His infestation was then eradicated by a combination of topical treatment and oral ivermectin. In total, 14 (88%) out of 19 ward staff became symptomatic, and four had evidence of scabies on examination of skin scrapings. Ward policy was changed to distinguish crusted scabies patients from ordinary scabies patients. A second patient with crusted scabies was treated with combined oral and topical therapy early in his admission and nursed with more stringent isolation procedures. No nosocomial transmission occurred, and the infestation responded rapidly to treatment. Patients with crusted scabies require strict barrier nursing if nosocomial transmission is to be avoided. Virtually all reviews of scabies in Europe note that the incidence of both uncomplicated and Norwegian scabies, the latter in particular, are on the rise. The reasons for such an increase are variously ascribed to greater mobility of human populations, more promiscuity, and, in the case of Norwegian scabies, to the much greater susceptibility of immunosuppressed individuals. The systemic drug, ivermectin, usually provides effective control in individuals, whereas the pyrethroids insecticide permethrin is thought to provide safer and more effective control (Walker and Johnstone, 2000 *ibid*).

Infestations with human pubic lice, *Phthirus pubis*, have also greatly increased, due to increasing promiscuity; pubic lice are not vectors of any disease, but, as with scabies, infestations by this species should lend suspicion to the presence of possible infections with venereal diseases. Scabies infestations may have a direct public health impact; from 1966 to 1986, 1 675 213 cases of scabies in Poland were recorded. The highest incidence (580.5 per 100,000 inhabitants) was noted in 1968, the lowest (41.7) in 1986. During this period, the losses brought about by this disease among people 20–64 years amounted to 1 836 234 days of sick leave, while the average absence in 1980 was 82 500 days (Murkowski, 1989). There are reports from several countries of an overall increase in the incidence of scabies. This is particularly evident in institutional outbreaks and among persons living under poor socioeconomic conditions. Reports of increased incidence of scabies infections have been received from Denmark, Germany, Italy, the Russian Federation, Sweden and the United Kingdom. Effective treatment and control is enhanced by rapid diagnosis. Scabies control by the application of topical pesticides has become increasingly difficult, as toxicological concerns have reduced the number of compounds available. Fortunately, ivermectin, a potent macro-cyclic lactone of the avermectin family, has now been approved and is widely available. The drug has a high degree of safety and is effective in the control of the mites. Used as a systemic, it is well tolerated.

## MITE-BORNE DISEASES

### Rickettsialpox

The causative agent of rickettsialpox is *Rickettsia akari*. It is a member of the spotted fever group of rickettsia. This rickettsial agent is transmitted by the house

mouse mite, *Liponyssoides sanguineus*, from rodents, particularly the house mouse, *Mus musculus*, to man. Rickettsialpox is a mild, self-limited, zoonotic febrile illness characterized by a papulovesicular skin rash at the site of the mite bite. It was first recognized clinically in New York City in 1946 (Huebner et al, 1946).

The infection appears to be widespread in the United States and has been found in Europe; it was detected for the first time in southern Europe with the isolation of *R. akari* from the blood of a sick patient in Croatia (Radulovic et al, 1996). The authors considered that rickettsialpox would probably be found more often on the continent if physicians gave greater consideration to the possibility of its presence, and if laboratory diagnostic methods were better able to distinguish between the different spotted fever group rickettsiosis. The infection has also been reported from Ukraine (Eremeeva et al, 1995). In view of the scarcity of cases and its lack of pathogenicity, rickettsialpox is not, at present, an infection of public health importance in Europe.

### **MITES AND ALLERGIES**

Although not an infectious disease, allergy due to house-dust mites, (*Dermatophagoides pteronissinus* and *D. farinae*) is an important causative factor for allergic asthma or rhinitis in children throughout the world, and it may, in part, be a factor in 50 to 80% of asthmatics. There is a clear relationship between the degree of allergen exposure and the subsequent development of asthma or the risk of sensitization. In fact, allergens produced by these mites are probably the single most important allergens associated with asthma worldwide (Tovey, 1992). Within Europe, the problem of asthma resulting from exposure to house-dust mites is particularly severe in the United Kingdom. Mites can be found in great numbers in bedrooms and in bedding. Their presence has little to do with the degree of cleanliness of a home. The successful treatment of asthma can be achieved in good part through the control of house dust mites, although this is often difficult, and it may require vinyl covers for mattresses, hot washing of bedding, removal of carpets from bedrooms and the use of acaracides (WHO, 1988). Among farm or warehouse workers, allergies may also be caused by storage mites which are especially common under warm, humid conditions.

