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VECTOR BORNE-DISEASES AND INFLUENCING FACTORS

Surveillance of vector-borne diseases in Germany: trends and challenges in the view of disease emergence and climate change

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Abstract The changing epidemiology of vector-borne diseases represents a growing threat to human health. Contemporary surveillance systems have to adapt to these changes. We describe temporal trends and geographic origins of vector-borne diseases in Germany with regard to strengths of existing disease surveillance and to areas marked for improvement. We focused on hantavirus infection (endemic in Germany), chikungunya fever (recently emerging in Europe) and dengue fever (imported from tropical regions), representing important subgroups of vector-borne infections. Routine surveillance data on demographics, origin of infection and the date of reporting were analysed. From 2001 through 2007, 3,005 symptomatic hantavirus infections, and 85 cases of chikungunya fever were reported, similarly 1,048 cases of dengue fever in 2002 through 2007. The geographic origin of hantavirus infection was reported for 95.5% of all cases (dengue virus, 98.4%; chikungunya virus, 100%). Hantavirus infections were acquired in Germany in 97.6% of cases (n=2800). In 2007, there was a marked increase of hantavirus cases, mainly in areas known to be endemic for hantavirus. In 2006, imported cases of chikungunya fever primarily returned from several islands of the Indian Ocean, while the majority of imported cases in 2007 came from India. The reported number of dengue fever cases have increased since 2004. Thailand contributed the largest proportion of cases (17–43% in individual years), followed by India, Brazil and Indonesia. Surveillance of notifiable vector-borne diseases in Germany is able to timely detect spatial and temporal changes of autochthonous an imported infections. Geographic and temporal data obtained by routine surveillance served as a basis for public health recommendations. In addition to surveillance of vector-borne infections in humans, nationwide monitoring programs and inventory techniques for emerging and reemerging vectors and for wildlife disease are warranted.

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Introduction

Vector-borne diseases represent an increasing and significant threat to human health. Within the last decade, almost 30% of all emerging infectious diseases were caused by vector-borne pathogens (Jones et al. 2008). These emerging pathogens include infectious agents that are imported into non-endemic areas by travellers or trade (e.g. West Nile virus in North America, chikungunya virus in Northern Italy) and organisms that have been newly identified and associated with a new disease (e.g. Nipah virus). Additionally, pathogens that were already endemic in a certain country or region might become more widely spread due to ecological or other changes (Sutherst 2004). Among other reasons for disease emergence, climate change potentially alters the exposure of humans to vector-borne pathogens by changing the spatial and seasonal distribution of conditions that are favourable for the establishment and survival of vectors and vector-borne agents (Kovats et al. 1999; Haines et al. 2006). In addition to other requirements (e.g. risk assessment studies, emergency preparedness plans), adaptation to climate change needs a surveillance system which is capable of documenting the incidence and geographical distribution of vector-borne diseases and timely detecting new events of autochthonous transmission.

The objective of this report was to describe the epidemiology of selected imported and autochthonous vector-borne diseases (i.e. hantavirus infection, chikungunya fever and dengue fever) in Germany based on routine surveillance data. We focused on long-term trends in disease incidence and distribution and on the geographic origins of infections. Our aim was to assess the usefulness of the surveillance system for evaluating the impact of ecological factors (including climate) on autochthonous vector-borne infections and for monitoring trends in imported infections.

Materials and methods

Germany is a federal republic with 16 states (Bundesländer) and 413 counties (Stadt-/Landkreise). Because of the modernisation of the national surveillance system for notifiable infectious diseases, a new law for the prevention and control of infectious diseases (Infektionsschutzgesetz, IfSG) was enacted in Germany in 2001 (Krause 2004). The IfSG defines 47 pathogens and 14 diseases that laboratories and clinicians, respectively, have to notify to the local health department. Usually, one local health department per county is responsible for managing single cases and outbreaks of infectious diseases and conducting necessary prevention and control activities. The local health authorities verify locally identified notifiable diseases with reference to national case definitions (Poggensee et al. 2006) and send case reports electronically through the 16 state health departments to the national surveillance unit at the Robert Koch Institute (RKI), the central national agency for infectious disease epidemiology. The SurvNet software organises the transmission of case-based datasets from peripheral databases in each local health department to databases of the respective state health department and finally to the RKI. Outbreak detection and reporting is integrated in the system (Krause et al. 2007).

