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Introduction

The vector and rodent-borne diseases are a heavy burden on public health in much of the tropical and semitropical regions of the world; among these diseases are malaria, leishmaniasis, sleeping sickness, many arboviruses and a plethora of other infections. Despite their largely temperate climates, Europe, the USA and Canada have not been spared by this group of infections; moreover, some endemic diseases thought to have been under control in these regions are now resurging and new infections are emerging on both continents. Co-infections of HIV virus and leishmaniasis and of Lyme disease and tick-borne encephalitis, pose diagnostic and treatment problems to clinicians. Ecological and climate changes have favoured increases in the densities of insect and tick vectors and rodent reservoir hosts and in the agents they transmit. With increased travel to tropical disease-endemic areas, the number of imported cases of malaria and other vector-borne diseases has sharply risen and some of these have become established, with grave consequences.

The following chapters will review the status of the vector and rodent-borne diseases which are endemic or imported into Europe and the USA and Canada as well as the literature describing their epidemiology, incidence, distribution, vectors and reservoir hosts. Emphasis will be placed on the epidemiology of the infections rather than on clinical aspects or treatment. To plan the prevention and control of this group of infections, knowledge of their epidemiology and distribution is essential for public health officials and health scientists; clinicians must be aware of the infections they may encounter to ensure a rapid diagnosis and timely treatment, especially those introduced from abroad.

An extensive bibliography is provided as much of the literature on this group of infections is scattered through a wide spectrum of journals. Furthermore, as will be seen, the incidence of many of the vector and rodent-borne diseases

in both Europe and North America are actually increasing, some quite seriously, while new diseases are emerging and old ones resurging; to substantiate this, an effort has been made to provide references to as many relevant studies as possible as well as an evaluation of the current public health importance of the infections which will be reviewed. The literature has been reviewed to June 2005.

PART I THE VECTOR- AND RODENT-BORNE DISEASES OF EUROPE

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Vector- and rodent-borne diseases in European history

Plague

The most serious of the vector- and rodent-borne disease epidemics in European history were the pandemics of plague that swept through the continent decimating the population. The first recorded epidemic began in Arabia at the time of Justinian, reaching Egypt in AD 542; it then spread through Palestine and Syria to Europe and throughout the Roman Empire to the British Isles and Ireland. The most infamous of the plague pandemics was the 'Black death' which ravaged the continent from the middle of the fourteenth century until the end of the sixteenth century. In Great Britain, one-half to two-thirds of the population is believed to have been killed and it is generally believed that 25 million people or as much as a quarter of the European population fell victim to this pandemic. The last outbreak of plague in Europe occurred in Marseilles, France in 1720, probably introduced by a plague-infested ship arriving from Syria. Some 50 000 people died in the city; the disease spread over a great part of Provence but disappeared in 1722 (Pollitzer, 1954).

There has been some controversy as to whether or not the epidemics described above were indeed caused by *Yersinia pestis* inasmuch as diagnosis of ancient septicaemia or other forms of plague solely on the basis of historical clinical observations is not possible. Furthermore, the lack of suitable infected material prevented direct demonstration of ancient septicaemia; thus, the history of most infections such as plague has remained hypothetical. Some recent investigations have supported the contention that these ancient epidemics were indeed caused by infections with *Y. pestis*. Drancourt *et al.* (1998) made DNA extracts from the dental pulp of 12 unerupted teeth extracted from skeletons excavated from sixteenth and eighteenth century French graves of persons thought to have died

of plague and from seven ancient negative control teeth. Polymerase chain reaction (PCR) probes incorporating ancient DNA extracts and primers specific for the human beta-globin gene demonstrated the absence of inhibitors in these preparations. The incorporation of primers specific for *Y. pestis rpoB* (the RNA polymerase beta-subunit-encoding gene) and the recognized virulence-associated *pla* (the plasminogen activator-encoding gene) repeatedly yielded products that had a nucleotide sequence indistinguishable from that of modern-day isolates of the bacterium. The specific *pla* sequence was obtained from 6 of 12 plague skeleton teeth but none of seven negative controls thus confirming presence of the disease at the end of the sixteenth century in France. Further DNA extractions of dental pulp were also positive in a study in the south of France (Raoult *et al*., 2000).

In Germany, in an area which was also struck by the purported plague epidemics, Wiechmann & Grupe (2004) carried out a molecular genetic investigation of a double inhumation, presumably a mother and child burial from Aschheim (Upper Bavaria, sixth century), which included analysis of mitochondrial DNA, molecular sexing and polymorphic nuclear DNA. *Y. pestis*-specific DNA was detected confirming the presence of *Y. pestis* in southern Germany during the first plague pandemic recorded.

Malaria

Malaria has existed in the Mediterranean basin since the prehistoric era and the arrival of man. The ancient Romans associated the malarial fevers with proximity to marshes. The modern term 'malaria' originates from Italy of the Middle Ages when the two words 'mala' and 'aria' became the word known today as 'malaria' which gradually came into common use.