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## ARTHROPOD PEST CONTROL

Many different species of arthropods may be the cause of local annoyance in homes and recreational areas. As elsewhere in the world, large sums of money are spent in Europe on the control of insect pests, particularly cockroaches, flies, ants and similar pests. Expenditures are made for the purchase of household sprays or baits or the hiring of commercial pest control operators. While control of these pests represents important economic expenditures, it is only rarely that most of this group serves as vectors of diseases, and they will not be considered here.

## FACTORS AUGMENTING THE INCIDENCE, PREVALENCE AND DISTRIBUTION OF VECTOR-BORNE DISEASES

After decades of decline following the Second World War, there is now a serious recrudescence of several vector-borne diseases in the European region; at the same time, the population densities of vector and potential vector populations of mosquitoes and ticks are increasing in many areas. New diseases and disease syndromes such as the co-infection of HIV/leishmaniasis have appeared. It is important to understand the reasons for the recrudescence of these diseases as a basis for their control and prevention.

### ECOLOGICAL CHANGES

As elsewhere, massive ecological changes have occurred over the European continent within the last 50 years. These include increases in human populations and increased population densities as a result of urbanization. After years of urban growth, there has been a trend towards movement of populations to suburban areas in more affluent countries, resulting in greater exposure to vectors and to animal reservoirs of infections. Changed leisure habits have also increased exposure to vectors, especially ticks.

Unfortunately, there have been major displacements of human populations from some countries within the European region due to conflict; the search for economic betterment has also been the cause of population migration. Substantial immigration from outside Europe has taken place, much of it from countries where vector-borne diseases are endemic. This has resulted in the frequent introduction of exotic infections and occasional secondary transmission of both tick and mosquito-borne diseases, with the risk that new infections may be established, as has occurred with West Nile virus in North America. Greatly increased tourism has brought with it the introduction of tropical diseases, particularly malaria, among persons returning from trips to disease-endemic areas. As physicians and health care workers are often not familiar with the symptoms of these tropical diseases, diagnosis and treatment may be delayed. The frequent appearance of Mediterranean spotted fever in dogs brought back from family travel to southern Europe has been discussed above.

Changes in agricultural practices, particularly increases in the extent of irrigated areas and the use of pesticides, have been the cause of important changes in vector and potential vector population densities. The spread of rice cultivation in Italy resulted in the reappearance of *An. labranthiae* in areas from which it had previously been eliminated (Bettini et al, 1978). Reforestation has increased, and along with it, there have been changes in the fauna and flora of newly wooded

areas. As has been noted above, the extension of forested areas has increased the density of deer populations, and hence the density of deer ticks and the incidence of Lyme disease and babesiosis.

Virtually all of these changes have had an impact on the distribution and incidence of vector-borne diseases; while some ecological changes have resulted in a decline in vector densities and vector-borne diseases, others have resulted in increased densities and greater exposure of human populations. These changes will continue, and continued surveillance of vector densities and the incidence of vector-borne diseases is required.

## THE PROBLEM AND RISK OF INTRODUCED VECTORS

More extensive travel and the increased exchange of goods and the manner in which they are transported, particularly by containers, has resulted in the introduction and establishment of vector species not previously found in Europe. The most notable example of this is the mosquito *Aedes albopictus*. This mosquito, of Asian origin, spread to the American and African continents in the last two decades: it is now established in North and South America, Africa, Oceania and Europe. It was first detected in Europe in 1979 in Albania (Adhami and Murati, 1987). The species was probably introduced into that country from China in the mid-1970s. The initial infestation was likely to have taken place at a rubber factory adjacent to the port of Durres (Durazzo); from there the eggs of the mosquito were shipped in tires to recapping plants in other parts of the country. This was the first recorded infestation of *Ae. albopictus* outside Oriental and Australasian regions (Adhami and Reiter, 1998). *Ae. albopictus* was thereafter found in Genoa, Italy in 1990 (Sabatini et al, 1990), as well as in Padua. The Padua introduction may have resulted from tire imports from the United States. Eighty-five percent of the imported tires came from a single source in Atlanta, Georgia; the remaining 15% of the tires came from the Netherlands. By late 2001, *Ae. albopictus* had rapidly become the most important pest mosquito species in areas of northern Italy, and it is now present in nine of Italy's 21 political regions, including Veneto, Lombardy, Emilia Romagna, Liguria, Tuscany, Lazio, Piedmont, Campania, and Sardinia. It has become a serious pest mosquito in Rome (Di Luca et al, 2001). Because of its cold tolerance, it is an active feeder throughout much of the year, even in the colder regions of northern Italy. The species appeared in France in 1999, when it was found in villages in the Basse-Normandie and Poitou-Charentes departments. Larvae, pupae and adults were collected in the used tire stock of a tire recycling company which imported tires, particularly from the United States, Italy, and Japan (Schaffner et al, 2001). The international shipping trade of used tires provides *Ae. albopictus* with an ideal mechanism for dissemination.