Three vector-borne diseases were selected for this study: a rodent-borne disease endemic in the South and some other regions of Germany (hantavirus infection), an infection that has recently emerged in Europe and that was responsible for the first autochthonous outbreak of a tropical arbovirosis affecting a population in Europe (chikungunya fever), and a disease that is endemic in more than 100 tropical countries and that is one of the major travel-associated infections in Germany (dengue fever). These infection are mandatorily reportable in Germany. Laboratories must notify local public health authorities of test results fulfilling the case definitions for acute infection. Only symptomatic infections are counted. For acute hantavirus infections, laboratory diagnosis is based on detection of nucleic acid, a marked rise of immunoglobulin G antibodies in a paired sample or detection of immunoglobulin (Ig) M or IgA antibodies confirmed by IgG antibodies.

For acute chikungunya infections, laboratory diagnosis is based on virus isolation, detection of nucleic acid, detection of IgM antibodies or a marked rise of immunoglobulin G antibodies in a paired sample. For acute dengue virus infection, detection of viral antigen or RNA, a fourfold or greater increase in antibody titers between acute- and convalescent-phase serum samples or detection of IgM antibodies to a dengue virus is required.

Reported data on hantavirus and chikungunya fever (2001 through 2007) were analysed as to the origin of infection, demographics and seasonality. For dengue fever, the same analysis were conducted on data from 2002 through 2007, as completeness of dengue reporting during these years was likely superior to 2001, the first year of reporting.

Results

Hantavirus infections

From the beginning of 2001 to the end of 2007, a total of 3,005 laboratory-confirmed hantavirus infections were notified to the RKI (Fig. 1). Of these, 73% were men and 87% were between 20 and 64 years old. The incidence of hantavirus infection fluctuated substantially in different years and generally reached a seasonal maximum in the summer months of May through August, when the breeding season of the bank vole as the predominating reservoir is at its maximum. Years of high incidences (0.3–2.0 cases/100,000 population) such as 2002, 2004, 2005 and 2007 alternated with years of low activity (<0.2 cases/100,000 population) such as 2003 and 2006 (Fig. 1). The rates are highest in the southwest and lowest in the northeast of Germany. Hantavirus infections mainly occur in well-known endemic areas in the federal states of Baden-Württemberg, Bavaria, Hesse, Lower Saxony and North Rhine Westphalia (Fig. 2). The Swabian Mountains in the south of Germany are the spatially most extended region where most of the reported infections were acquired each year. The annual incidence of hantavirus infections reached its maximum in 2007 when 1,687 cases were reported (2.0 cases/100,000), four times as much as in 2005, the year with the second highest annual incidence with 448 cases. The seasonal increase of hantavirus infections in the endemic areas did not appear always at the same time. The annual beginning of the hantavirus season differed from year to year. The geographic origin of infection was reported for 95.5% of all hantavirus cases. Among those, where a place of infection was reported, 97.6% (n=2,800) were acquired in Germany. The predominant virus species was Puumala (PUU). PUU was responsible for 93% of

