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Chikungunya infection has been increasingly reported in international travellers following its epidemic re-emergence in the Indian Ocean islands in 2006 and its spread to southern Asia thereafter. We describe the first case of chikungunya in a Belgian traveller returning from Phuket, Thailand and discuss the potential implications of chikungunya cases imported to European countries for patient management and public health.

Introduction
Chikungunya is a tropical arboviral disease transmitted by mosquitoes belonging to the genus Aedes. Infection is characterised by an acute-onset fever, rash and incapacitating joint pain. Chikungunya virus belongs to the Alphavirus genus of the family Togaviridae, and was first isolated in Tanzania in 1953 [1]. Although periodic outbreaks occurred ever since throughout Africa as well as in southeast Asia, they were typically self-limiting and rarely had a broad geographic extension. After a long period of quiescence, chikungunya re-emerged in 2004 on the coast of Kenya and hit the islands of Comoros and Réunion in 2005, where high attack rates and large epidemics were reported. It spread then in a sweeping succession of outbreaks to other islands of the Indian Ocean and reached India in 2006 where more than 1,000,000 suspected cases were reported [1]. In the following years, Sri Lanka, Indonesia, Singapore and Malaysia were successively affected, including the south of Thailand in the late 2008. Since January 2009, more than 20,000 cases have been reported in Thailand, with evidence of spreading to the northern provinces [2]. We describe here the case of a Belgian traveller who presented in our centre with a chikungunya infection after having stayed exclusively in the popular tourist destination of Phuket (Thailand).

Case report
A Belgian woman in her forties presented in mid April 2009 at the travel clinic of the Institute of Tropical Medicine, Antwerp, Belgium with symptoms of recurrent high-grade fever (up to 39.5°C), headache, generalised muscle aches and skin rash for the last four days. She had returned two days before from a holiday trip to Thailand where she had stayed exclusively in Phuket for 14 days. She had consulted in a hospital in Phuket when the symptoms started and a dengue NS1 antigenic test was performed and reported as negative. In our centre, the patient presented with a slight macular skin rash on the trunk and limbs and a slightly swollen right ankle. Laboratory tests at the time of presentation showed a leukocytosis (2.290 WBC/µL), a borderline thrombocytopenia (138,000 platelets/µL) and elevated alanine aminotransferase (78 IU/L; normal 9-52 IU/L), aspartate aminotransferase (81 IU/L; normal 14-36 IU/L) and lactate dehydrogenase (742 IU/L; normal 313-618 IU/L). Blood smears for malaria and blood cultures were negative. Dengue fever was considered to be the most likely diagnosis.

Fever decreased the day following the consultation, but during the next two-three weeks, the patient developed severe joint aches in the feet, fingers and right wrist without evident swelling. Paired serology against dengue remained negative, as well as testing for leptospirosis, rickettsiosis, Q fever, West Nile virus, Toxoplasma gondii and cytomegalovirus. Chikungunya was considered as a differential diagnosis and serology by indirect immunofluorescence, adapted from Panning et al. (2008) [3], revealed a more than 4-fold increase of immunoglobulin (Ig) G titres against chikungunya (from 1/16 to 1/256 within 14 days). A real-time polymerase chain reaction testing, adapted from Panning et al. [3], of the acute-phase serum taken upon the first presentation in our clinic, was positive for the chikungunya virus (cycle threshold-value 33.48), while the serum sample taken 14 days later was negative. The patient fully recovered, but joint pain persisted until the beginning of June despite symptomatic treatment.

Upon receipt of the positive test result, national and regional health authorities were notified. A specific project called “Emerging Threats” has been indeed established in the Scientific Institute of Public Health of Belgium since September 2008. Its main objective is to implement a national surveillance for tick-borne encephalitis, West Nile fever and chikungunya. Our laboratory, which is the national reference centre for tropical diseases, takes part in this project by reporting monthly all serological and/or molecular diagnoses of West Nile and chikungunya infection.

Discussion and conclusion
Following the successive waves of outbreaks spreading from east Africa to southeast Asia, chikungunya infection has been reported increasingly in returning western travellers or immigrants returning from visits to their home countries during the last couple of years [3-8]. In Belgium for example, 54 cases of chikungunya have been confirmed since 2006 (38 in 2006, 9 in 2007, 7 in 2008) mainly in travellers returning from countries with recent epidemics such as Mauritius (n=17), Réunion Island (n=10), Sri Lanka (n=4), Madagascar and India (n=3 for each) (unpublished data). Compared to this, approximately 50 imported cases of dengue are diagnosed every year in our country, mainly acquired in southeast Asia/western

Chikungunya infection was confirmed in a Belgian traveller returning from Phuket (Thailand)

E Bottleau (ebottleau@itg.be), M Van Esbroeck, L Cnops, J Clerinx, A Van Gompel
1. Department of Clinical Sciences, Institute of Tropical Medicine, Antwerp, Belgium
Pacific and Latin America, with Thailand, Indonesia and India being the leading countries of infection [9]. To our knowledge, this is the first imported case in Europe of chikungunya acquired undoubtedly in Phuket, Thailand. Our observation is worth reporting because this region is probably one of the most popular travel destinations in southeast Asia. We therefore expect that significant numbers of susceptible travellers might become infected in Phuket. This would result in an increase in symptomatic travellers returning from this area attending the travel or primary care settings in various western countries and make chikungunya an important differential diagnosis in these patients.