In 1996, another introduced mosquito species, *Aedes atropalpus*, was discovered in the Ventao region of northern Italy. It was also found breeding in tires stored at a recapping company, this one importing used tires from eastern Europe and North America (Romi et al, 1997). The species now appears established in Italy. Hitherto, *Ae. atropalpus* was known only in North America; unlike *Ae. albopictus*, its distribution in Italy remains limited to the area in which it was first found (Romi et al, 1999). Most recently, *Ochlerotatus japonicus*, an Asian mosquito, has been reported from Normandy, France, where it was found breeding

in tires (Schaffner et al, 2003). This same species was introduced into the United States in 1998, and has since spread very widely there. West Nile virus has been isolated from the species.

The establishment of exotic mosquito species in Europe is a cause for serious concern, as the newly introduced species may be vectors or potential vectors of disease, and they may possibly be more efficient vectors than indigenous species of mosquitoes. Introduced species may spread rapidly, as has occurred with *Ae. albopictus* and *Oc. japonicus* in the USA. Both in Europe and the Americas, *Ae. albopictus* has become a pest as well as a potential vector. As has been discussed above, infected vectors may be introduced by aircraft, and, if infected with malaria parasites, they may transmit infections, such as has occurred with 'airport malaria.'

As discussed, the tick, *R. sanguineus*, the vector of MSF, is a southern European species; however, it is frequently found on dogs which have been taken to southern Europe and back. There have been several instances in which introduced ticks have transmitted *R. conorii*, for which it serves as both vector and reservoir in areas outside their normal range of distribution. There have been many findings of the species as an occasional invader in countries where it is not normally present, and its distribution now appears to be moving north. As an example of this phenomenon, *R. sanguineus* has been reported in Switzerland as an introduced species since 1940, but it has now become established in the Canton of Ticino in southern Switzerland, where two different tick species coexist, those of *R. sanguineus* sensu stricto and *Rhipicephalus turanicus*. In this area, it has been found infected with *Rickettsia* and *Coxiella* (Bernasconi et al, 2002 *ibid*).

Jaenson et al (1994) reported the regular introduction of several tick species into Sweden, among them *I. persulcatus*, *Hyalomma marginatum* and *R. sanguineus*, as well as the first European record of the American dog tick, *Dermacentor variabilis*, and remarked that the potential introduction to Sweden of exotic pathogens with infected ticks (e.g., *I. persulcatus* and *H. marginatum* on birds or *Dermacentor* spp. and *R. sanguineus* on mammals) is evident. Imported ticks have been found in most countries of Europe, even those in which they have not become established. *R. sanguineus* and *H. detritum* were found on seven occasions between 1975 and 1985 in Brittany; they were found in houses and on dogs, and *H. detritum* was found on a man (Couatmanac'h et al, 1989). *Argas reflexus*, a pigeon tick which may cause severe allergic reactions in humans exposed to it, has been found in many houses in Berlin, and is probably an introduced species (Dautel et al, 1991). Migrating birds are a common source of introduction of ticks; according to Bjoersdorff et al (2001); during the spring of 1996, an estimated 581 395 *Ehrlichia*-infected ticks were imported into Sweden by migrating birds. The gene sequences of the *Ehrlichia* in the birds were similar to the granulocytic ehrlichiosis found in domestic animals and humans in Sweden, thus demonstrating that birds play a role in the dispersal of both ticks and disease.