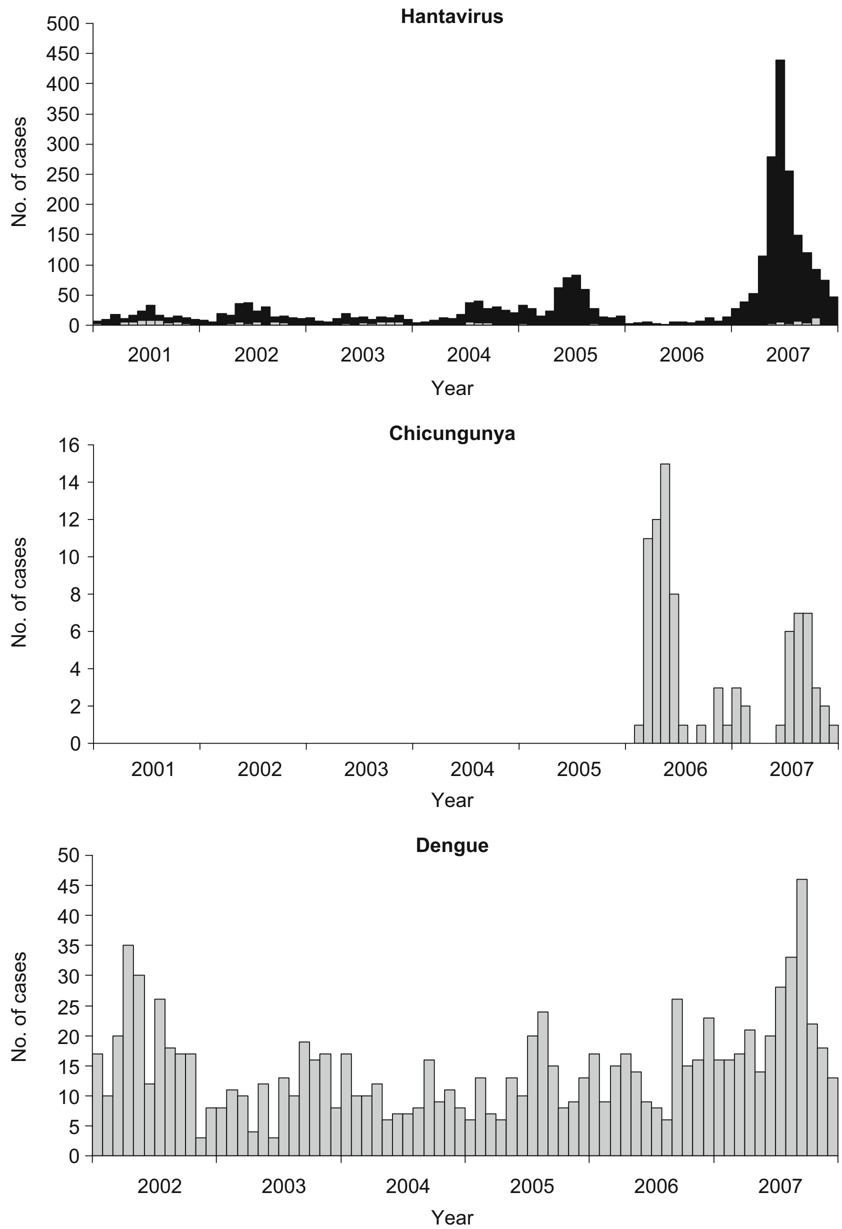

Fig. 1 Number of reported cases of hantavirus, dengue fever, and chikungunya fever in Germany, 2001–2007. Imported cases are shown in *light grey*, autochthonous cases in *dark grey*

infections among those where the causing virus species was known (2,727 infections).

Chikungunya fever

Cases of chikungunya fever imported to Germany were not reported until 2005 (Fig. 1). Subsequently, 85 cases were reported in 2006 (53) and 2007 (32). Of these patients, 37 (44%) were men. The infection affected individuals between 14 and 77 years of age, with highest incidence in the age groups 30–69 years. Twenty-one cases were hospitalised; no fatal case was reported. All cases acquired the infection outside of Germany or other European countries. In 2006, the majority (88%) of cases contracted the infection while visiting islands of the Indian Ocean, including Mauritius, Reunion, Madagascar and the Seychelles (Fig. 3). In 2007, most imported infections (76%) with chikungunya virus originated from India and Sri Lanka.