We demonstrated recently that the pre-test probability for a traveller returning from southern Asia with fever to be diagnosed with dengue was about 15% [10]. If a skin rash, a leucopenia and a thrombocytopenia are present like in the case under discussion here, with respective adjusted positive likelihood ratios of 2.8, 3.3 and 2 [10], the post-test(s) probability for dengue rises above 50%, explaining why this was the foremost diagnosis we considered. The differentiation between chikungunya and dengue infections is often difficult [4,6]. Skin rash tends to be more frequent in chikungunya patients (75-80%) than in dengue patients (about 50%) [4-8,10]. In contrast, leucopenia and thrombocytopenia seem to occur rather similarly in both diseases, although no large comparative series have been published so far. In our case, joint symptoms became prominent during the course of the disease [7,8] and paired serology against dengue remained negative. This encouraged us to look for chikungunya as an alternative diagnosis which was ultimately confirmed by further serological and molecular investigations.

Potential implications for Europe

Besides the implications for managing individual patients, chikungunya has a potential for autochthonous transmission in Europe. This was amply demonstrated by the outbreak of chikungunya in Italy in the summer of 2007, presumably triggered by a viraemic index case – an Indian traveller returning from a visit to friends and relatives in India [11,12]. Local transmission was made possible by the presence of the receptive vector, Aedes albopictus, in Italy. This vector is established in other southern European countries as well, but not in Belgium so far although it has been sporadically introduced [13]. However, several models with different climate change scenarios predict a further spread of A. albopictus to northern Europe and consider parts of Belgium as suitable for the mosquito establishment [13]. Since the vector is sporadically introduced and might be established in Belgium in the future and since both chikungunya and dengue viruses are diagnosed repetitively in returning travellers, the risk for local epidemics, although extremely limited now, is likely to increase.

In conclusion, we have observed a case of dengue-like illness finally diagnosed as chikungunya infection and acquired in Phuket, Thailand. Phuket is a popular tourist spot in southeast Asia, increasing the likelihood of further imported cases in western countries while the local epidemic in Thailand is ongoing. Despite the similarity with dengue features, chikungunya infection should be recognised early in returning travellers because of its specific protracted morbidity and its potential for local outbreaks in European countries.

References


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Dengue fever continues to spread globally, causing major epidemics and putting major strain on health systems in affected countries. For imported dengue in Europe, south east Asia is the most important region of origin, followed by Latin America, the Indian subcontinent, the Caribbean, and Africa. Information regarding mosquito protective measures is highly recommended for all travellers to affected areas.

Introduction
Dengue fever has developed into one of the world’s major emerging infectious diseases. The infection is by now seen as a global epidemic with recorded prevalence in more than 120 countries [1]. It appears that dengue originated from Africa and was introduced to Asia some 600 years ago. The first recognised dengue epidemics occurred almost simultaneously in Asia, Africa, and North America in the 1780s. Dengue is transmitted by Aedes mosquitoes, particularly A. aegypti and, less important, A. albopictus. These mosquitoes travel well, particularly in cargo ships and the four subtypes of dengue virus have spread to most tropical and subtropical countries in their wake. During the last 200 years, spread of the disease has increased, reaching epidemic proportions during the last three decades. Since the late 1990s, dengue is the most important mosquito-borne disease affecting humans after malaria, with around 40 million cases of dengue fever and several hundred thousand cases of dengue haemorrhagic fever (DHF) each year. The main endemic areas are Latin America, the Caribbean, Africa, south and southeast Asia, and parts of the Pacific Region. For Europe, dengue remains an imported disease, even though A. albopictus has become established in some parts of the continent.

The pathogenesis of DHF is not fully understood, but it has been well documented that secondary dengue infection is a major risk factor of the disease [2,3]. As a consequence, and maybe also under genetic control, European travellers rarely develop DHF [4]. A high percentage of dengue infections in travellers occur without any symptoms [5]. However, the important role of travellers is recognised to introduce more virulent dengue strains into endemic areas where usually only mild disease occurs [6], or into non-endemic areas but where the mosquito vector is common [7].