Many species of arthropods are found as occasional introductions in countries in which they do not become established. Dipteran larvae, a cause of myiasis, are often found on travelers returning from tropical countries; among the species recorded are *Cordylobia anthropophaga*, (the “tumbu-fly”), *Cordylobia rodhaini*, *Dermatobia hominis*, *Hypoderma lineatum*, *Oestrus ovis* and *Wohlfahrtia magnifica*. Instances of myiasis are probably more common than reported, but most cases are self-limited: if there is no secondary bacterial infection, they frequently go unreported. The sand flea, *Tunga penetrans*, is occasionally found infesting travelers returning from Africa or South America, but it rarely constitutes a serious medical problem.

Cockroaches are ubiquitous pests aboard ships and aircraft, and exotic species are quite often transferred from one country to another. Some species may become established, such as *Pyenoscelus surinamensis*, a southeast Asian species which was found in a heated greenhouse in Sweden (Hagstrom and Ljungberg, 1999). *Periplaneta australasiae* have been recorded as introduced into the Czech Republic and Slovakia, as well as *Periplaneta brunnea* and *Supella longipalpa* in the Czech Republic (Kocarek et al, 1999). *P. brunnea* was found in an airport in the United Kingdom; the species was probably imported from the southern United States on an aircraft, and it seems to have established itself in the heated rooms at the airport (Bills, 1965).

## THE RISK OF IMPORTED VECTOR-BORNE DISEASES BEING ESTABLISHED

While global warming may lead to the increase and spread of existing vector-borne diseases in Europe, there are a number of infections whose importation may result in epidemic transmission in Europe due to the presence of potential vectors. Rift Valley fever must be considered a serious threat. Until 2000, the distribution of this serious disease was limited to the African continent. In that year, however, the virus invaded Saudi Arabia and Yemen, and it caused a serious epidemic with a high morbidity and mortality among animals and man in the first confirmed occurrence of the disease outside Africa. Statistics provided at the end of the outbreak in April 2001 from the Saudi Ministry of Health documented a total of 882 confirmed human cases with 124 deaths. Both the severity of the disease and the relatively high death rate (14%) may be the consequence of under-reporting of the less severe disease (Balkhy and Memish, 2003). In Yemen, 1 087 cases were estimated to have occurred, with 121 deaths (Shoemaker et al, 2002). Isolations of the virus were made from two mosquito species, *Cx. tritaeniorhynchus* and *Ae. vexans arabiensis*; both species were considered as vectors on grounds of their abundance, distribution, preference for humans and sheep, isolations of virus from them, and vector competence tests (Jupp et al, 2002). Inasmuch as the closely related mosquito species *Ae. vexans* is one of the most widespread in Europe and *Cx. tritaeniorhynchus* is found in Turkey, the risk of spread to Europe is obvious. Should RVF virus be introduced in an infected animal from Africa or the Middle East, local transmission could occur, with very serious consequences for both human and animal populations.

The recent spread of Israel spotted fever to Portugal and the appearance of Boutonneuse fever in Switzerland demonstrate that if a suitable local vector is present, local transmission of introduced diseases can occur. The spread of Mediterranean spotted fever and its vector, *R. sanguineus*, to countries in which it has never been reported previously has already been described above. Several cases of African tick-bite fever have been reported in France, but all were among travelers returning from endemic areas in Southern Africa. Combermerle et al (1998), however, reported a case in a man who had never left France. He had developed a fever, and he had black spots on his legs, lymphangitis and enlarged nodes. Western blot confirmed the diagnosis of *R. africae*, which was probably transmitted by a tick imported into France in the luggage of the patient's daughter, who had spent three months in Zimbabwe.