Dengue fever

During 2002 through 2007, 1,048 patients with confirmed dengue virus infection were reported (median annual incidence of 0.17 cases/100,000 population), with annual numbers of cases ranging from 121 to 264, increasing steadily since 2004 (Fig. 1). A large majority of notified cases (76.4%) was between 20 and 49 years of age; 54%

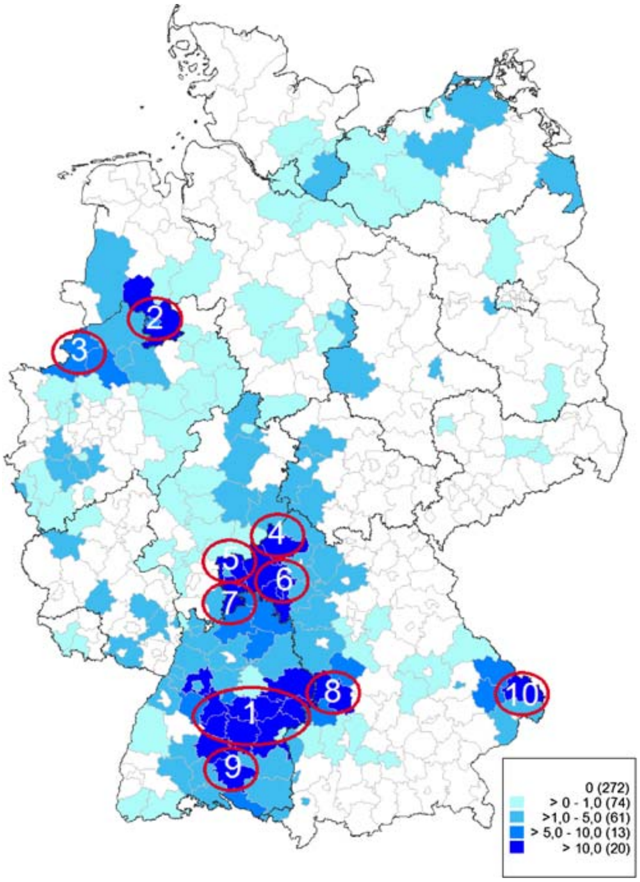

Fig. 2 Incidences of reported hantavirus infections per 100,000 inhabitants by administrative district, Germany, 2007. *Circles* represent areas in which hantaviruses were known to be endemic (*1* Swabian mountains, *2* Area Osnabruck, *3* Munsterland, *4* Unterfranken, *5* Spessart, *6* Area Würzburg, *7* Odenwald, *8* Fränkischen Alb, *9* Oberschwaben, *10* Bavarian Forrest)

were male. Data on the country or region of infection was available for 1,031 of these cases (98.4%). For a single case, autochthonous nosocomial transmission was reported after a needle stick injury in a German hospital in 2002 (Wagner et al. 2004), while all other patients acquired the infection abroad. In each year, Thailand contributed the largest percentage of cases (25% overall, 17–43% in individual years). The other three countries contributing large numbers of cases on the whole and in individual years were India (9% overall, 17% in 2003), Brazil (8% overall, 16% in 2002) and Indonesia (8% overall, 10% in 2005 and 2006; Fig. 4). The only region with a clear trend, the percentage of infections acquired in Central American countries has steadily risen from 9% in 2002 to 24% in 2007. In most years, only 2–6% of the cases got infected while travelling in Africa; however, in 2004, 15% of the cases came from Africa, mainly from the Seychelles and Tanzania. There is no clear seasonality overall with each calendar month contributing 6–13% of the cases. For some individual countries, seasonality is apparent, with most cases from Thailand reported during the summer months, those from India in the last quarter and those from Brazil from March through May.