Recent developments
While dengue activity remains quite high in Asia, Latin America has seen a particular increase of major epidemics during the last two years. Rio de Janeiro experienced serious outbreaks in 2002 and again in 2008, each straining the health infrastructure severely [8]. A severe epidemic developed in Bolivia in early 2009 with several 10,000 patients, prompting the government to declare a state of emergency for the nation [9]. Most recently, Argentina declared a dengue outbreak in the northern provinces of Salta, Jujuy, Catamarca, Chaco, and Corrientes with more than 26,000 cases [10]. The disease has spread as far as the capital Buenos Aires. On the other side of the Pacific Ocean, an outbreak of dengue fever erupted in December 2008 in northern Queensland, Australia. Located around a focus in Cairns, it spread to other parts of the tropical north of Australia [11].

Dengue importation into Europe
Reports on dengue in international travellers have increased, too. Both the increasing international air travel and the increasing activity of dengue in the tropics are responsible for the increased chance that healthcare providers, including those in western countries, are more and more likely to be confronted with imported dengue infections. In various studies at travel clinics, dengue infection was the most common cause for fever in returning travellers [4,12,13]. Since dengue surveillance, if performed at all, is passive, and since dengue infection presents either as a short and self-limiting viral disease or even asymptomatically, it is certainly one of the under-diagnosed tropical infections in travellers.

The European Network on Imported Infectious Disease Surveillance (TropNetEurop) was founded in 1999 to detect emerging infections of potential regional, national, or global impact at their point of importation into the European area. The network currently consists of 57 collaborating centres in 17 European countries. Annually, the collaborating centres give approximately 220,000 consultations prior to travel, and treat 57,000 patients post-travel [14]. From comparisons between national notification numbers and patients reported to the network, it can be safely assumed that TropNetEurop is covering around 12% of the European patients with imported infectious diseases. Within this network, the number of reported dengue cases increased from 64 in 1999 to a maximum of 224 in 2002 and remained at 100-170 since then. For 2008, 116 cases have been reported. The median age in this population is 38 years (range 12–73 years). The median duration of travel during which patients acquired the dengue infection decreased from 38 days in 1999 to a maximum of 224 in 2002 and remained at 100-170 since then. For 2008, 116 cases have been reported. The median age in this population is 38 years (range 12–73 years). The median duration of travel during which patients acquired the dengue infection decreased from 38 days in 1999 to 21 days in 2008 [15].

In 2008, 43% of the dengue cases were acquired by patients who returned from travel to countries in south east Asia, 14% were...
imported from Latin America, 12% from the Indian subcontinent, 11% from the Caribbean, and 4% from Africa (Figure 1).

This distribution reflects two different aspects: worldwide dengue activity and countries’ popularity as tourist destinations. Thailand, Vietnam, and Indonesia are not only highly endemic areas for dengue viruses, but they are also very popular destinations for European tourists. Thailand alone is responsible for almost 30% of all travel associated dengue infections in our network over the past six years. Current developments mirror the epidemics in south America, with stronger reporting from Bolivia and Argentina. In addition, unusually strong signals come also from Eritrea, Jordan, Pakistan, Papua New Guinea, South Africa, Dominican Republic, and Suriname (Figure 2).

Reporting over the past years in Europe has shown that most dengue patients are European travellers (87% in 2008). Dengue haemorrhagic fever and death have remained rare events in European travellers but are being reported almost every year. In 2008, two out of 116 patients developed complications, and one patient died of DHF.

Overall, TropNetEurop has documented a clear increase of reported dengue cases during the early 2000s, reaching a plateau since 2002. This is in line with national reporting in most European countries, as documented by the World Health Organization (WHO) Europe centralized information system for infectious diseases (CISID) database [16]. The exceptions of the rule are France with several recent dengue outbreaks in its overseas territories, and Germany, with an increase from 218 reported patients in 2002 to 263 in 2007.

**Future outlook**

It appears that the spread of dengue is only limited by the spread of its vector mosquitoes, in particular A. aegypti. Since Aedes spp. has proven to be exceptionally adapted to human habitation, its global spread cannot be controlled effectively. Dengue has moved to North America, Australia, east Asia, the Pacific, and eastern Africa. Its imminent spread to Europe has to be anticipated. However, a series of phase 2 trials for efficacy and reactogenicity of dengue tetravalent vaccines has been started in early 2009 [17]. Further trials are listed to follow soon, promising the availability of effective control tools within a few years. A dengue vaccine with high protective efficacy could change the whole picture of the current epidemic. However, as long as no effective vaccine is available, dengue viruses will present a serious threat to European travellers, to European countries with growing populations of potential vector mosquitoes, and an even greater threat to those living in already endemic countries.