In the nineteenth century malaria transmission extended from part of Norway, through southern Sweden, Finland, Russia, Poland, along the countries of the Baltic coast including northern Germany, through Denmark and the Netherlands, south along the coasts of Belgium, France, Spain and Portugal and all of the countries of the Mediterranean and Adriatic, in the Balkans where it was particularly severe and throughout Greece and the Danube peninsula (Strong, 1944). Coastal southern and eastern England had unusually high levels of mortality from malaria from the sixteenth to the nineteenth century (Dobson, 1994).

In the beginning of the 1950s eradication programmes were launched by national governments with the support of the World Health Organization and successfully eradicated the disease from virtually all the continent. By 1969, Hungary, Bulgaria, Romania, Yugoslavia, Spain, Poland, Italy, the Netherlands and Portugal had completely eradicated endemic malaria.

Typhus

Epidemic or louse-borne typhus *Rickettsia prowazekii* transmitted to humans by the human body louse *Pediculus humanus* may cause a mortality of 60% in untreated people. Widespread epidemics have occurred in Europe. Armies have been virtually wiped out by epidemics of typhus. Between 1915 and 1918, typhus was responsible for one-fifth to one-third of all illnesses in the British forces, and for about one-fifth of the German and Austrian armies. An outbreak of louse-borne typhus occurred in Serbia in November 1914; within six months 500 000 people developed typhus fever. Over 200 000, of whom 70 000 were Serbian troops, died from the disease. One half of the 60 000 Austrian prisoners also died from typhus. At its peak new cases ran at 10 000 per day. Mortality ranged from 20% at the start to 60–70% at the end of the epidemic.

In the 1917–1921 epidemic in Russia the epidemic raged amidst the famine and dislocation of the revolution and 20–25 million cases were estimated to have occurred. For a while it looked as if the fate of the revolution was at the mercy of typhus fever. Lenin, in 1919, put it succinctly: 'Either socialism will defeat the louse, or the louse will defeat socialism' (Tschanz, D. W. http://scarab.msu.montana.edu /historybug /WWI/TEF.htm, accessed 21 June 2005).

Murine typhus caused by *Rickettsia typhi*, is endemic in southern Europe. One tale has it that this milder rickettsial infection transmitted from rats to man by fleas, has an historical basis in the thirteenth century legend of the Pied Piper, who led away the rats from the town of Hamelin, Germany; when refused payment for his services, he led away 130 children and disappeared with them in the mountains. It is suggested that the children actually died in an outbreak of disease and were buried in a common grave at the site of the legendary disappearance. The association with rats points to a rodent-borne infection, and the pied (mottled) coat of the piper seems to indicate a disease causing conspicuous macular lesions (Dirckx, 1980).

Arboviruses

At the end of the eighteenth century and into the nineteenth, yellow fever broke out in Spanish ports, having been brought by vessels mainly from infected ports in the New World. Cadiz suffered five epidemics in the eighteenth century, and Malaga one; from 1800–1821 the disease assumed alarming proportions, Cadiz being still affected (Waddell 1990), while Seville, Malaga, Cartagena, Barcelona (Angolotti, 1980), Palma, Gibraltar (Sawchuk & Burke, 1998) and other ports and their surroundings suffered severely. In the epidemic at Barcelona in the summer of 1821, some 12 000 persons died (Chastel, 1999). Yellow fever

also invaded the port of Saint Nazaire in France in the 1860s (Coleman, 1984) and at Lisbon in 1857 some 6000 died. An outbreak of yellow fever occurred in Swansea, UK in 1865; both this outbreak and the Saint Nazaire one were caused by infected mosquitoes flying to the mainland from ships in harbour.

Dengue was long endemic in most of the countries of the Mediterranean; in 1928 approximately 650 000 residents of Athens and Piraeus contracted dengue and 1061 died (Halstead & Papaevangelou, 1980). The disease disappeared from Europe with the disappearance of its vector, *Aedes aegypti*.

From the beginning of the twentieth century, sanitary conditions improved in urban and rural areas, farming and irrigation practices changed, and the great epidemics described above have ceased. However, a substantial number of vector and rodent-borne infections persist both in Europe and North America and new infectious agents are emerging, some of which represent no small threat to public health.

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The arboviruses

There are between 500 and 600 known arthropod-borne viruses, or arboviruses, in the world of which some 100 may give rise to human disease. There are six families of arboviruses; Togaviridae, Flaviviridae, Bunyaviridae, Reoviridae, Rhabdoviridae and Orthomyxoviridae. By 1996, 51 arboviruses had been reported from Europe – they are the subject of a comprehensive review by Hubalek & Halouzka (1996). Many of these viruses are not known to cause human illness; some have only been isolated from arthropods, birds or other animals and their public health significance is unknown. Others, however, may cause significant human illness and mortality. The arboviruses will be considered by the four groups of arthropods that transmit them, i.e. mosquitoes, sandflies, biting midges and ticks. The epidemiology of the arboviruses is rapidly evolving and their distribution is spreading to areas in which they have not been previously endemic and, in some cases, as appear to be occurring with West Nile virus, increased virulence has been seen in some recent outbreaks.