Discussion

Vector-borne pathogens play an important role in the emergence, resurgence and redistribution of infectious diseases. In addition, the potential impact of climate change on vector-borne diseases has been identified as an important public health issue (Sutherst 2004). Hence, contemporary surveillance of vector-borne diseases that are sensitive to climate—including both autochthonous and imported infections—needs to detect and respond to the impacts of climate change on human health. We investigated routine surveillance data of imported and autochthonous vector-borne diseases in Germany to evaluate the performance of the national surveillance system with respect to geographic and temporal trends of vector-borne infections.

Looking at hantavirus infection as an example for a vector-borne disease endemic in Germany, national trends are accurately and timely detected by routine surveillance. In 2005, the increase in hantavirus cases affecting not only the known endemic areas but also several urban areas prompted us, in collaboration with federal and local public health departments, to carry out a nationwide case-control study into the risk factors of hantavirus infection. The results formed the basis for increased surveillance and control of rodent populations in selected areas and for targeted prevention measures (Abu Sin et al. 2007). In early 2007, it has been recognised that the number of notified hantavirus infections strongly increased (Koch et al. 2007). As in previous years, most infections were reported from the federal state of Baden-Württemberg, but in most

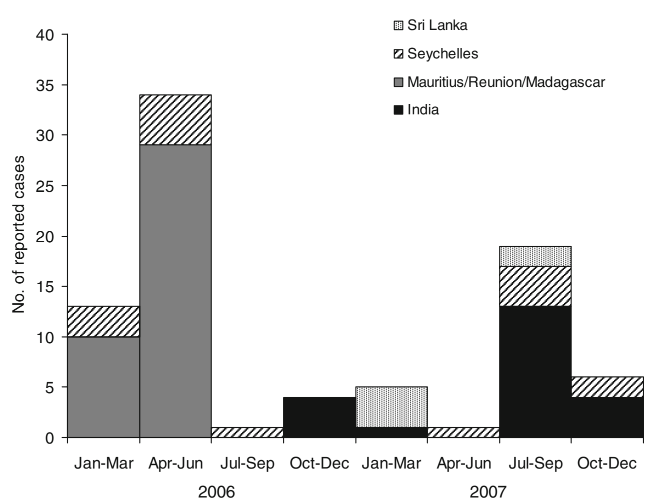

Fig. 3 Countries of origin for reported cases with chikungunya fever, Germany, 2006–2007 (*n* =85)