**References**


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Parvovirus B19 infection may be mistakenly reported as measles or rubella if laboratory testing is not performed. As Europe is seeking to eliminate measles, an accurate diagnosis of fever/rash illnesses is needed. The main purpose of this study was to describe the epidemiological pattern of parvovirus B19, a common cause of rash, in Ireland between January 1996 and June 2008, using times series analysis of laboratory diagnostic data from the National Virus Reference Laboratory. Most diagnostic tests for presumptive parvovirus B19 infection were done in children under the age of five years and in women of child-bearing age (between 20-39 years-old). As a consequence, most of the acute diagnoses of B19 infection were made in these populations. The most commonly reported reasons for testing were: clinical presentation with rash, acute arthritis, influenza-like symptoms or pregnancy. The time series analysis identified seasonal trends in parvovirus B19 infection, with annual cycles peaking in late winter/spring and a six-year cycle for parvovirus B19 outbreaks in Ireland.

Introduction

Human parvovirus B19 infection is the cause of erythema infectiosum, or “slapped cheek” disease, a fever/rash illness occurring most frequently in childhood. The clinical presentation of parvovirus B19 infection is sometimes mistakenly diagnosed as rubella or measles. Although typically a mild, self-limiting disease, the infection can cause severe adverse outcomes in certain groups. In pregnant women infection can result in foetal death or hydrops foetalis, and among individuals with haematological disorders, complications such as anaemia or aplastic crisis can occur [1].

An accurate diagnosis of fever/rash illness is necessary not only for case management but also for public health control activities, particularly in outbreak situations in which measles or rubella is suspected [2]. As Europe seeks to eliminate measles as part of the World Health Organization’s European strategy it is important that fever/rash illnesses are accurately diagnosed and that parvovirus B19 infection is not mistakenly reported as measles or rubella [3,4]. The lack of commercially available, convenient and non-invasive diagnostic tests for parvovirus B19 may play a role in the misdiagnosis of measles and rubella cases [5,6]. Because many individuals with fever/rash illnesses are not routinely tested, each year many notified measles and rubella cases are not laboratory-confirmed. In Ireland in 2007, for instance, only 20 of 53 notified measles cases were laboratory-confirmed [7].

No data are available on the prevalence of parvovirus B19 infection in the Irish population, nor on the pattern of disease incidence in Ireland. As the infection is often asymptomatic, it is difficult to have a comprehensive picture of disease incidence. Due to the limited information available to us on the epidemiology of B19 in Ireland, we collaborated with the National Virus Reference Laboratory (NVRL) on a study to describe which population groups were most commonly tested for parvovirus B19, and to describe, using the pattern of laboratory diagnosis of acute infection, the epidemic pattern of acute parvovirus B19 in Ireland between January 1996 and June 2008.

Materials and methods

The NVRL is the main diagnostic facility in Ireland for the diagnosis of parvovirus B19 infection. During our study we identified three regional hospitals which also offer local testing but they represented a minority of all tests done in Ireland. Upon suspicion of acute parvovirus B19 disease, a clinician may request diagnostic testing. Serum samples are sent to the diagnostic laboratory either directly, by individual clinicians, or via any of the hospitals’ microbiological laboratories. Acute infection is diagnosed by the detection of parvovirus B19-specific immunoglobulin M (IgM). These samples are tested by enzyme immunoassay (EIA) in serum or plasma (Parvovirus B19 IgM (mu capture) EIA, Biotrin International).

To estimate the incidence of laboratory-confirmed disease in Ireland, information relating to each individual testing positive for parvovirus B19-specific IgM was extracted from the laboratory information system at the NVRL and sent to the Health Protection Surveillance Centre (HPSC) for analysis. The initial database consisted of a listing of all the positive tests performed at the NVRL with details on place and date of blood samples, age and sex of the patient, clinical symptoms associated with disease or an underlying condition consistent with this diagnosis, results for parvovirus IgM testing and parvovirus IgG testing in laboratory-confirmed acute cases. To eliminate duplicate results originating from patients presenting to clinicians for the same event, all the line listings were reviewed. Duplicates were defined as similar records based on same dates of birth, sex, place of testing, within a period of three days. Duplicate records were excluded from subsequent analysis. Age and sex distribution, clinical features according to the age and sex of the patient, time and place of occurrence of positive tests for parvovirus IgM were described.
Times series analysis was carried out for the series of laboratory-confirmed acute parvovirus B19 cases reported per month. A linear function was used for analysing secular trends. In order to describe cycles and seasonality in the series, secular trend was removed and data were log transformed for stabilising minor changes in the variance along the series. From the new working series, cyclic components were identified using a Fast Fourier Transformation. Cycles with energy above the upper limit of the 95% confidence interval for the mean energy of the cycles were estimated using the least squares period. An equation with the following structure was obtained:

\[ y = f(x) + \sum A \cos \left( \frac{2\pi (x - \theta)}{p} \right) \]

where \( A \) is the amplitude, \( \theta \) is the phase and \( p \) is the period of cosine function of significant cycles.