## THE POSSIBLE EFFECT OF CLIMATE CHANGE ON VECTOR-BORNE DISEASES

The International Council of Scientific Unions and the Intergovernmental Panel on Climate Change, established by the World Meteorological Organization and the United Nations Environmental Program, have estimated that by the year 2100, average global temperatures will have risen by between 1.0°C to 3.5° C. Important ecological changes may come about in the future due to global warming. Globally, 1998 was the warmest year ever, and the 1990s was the warmest decade on record. The distribution and seasonality of diseases that are transmitted by cold-blooded insects or ticks are likely to be affected by climate change. Such increases in temperatures in Europe might allow the establishment of tropical and semitropical vector species, permitting transmission of diseases in areas where low temperatures have hitherto prevented their over-wintering. Kovats et al (1999) have pointed out that for the last few decades, Europe has experienced significant warming, and this is likely to continue. A change in the distribution of important vector species may be among the first signs of the effect of global climate change on human health. Indeed, Lindgren et al (2000) cite evidence that the distribution of tick vectors in Sweden has expanded northward between 1980 and 1994, consistent with observed changes in climate. The Swedish study indicated that the reported northern shift in the distribution limit of ticks was related to fewer days during the winter seasons with low minimum temperatures below -12°C. At high latitudes, low winter temperatures had the clearest impact on tick distribution, whereas in the south of the country, the increased temperatures resulted in increased tick population densities. Another consequence of the warmer weather in Sweden has been a rise in the incidence of TBE, which has substantially increased since the mid-1980s. Lindgren and Gustafson (2001 *ibid*) believe this is associated with increased tick abundance, a longer life-span of the tick vectors, (*I. ricinus*), more persons visiting endemic areas, and increases in host animal abundance. In any event, documented increases in the incidence of TBE over the last decades have been reported from Belarus, the Czech Republic, France, Germany, Latvia, Lithuania, Poland, the Russian Federation, Slovakia, Sweden, and Switzerland. It is generally agreed that the rising trend in TBE incidence in central and northern Europe has resulted from increased densities of *I. ricinus*, the vector tick. In France, where there has been a notable increase in TBE incidence in the region of Lorraine since the mid 1990s, the proliferation of ticks is a major factor in the increased incidence of cases, and is mainly due to a modification of the ecosystem (George and Chastel, 2002 *ibid*). In the area of St. Petersburg, Russian Federation, the increase in incidence of TBE is ascribed to changing rec-

reational habits which bring people into greater contact with ticks (Antykova and Kurchanov, 2001). Randolph (2002) believes that increased incidence in TBE in northern Europe is related to climate change, either directly by increasing tick population densities, or indirectly, in that warmer weather in spring and autumn may permit longer activity seasons for both ticks and humans, which is likely to be an important factor in northern regions such as Scandinavia, where prolonged low temperatures are limiting factors for tick development and activity.

Global warming may have a more immediate effect on mosquito populations and only later on mosquito-borne diseases. With increased average temperatures, the length of the breeding seasons for mosquito populations would be extended and population densities would increase. Warmer northern climates would cause an expansion of the distribution of species now found only in warmer climates. Should these changes occur, it seems likely that the distribution of mosquito-borne diseases would also subsequently expand.

With a rise of temperatures in Europe, there is concern about the possible recrudescence of malaria transmission. Such a recrudescence has already been seen in eastern Europe (Table 5). In light of the constant introduction of malaria cases from endemic countries, local transmission could reoccur in western Europe, should the densities of vector populations increase. Increased temperatures would also favour the development of *P. falciparum*. Although the well-established surveillance programmes throughout western Europe should provide adequate warning of any marked increase in malaria incidence and allow for the organization of effective control operations, the reestablishment of transmission would prove costly in terms of medical care and control operations. In eastern Europe, where recrudescence of malaria transmission has occurred, the health services of some countries have had only limited success in containing malaria transmission, and there is a need for donor support of surveillance and control operations.

## CONCLUSIONS

The incidence of vector-borne diseases in Europe is much greater than is generally recognized by physicians and health authorities. As a result, diagnosis and treatment are often delayed by health care professionals who are unaware of the presence of these infections and thus do not take them into consideration when attempting to determine the cause of a patient's illness. In the absence of major and dramatic outbreaks, health authorities often fail to allocate adequate funding for the surveillance and control of this group of diseases. It is important that those engaged in all aspects of public health surveillance in Europe are aware of the distribution and epidemiology of this group of diseases and are able to prepare for their control when necessary.



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While the number of vector-borne diseases and their incidence in Europe is much less than that of the tropical, developing countries, there are, nevertheless, a substantial number of such infections in Europe. Furthermore, the incidence of many of these diseases has been on the rise, and their distribution is spreading. This publication reviews the distribution of all of the vector-borne diseases of public health importance in Europe, their principal vectors, and the extent of their public health burden. Such an overall review is necessary to understand the importance of this group of infections and the resources that must be allocated to their control by public health authorities. Medical personnel must be aware of these infections and their distribution to ensure their timely diagnosis and treatment.

New combinations of diseases have also been noted, such as the appearance and spread of co-infections of HIV virus and leishmaniasis.

The effect of global warming may lead to the resurgence of some diseases or the establishment of others never before transmitted on the continent. Tropical infections are constantly being introduced into Europe by returning tourists and immigrants and local transmission of some of these, such as malaria, has already taken place as a result.



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