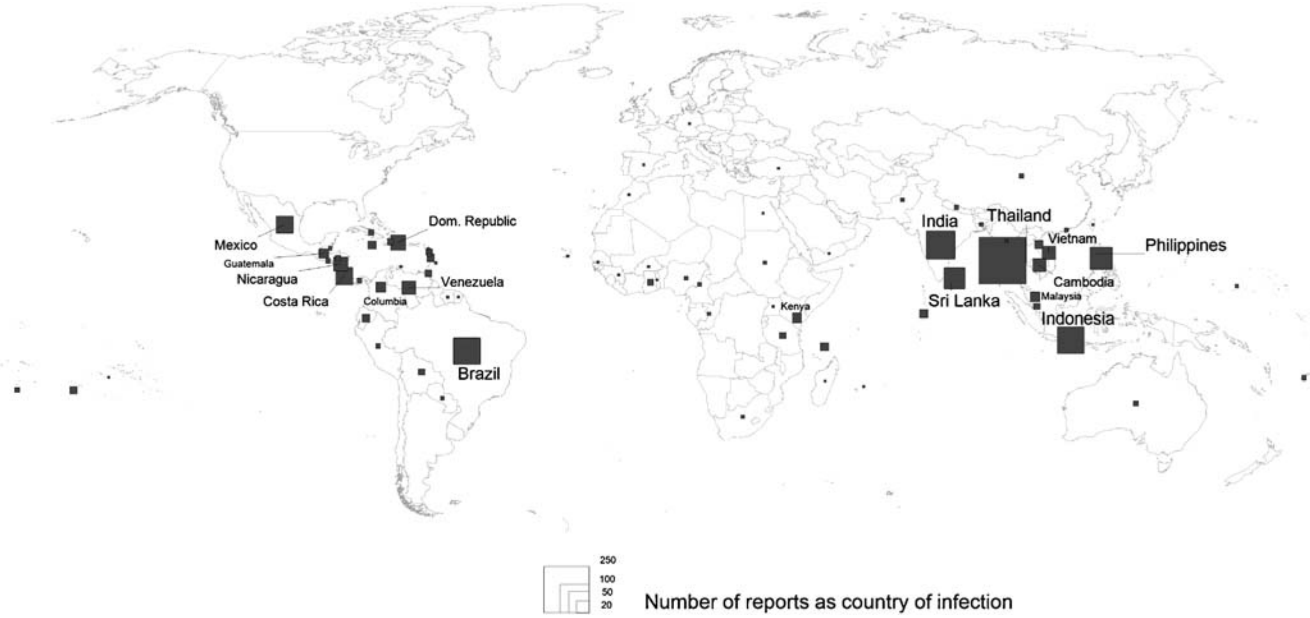

Fig. 4 Countries in which dengue infection was acquired 2002–2007 (n=1,021 mentions of individual countries)

endemic regions, infection rates never had been as high as in 2007. The incidence of human hantavirus infections is known to be correlated with the population size of the bank voles, which serve as the main reservoir of hantavirus in Germany and which are particularly abundant in endemic regions. It is well known that the geographical distribution and epidemiology of hantavirus reflects the distribution and density of the reservoir rodent (Augot et al. 2006). The dynamic of the bank vole population follows a 3- to 4-year cycle, often with two consecutive high density years (Rose et al. 2003). The winter season 2006/2007 was exceptionally mild, and in many endemic regions, there was no snow cover. In addition, there was an abundant supply of beech mast in the autumn of 2006. These conditions resulted in higher overwinter survival rates of rodents and in rapid onset of the breeding season in early spring or an extension of the reproductive activity over the winter (Krautkrämer and Zeier 2008). Due to the early detection of the upcoming hantavirus epidemic in 2007, it was possible to timely inform public health authorities and to address general recommendation for the prevention of hantavirus infections. The efficacy and performance of these recommendations, however, need to be evaluated and possibly adapted in forthcoming hantavirus seasons. In addition, further studies about the interrelation of ecologic factors (including climate), bank vole population cycles and disease incidence among humans are necessary. In this context, systematic monitoring programs of the rodent population are warranted. Such information may help to predict future epidemics in time.

With respect to newly emerging pathogens, the German surveillance system has shown a sound flexibility as demonstrated by the emergence of chikungunya virus infections among travellers from Germany. In 2006, an outbreak of chikungunya virus affected a number of islands in the Indian Ocean, including the Comoros Islands, Reunion, Mauritius, Madagascar and other islands in the southwest Indian Ocean (Charrel et al. 2007). Subsequently, the epidemic jumped to India (Panning et al. 2008), and the first outbreak in a temperate region (Italy) has been documented in 2007 when the virus was transmitted by abundant populations of *Aedes albopictus* (Rezza et al. 2007). From 2006 to 2007, the virus affected 85 German travellers. Corresponding to the spread of the virus in the Indian Ocean and India, the countries where the infections were acquired by German travellers changed during that time. Keeping in mind that these changes are also influenced by changes in travelling behaviour, German surveillance data can provide some hints regarding disease emergence in foreign countries. In autumn 2007, press reports indicated the presence of *A. albopictus* eggs in the Upper Rhine valley for the first time. At present, however, it remains unclear whether this was an isolated finding or *A. albopictus* is already about to establish itself in certain areas of Germany. Under certain conditions (existence of *A. albopictus* populations, temperatures high enough over longer time periods for virus propagation in the mosquito, viraemic human patients), it cannot be ruled out that outbreaks similar to that in Northern Italy could occur in parts of Germany as well. We assume that the networks of physicians, infectious disease specialists and public health departments will be able to timely detect the first cases of autochthonous transmission so that the extent of such an outbreak could be determined and controlled. However, it remains to be seen how the public health system would cope with larger and geographically disperse outbreaks of newly introduced vector-borne infections.