Analyses were performed using Stata V9.2 (Stata Corporation) and the Fourier Transformation was done using R V2.8.1 (R foundation, www.r-project.org).

**Results**

**Descriptive results**

Parvovirus B19 tests undertaken by NVRL

Between January 1996 and June 2008, a total of 12,430 tests for parvovirus B19 were carried out at the NVRL. Of those, 546

**Figure 1**
Requests for parvovirus B19-specific immunoglobulin M detection by year, National Virus Reference Laboratory, Ireland, January 1996-June 2008 (n=11,437)

**Figure 2**
Requests for parvovirus B19-specific immunoglobulin M detection by age group and sex, National Virus Reference Laboratory, Ireland, January 1996 -June 2008 (n=11,437)

**Figure 3**
Number of positive tests for parvovirus B19-specific Immunoglobulin M by age and sex, National Virus Reference Laboratory, Ireland, January 1996-June 2008 (n=497)*

* Age is unknown for 15 patients and sex is unknown for two patients under the age of 10 years

**Table**

Most common clinical associations observed in patients with parvovirus B19-specific immunoglobulin M by age group, National Virus Reference Laboratory, Ireland, January 1996-June 2008

<table>
<thead>
<tr>
<th>Age group</th>
<th>&lt;15 years (n=86)*</th>
<th>≥15 years (n=190)*</th>
<th>Total (n=196) †</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical features</td>
<td>No. of reports (% Total)</td>
<td>No. of reports (% Total)</td>
<td>No. of reports (% Total)</td>
</tr>
<tr>
<td>Rash</td>
<td>28 (34)</td>
<td>52 (63)</td>
<td>83 (42)</td>
</tr>
<tr>
<td>“Slapped cheek” appearance</td>
<td>5 (71)</td>
<td>2 (28)</td>
<td>7 (3.5)</td>
</tr>
<tr>
<td>Acute arthritis</td>
<td>7 (16)</td>
<td>35 (79)</td>
<td>44 (22)</td>
</tr>
<tr>
<td>Fever</td>
<td>9 (32)</td>
<td>18 (64)</td>
<td>28 (14)</td>
</tr>
<tr>
<td>Influenza-like symptoms</td>
<td>1 (4)</td>
<td>24 (92)</td>
<td>26 (13)</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>0</td>
<td>23 (96)</td>
<td>24 (12)</td>
</tr>
<tr>
<td>Intrauterine death</td>
<td>0</td>
<td>8 (100)</td>
<td>8 (4)</td>
</tr>
<tr>
<td>Preterm delivery</td>
<td>0</td>
<td>1 (100)</td>
<td>1 (0.5)</td>
</tr>
<tr>
<td>Anaemia</td>
<td>11 (73)</td>
<td>4 (26)</td>
<td>15 (8)</td>
</tr>
<tr>
<td>Haemophilia/Sickle cell anaemia</td>
<td>7 (70)</td>
<td>1 (10)</td>
<td>10 (5)</td>
</tr>
<tr>
<td>Sore throat</td>
<td>3 (42)</td>
<td>4 (57)</td>
<td>7 (4)</td>
</tr>
<tr>
<td>Lymphadenopathy</td>
<td>0</td>
<td>5 (100)</td>
<td>5 (3)</td>
</tr>
<tr>
<td>Headache</td>
<td>3 (75)</td>
<td>1 (25)</td>
<td>4 (2)</td>
</tr>
<tr>
<td>Bone marrow transplant</td>
<td>2 (100)</td>
<td>0</td>
<td>2 (1)</td>
</tr>
</tbody>
</table>

* The total number of symptoms exceeds the total number of cases as more than one symptom could be mentioned per case.
† Age is unknown for eight patients for whom clinical details were given.
were positive, and 993 duplicates tests were identified. Following de-duplication, 514 (4.5%) acute cases of parvovirus B19 were identified out of 11,437 tests performed (Figure 1).

The number of test requests increased over the time period, from 500 requests in January 1996 to 1,388 in 2007. The proportion of IgM-positive tests varied depending on the year and the seasonality of parvovirus B19 in the community.

Most samples (27%) originated from children under the age of 10 years, the majority of whom were under five years old (19% of all events). The next largest age group was the age group of 30-39 year-olds (23%), followed by 20-29 year-olds (16%). Females were more likely to be tested than males (64% of all requests), most marked in the women of child-bearing age; 77% of requests were made for the 30-39 year-old group and 83% for the 20-29 year-olds (Figure 2).

Positive tests (n=514)
Overall, 76% of all positive tests occurred in female patients, giving a female:male ratio of 3.3:1 (Figure 3). The median age of all cases for whom the age was known was 31 years (range 7 days to 92 years); information on age was missing for 15 positive patients. Males tested positive were more likely to be younger than females (p<10^-3). The median age for male patients was nine years and for female patients 33 years.