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The mosquito-borne arboviruses of Europe

West Nile virus

West Nile virus (WNV), a member of the Japanese encephalitis complex, is a neurotropic flavivirus virus that produces damage of varying severity in human, animal and avian hosts. The virus is amplified in birds and transmitted to humans usually by *Culex* mosquitoes. Most cases of WNV are subclinical, with overt clinical illness affecting 1:100 to 1:150 cases. Meningoencephalitis is the most common diagnosis in hospitalized WNV patients, affecting 50–84%. In the elderly the mortality rate may range as high as 10% though it is much lower in the current outbreak in the USA. The epidemiological cycle of WNV is shown in Figure 4.1.

West Nile virus was first isolated from a febrile woman in the West Nile District of Uganda in 1937 (Smithburn *et al.*, 1940); in 1950 it was found that the virus was present in a large percentage of normal individuals in the vicinity of Cairo, Egypt. The majority of the children from whom the sera were collected appeared to be normal; there was no evidence that children with viremia were severely ill. In 1950 more than 70% of the Cairo inhabitants aged 4 years and over had antibodies to WNV (Melnick *et al.* 1950).

In 1951, WNV was recognized in Israel; the disease had probably already been present in that country for several years. There were large outbreaks in 1950–1951 and it is estimated that the number of cases was in the hundreds (Goldblum *et al.*, 1954); none of the cases was fatal and there were apparently many subclinical cases. Israel is an important path for migrating birds to and from Africa and to Europe and the virus may have been introduced in this manner.

The known distribution of WNV is shown in Figure 4.2.

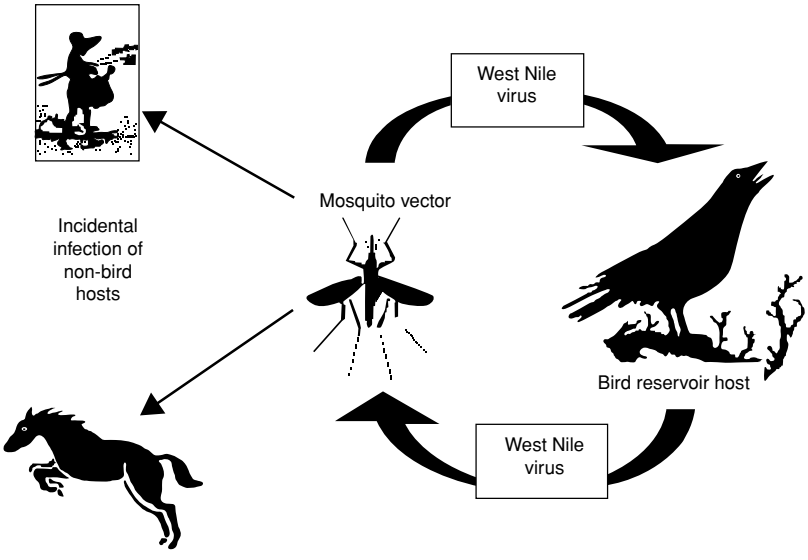

Figure 4.1 Transmission cycle of West Nile virus.

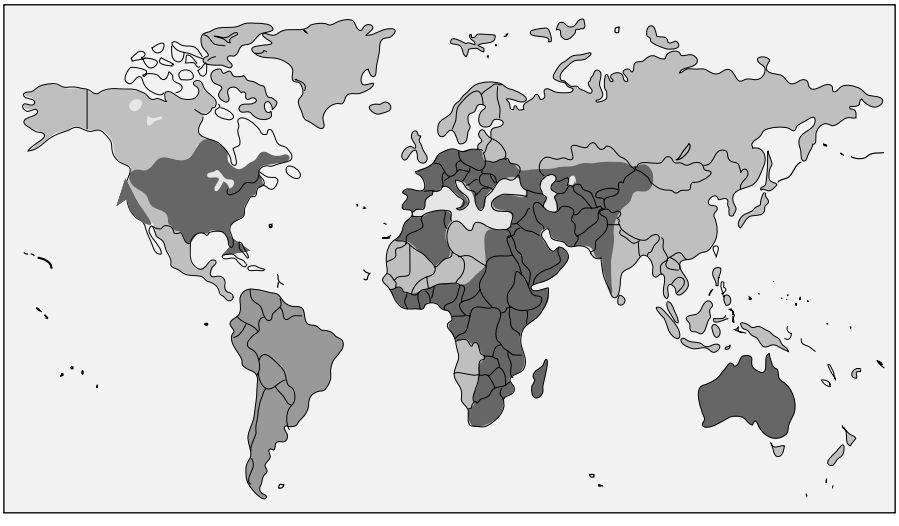

Figure 4.2 The global distribution (dark shading) of West Nile and Kunjin viruses.

Albania

The first report of WNV in Europe was the detection of the virus in 1958, in two Albanians found to have specific WNV antibodies (Bárdos *et al.*, 1959). The virus remains endemic in the country (Eltari *et al.*, 1993).

The subsequent spread of WNV through Europe is reflected in Table 4.1 which records the presence of WNV as indicated by the occurrence of human cases