With dengue fever as an example for imported vector-borne infections, the national surveillance system of the RKI has proven to be a powerful tool in the reporting of notifiable diseases imported from tropical countries. Spatial and temporal trends are mirrored in the surveillance data with a reasonable degree of discrimination, as demonstrated by the increase in dengue virus infections imported from Brazil in 2002. At that time, the state of Rio de Janeiro recorded an incidence of dengue infections that was 6.5 times higher than it had been in January through March of 2001, and an urban epidemic in the city of Rio de Janeiro was observed (Frank et al. 2004). The city draws large numbers of German tourists (especially during the festival of Carnival), likely explaining the high number of infections acquired there. The current increase of dengue fever in German travellers returning from Central America is again reflected by reports of dengue increase in countries of the region as documented by the Pan American Health Organization (http://www.paho.org).

In general, the comparison of the number of infections acquired per country has to be weighted by the number of German travellers with this destination, i.e. the risk of acquiring dengue in Thailand, where approximately 378,500 Germans travel every year, may be similar to that of the approximately 76,000 German Sri Lanka travellers, despite vastly different absolute case numbers. Nevertheless, while comparisons between countries are problematic without good traveller data, trends can be closely monitored and current developments compared to previous years' data. The close surveillance of notification data is then used for the analysis of acute travel health risks and serves as a basis for travel warnings in Germany (http://www.rki.de: Epidemiologisches Bulletin 48/03, 41/05 and 42/07).

It has to be emphasised that no human epidemic related to an emerging and highly contagious pathogen (e.g. H5N1 influenza virus, Ebola virus) has occurred in Germany in recent years. During the severe acute respiratory syndrome (SARS) pandemic in 2003, a nationwide surveillance system for SARS was rapidly established after occurrence of the first SARS case in Germany (Krause et al. 2003). Germany, however, was only confronted with two imported SARS cases, and it is difficult to predict how exactly the national surveillance system will cope with larger epidemics of emerging diseases, especially in urban areas (Porten et al. 2006). There is a need for modelling studies to determine the potential impact of climate in the complex interplay between ecological factors, vector population dynamics, human exposure and disease incidence.

Though surveillance is one of key elements in controlling emerging and reemerging vector-borne diseases, it is clear that surveillance in itself is not sufficient to adequately address the problem of these infections. Observation of vector-borne infections should also include systematic monitoring to determine the distribution and competence of autochthonous or newly emerging vectors, monitoring of non-human reservoir species (Jansen et al. 2007) and targeted studies on other pathogens which are not notifiable in Germany at present, e.g. West Nile virus (Linke et al. 2007). The availability of such studies in turn depends on priority allocation of resources to public health. Finally, physicians need to include emerging or reemerging infections in their differential diagnosis to timely diagnose, treat and control the infection (Haas et al. 2004). In addition to mandatory surveillance, well-functioning networks of medical institutions (infectious disease departments, institutes of tropical medicine, hospitals, general practitioners) are necessary to early detect imported tropical diseases and occurring cases of autochthonous transmission. Close cooperation between physicians, laboratories and the public health service on local, federal and state levels is warranted to accomplish this requirement. At present, though, the German surveillance system is well equipped to detect both large-scale and sporadic cases of imported or autochthonous vector-borne infections in a degree of spatial and temporal discrimination that is sufficient to serve as a basis for public health recommendations and preventive measures.

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