A total of 168 positive tests (32.7%) belonged to patients under the age of 15 years; 137 positive tests (21.3%) occurred in children between 0 and 9 years of age, with equal distribution between male and female children; 160 (31.1%) positive tests originated from patients between 30 and 39 years of age, 90% of whom were female. Of the 514 IgM-positive cases, 300 (58.4%) were also positive for IgG.

Regional distribution of events
There was marked regional distribution of positive tests. Most of the positive IgM samples (60.3%) were from the former Eastern Health Board region (encompassing the Dublin metropolitan region among others). Samples originating from the North Western Health Board, the Midland Health Board and the North Eastern Health Board represented 7.8%, 5.8% and 5.4% of positive tests, respectively. The lowest number of positive test results came from samples taken in the Western Health Board and in the Mid-Western Health Board regions (2.4%).

Clinical information provided with diagnostic samples
Clinical information accompanied the request for parvovirus B19-specific IgM testing for 198 (38.5%) of patients who tested positive for parvovirus IgM (Table). Parvovirus B19 infection was characterised by a variable combination of symptoms: rash, influenza-like symptoms, joint pain and haematologic abnormalities were often reported.

The most common symptom reported in parvovirus B19 IgM-positive patients was a rash (n=83, 42%) but the typical “slapped cheek” appearance was mentioned in only seven patients as shown in the Table. Joint pain was reported in 44 patients (22.1%) and was more common in adults than children. Fever was the third most commonly reported symptom (14%). Anaemia was the reason for testing in 15 patients (8%), and these were mainly young patients with 11 (68%) under the age of 15 years. Among these 11, six had sickle cell anaemia and four had haemophilia.

Finally, 24 women (12%) were tested because they were pregnant (the specific circumstances however were not reported for the majority of them). Among those women, eight experienced an abortion or a miscarriage (one in 1996, two in 1999, one in 2000, one in 2004, two in 2005 and one in 2008).

Other documented symptoms reported at the time of diagnostic test request were varied and often unspecific, including reporting influenza-like symptoms, fever and fatigue (30 patients, 15.1%). Three parvovirus infections occurred in patients known to be immunocompromised (Hodgkin's disease, renal transplant). One case was due to occupational exposure (unspecified).
Seasonal pattern and periodicity of epidemic years

The 514 acute cases of parvovirus B19 were reported over a period of 149 months between January 1996 to June 2008 (Figure 4). The average number of cases diagnosed per month was 3.4 (standard deviation (SD) +/- 3.7). The maximum number of cases was diagnosed during April 1999 (n=20). An increasing trend in the number of acute cases was observed over the study period.

The Fast Fourier Transformation analysis identified two statistically significant components, one annual and the other every 75 months, i.e. approximately six years (Figure 5). Annual cycles peak during winter/spring; each year the majority of cases occurred between March and July.

Discussion

In Ireland as well as in most other European countries, parvovirus B19 infection is not a notifiable disease, and neither clinical descriptive data nor epidemiological data are readily available. To our knowledge, this is the first Irish study which attempts to describe the clinical and epidemiological pattern of parvovirus infection based on acute cases identified by the reference laboratory.

Our initial objective was to describe the epidemic pattern of parvovirus infection. We identified a periodicity of six years and an annual seasonality pattern, with most cases diagnosed between March and July. Our results showed that there was no sex difference in testing patterns in young children, which was to be expected as parvovirus B19 affects both sexes equally. In older age groups, testing is done predominantly in women; during pregnancy, the disease can lead to severe adverse outcomes for the foetus. Of 24 parvovirus B19 positive women known to be pregnant in this report, nine experienced a foetal loss, of whom four had acquired the infection during a time of increased incidence (two in 1999 and two in 2005). A prospective study in the United Kingdom estimated the risk of transplacental infection at 30%, with 5-9% of foetal loss reported [8]. As the number of pregnancies as well as the coverage of the screening in pregnant women are unknown for our study period, the data are not comparable. Nevertheless, they remind us of how severe the disease can be in pregnant women and of the consequences for the foetus. A better knowledge of the prevalence of parvovirus B19 in the Irish population is needed for further interpretation.

Our data were obtained from the Irish National Reference Virus Laboratory. It is situated in Dublin, the metropolitan area of which accounts for approximately one quarter of the Irish population. Although this may explain in part why the majority of tests came from the Eastern region (including Dublin), it does not fully explain the under-representation of other regions in these results. The extent to which other alternative testing may be done at local level is a possibility. However, we could identify only three other regional hospitals that undertook testing, and the number of positive tests performed there during the period under investigation was small (n=50). Despite this lack of regional representation we believe that our data represent a fair approximation of the current endemic situation of symptomatic parvovirus B19 in Ireland. The overrepresentation of the Dublin area most likely reflects increased awareness of testing and submission to the laboratory by both clinicians and the local hospital laboratories. There is no reason to suspect that there is a connection between geography and susceptibility to this common illness. The epidemiology of parvovirus B19 infection has many of the characteristics of other common childhood communicable diseases which were common in the pre-vaccine era (e.g. measles, rubella or mumps), all of which demonstrated outbreak years followed by periods of low incidence before the next outbreak. However, our data are unlikely to be fully representative of the true distribution of acute parvovirus B19 infection in the general Irish population due to a testing bias for certain population groups (young children and women attending maternity hospitals). It is likely that people tested in the present study represent the most seriously affected cases or the population considered to be most at risk.

Because human parvovirus infection is not a notifiable disease in Ireland, we cannot test the assumption that IgM-positive results from a reference laboratory are representative of the pattern of acute infection in the community. Nevertheless previous studies have used data from reference laboratories to describe the seasonality of parvovirus B19 [9,10]. In Ireland, measles is a notifiable disease. By comparing the pattern of measles-specific positive samples tested by NVRL with the distribution pattern of measles notifications to the HPSC between 2000 and 2008, we find a similar trend, with an increase in laboratory testing for measles during periods of increased notification, thus supporting the main assumption we made for parvovirus B19. Published data on the seasonal activity of parvovirus B19 in temperate countries are limited. According to our data most of the cases occurred during winter and late spring. Based on the times series analysis, the periodicity of epidemic years is six years, which is concordant with data published for some other developed countries [10-12]. However we cannot exclude that the pattern of the disease may present with one or two consecutive epidemic years: both 2004 and 2005 had a substantial number of positive tests. Even though the data from a reference laboratory are not as informative as the data which could be provided by a national surveillance system, they can provide helpful insight into the epidemiological pattern of non-notifiable diseases. Awareness of the normal epidemiology of parvovirus B19 can help clinicians who are confronted with patients with rash illnesses in the differential diagnosis for all compatible rash illness, especially measles.

Assuming a periodicity of six years, we can expect the next epidemic year in the coming two years (2011). We hope that this study will alert clinicians and increase diagnostic testing of all rash illnesses as they present. Numerous studies have highlighted the difficulty in making an accurate diagnosis of rash diseases [5,6,13,14]. The development of new and non-invasive technology that allows the sampling of oral fluid to diagnose viral infections such as measles [15], mumps [16], and hepatitis A and B [17] has increased the number of laboratory-confirmed diagnoses in many countries. Such testing has been found to be both sensitive and specific and is routinely used in many countries in case diagnosis. Commercial tests for the serological diagnosis of parvovirus B19 are available, but none are validated for use on oral fluid samples. Such a diagnostic tool would be invaluable, particularly when investigating fever/rash illnesses in young children [2] who are not so ill as to require hospitalisation but are usually seen by general practitioners (GPs) in the community. Anecdotal reports indicate that Irish GPs are reluctant to undertake phlebotomy in such paediatric cases and hence accurate laboratory confirmation of fever illness is often not done. A recently developed test to diagnose acute parvovirus B19 infection using oral fluid samples is now being assessed by the NVRL as part of a collaborative study with HPSC and clinicians around the country.
The value in adding parvovirus testing to enhanced measles surveillance has been demonstrated in South Australia where measles, rubella and parvovirus testing are included in routine measles surveillance. Despite a low overall rate of measles testing, this was particularly obvious in an inter-epidemic period when most notified measles cases were not measles [18]. Between 2% and 10% of suspected measles cases tested in South Australia between 1999 and 2004 were parvovirus B19 cases [19]. An added value was also shown when including parvovirus testing in the rubella surveillance programme [14].

In countries in the elimination phase for measles and rubella, a better knowledge of the epidemiology of parvovirus B19 may help clinicians in the differential diagnosis of common rash diseases. Meanwhile, a better laboratory confirmation of common rash illnesses is required to improve the quality of national data and public health action. The anticipated availability of an oral fluid test for parvovirus B19 will be useful in this aim.

References

Strama (the Swedish Strategic Programme against Antibiotic Resistance) and the Swedish Institute for Infectious Disease Control (SMI) launched the seventh report on the use of antibiotics and resistance in human medicine in Sweden, Swedres 2008, on 10 June 2009 [1]. The report published jointly in conjunction with a similar veterinary report from the National Veterinary Institute (Svarm), shows a 1.6 % decrease in sales of antibiotics in Sweden compared with 2007, whereas from 2004 to 2007 there had been a continued slight increase. Swedres 2008 highlights a number of areas that require particular attention and further investigation such as the high antibiotic pressure and poor compliance to guidelines for the antibiotic treatment of the elderly and a considerable spread of vancomycin-resistant enterococci (VRE) over several Swedish counties, mainly affecting the elderly.

Use of antibiotics

Sales data are obtained from the National corporation of Swedish pharmacies. The use of antibiotics in Sweden is highest among the elderly and children with prescription rates varying considerably between different parts of the country. The fraction of children aged 0-6 years treated with at least one course of antibiotics ranges from 38 per cent in Stockholm county to 25 per cent in Västerbotten county, with a national average of 33 percent. The corresponding number among the group of people over 80 years of age was 36 % but this figure is likely to be an underestimate, as the prescription of antibiotics in hospitals and care homes frequently are not registered according to age. In this respect it is important to note that the elderly are particularly at risk concerning severe side effects of antibiotics, such as Clostridium difficile infections.

The use of antibiotics in hospital care seems to be changing in a desirable way, with broad spectrum antibiotics being replaced by narrow spectrum substances. Various types of penicillins have increased and the use of cephalosporins and fluoroquinolones is decreasing.

This is in accordance with the guidelines on the reduction of prescription of fluoroquinolones against lower urinary tract infections in women, a subject of information campaigns aimed at health professionals for several years [2]. The decrease in the use of cephalosporins in hospitals is remarkable as Sweden has a long tradition of extensive use of cephalosporins. To use less fluoroquinolones and cephalosporins is a recommendation in the antibiotic policy to reduce the risk for selection and spread of extended-spectrum beta-lactamases (ESBL) containing bacteria in hospitals [3].

Use of antifungals

The total use of antifungals for hospital in-patients remains practically unchanged from 2007 to 2008. The use of amphotericin B increased whereas the use of fluconazole decreased a little in 2008 after several years of steep increases. However, fluconazole still represents 80 % of the total antifungal drugs used for in-patients.

Antibiotic resistance

Four types of antibiotic resistance are mandatorily notifiable according to the Swedish Communicable Diseases Act. The major part of data on antibiotic resistance in Sweden, however, is gathered by the voluntary reporting by Swedish clinical microbiology laboratories via the annual resistance surveillance and quality control (RSQC) programme. Three quarters of the labs also supply data on defined invasive isolates to the European Antimicrobial Resistance Surveillance System (EARSS) network database.

The major trends in 2008 were an increase of notifiable ESBL-strains by almost 30 %, 2,957 cases, compared to 2007. On the positive side was that the transmission of meticillin resistant Staphylococcus aureus (MRSA) in the health-care sector seems to have stabilized, 1,307 cases, probably due to extensive case-finding and promotion of compliance to basal hygiene principles.

Other resistances covered in the report are Streptococcus pneumoniae and pyogenes, Enterococcus faecium and faecalis, Haemophilus influenzae, Klebsiella pneumoniae, Escherichia coli, Helicobacter pylori, Campylobacter jejuni/coli, Neisseria gonorrhoeae, and Mycobacterium tuberculosis.

References


This article was published on 25 June 2009.
The Robert-Koch Institute in Germany has just published their latest annual epidemiological report on notifiable infectious diseases, analysing the data from 2008 [1]. The report is in German, but contains an English summary as well as tables and graphs presenting the geographical and demographic distribution of the reported cases and showing trends over the past six years.

After an extraordinary surge in hantavirus infections in 2007, the incidence in 2008 returned to the low level seen in 2003-2006, with 0.3 per 100,000 population.

The number of newly diagnosed infections with human immunodeficiency virus (HIV) in 2008 was higher than in 2007, but compared to the steady increase seen between 2001 and 2007, this difference was small. The increase in 2008 is reported to be due mainly to infections in people originating from areas with a high HIV prevalence.

Seasonal influenza activity in 2007-8 was weak. The circulating viruses were mainly influenza A(H1N1) and later influenza B viruses. Resistance to oseltamivir was seen for the first time in 13% of influenza A(H1N1) viruses in 2008.

Regional outbreaks of measles led to an increase in reported cases in 2008 (n=916, incidence 1.1/100,000) compared to 2007 (n=566). The majority of cases were not vaccinated. Most cases occurred in southern Germany, in Bavaria and Baden-Württemberg. These areas are bordering Austria and Switzerland, two countries that also had a number of outbreaks in 2008 [2,3].

With 43% of all notified cases, norovirus gastroenteritis was the most commonly reported disease in 2008. The winter season 2007-8 saw the highest number of norovirus infections in Germany since the start of mandatory notification in 2001.

A total of 370 cases of Q fever were reported in 2008. There was no clear accumulation in the summer months as seen in the previous outbreak years 2003, 2005 and 2006. Rather, the cases occurred evenly throughout the year.

The steady decline in tuberculosis incidence since 2002 continued, and the number of reported cases in 2008 (n=4,526) was again almost 10% under the level of the previous year.

The full report [1] can be downloaded from the website of the Robert-Koch Institute, together with a comprehensive table listing case numbers and incidence rates by federal state for the years 2007 and 2008 [4].

References

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