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HEPATITIS A IN THE EUROPEAN UNION: RESPONDING TO CHALLENGES RELATED TO NEW EPIDEMIOLOGICAL PATTERNS

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Hepatitis A is a vaccine-preventable acute, usually self-limiting disease caused by infection with the hepatitis A virus (HAV). Transmission is usually by the faecal-oral route, including via person-to-person spread, contaminated water or food products. It has also been associated with injecting drug use and outbreaks among men having sex with men.

In the European Union (EU), though figures may vary among countries, the overall incidence of hepatitis A has decreased over the last 10 years from 15.1 per 100,000 population in 1996 to 3.9 per 100,000 in 2006 [1]. This decreasing trend has been attributed to continued improved sanitary and living conditions, with reduced exposure to infection, especially in early childhood. However, reduction in circulation of HAV leads to decreased acquisition of immunity and, in the absence of universal vaccination, an accumulation of susceptible individuals.

The impact of increasing susceptibility of the general population on the risk for outbreaks is clearly illustrated in independent outbreaks in Czech Republic, Latvia and Slovakia in 2008, described in three of the articles published in this week's issue of *Eurosurveillance* [2-4]. In these papers, the authors describe the extent to which hepatitis A can spread within at-risk susceptible populations and in the cases of Czech Republic and Latvia within the general population. In these reports, a significant proportion of cases are young adults, resulting in potentially more severe clinical presentation and posing a challenge to the health authorities in the area of safety of blood and tissue donation.

Experiences from the response to these outbreaks were the focus of a technical meeting organised by the European Centre for Disease Prevention and Control (ECDC) in collaboration with the Latvian Public Health Agency in Riga in November 2008, where the epidemiological pattern of hepatitis A outbreaks was reviewed, as well as the role of vaccination in outbreak settings. Discussions highlighted the fact that emergence of outbreaks in the EU generally follows the introduction of the virus from endemic countries through "seeding events". Non-immunised travellers to endemic areas are often at the origin of seeding events, as shown in this week's issue of *Eurosurveillance* in the three articles from France, Belgium and Germany [5-7] which describe clusters of travel-related cases following visits to Egypt.

To prevent the introduction of HAV in the EU travellers to endemic countries need to be vaccinated, and indeed vaccination

for travellers is recommended by the national guidelines of these three countries. However, as the authors point out, none of the cases reported in their articles had been vaccinated. These clusters therefore highlight the importance of effective travel medicine advice reaching EU travellers of all age groups.

Seeding events can be self-contained. However, when occurring in at-risk settings or communities, HAV transmission may be "amplified" and result in a wide spread of the disease, as described among injecting drug users in the reports by Czech Republic and Latvia, as well as among Roma populations as reported by Slovakia. Similarly, infected food-handlers may contribute to transmission amplification. Introduction of HAV by children attending day care centres or primary schools represents another type of situations at risk of increased transmission. The Slovak experience shows that immunisation targeting at-risk communities following such introduction may prevent the spread to the general community. However, the Czech example shows that such a strategy for control may not be effective with hard-to-reach communities such as injecting drug users.

Once the outbreak spreads to the general population, vaccination of contacts, as carried out in Czech Republic, represents an option to complement isolation of cases and health education measures, if done within a few days from exposure. Currently, there is no evidence-based guidance available regarding the use of HAV vaccine in outbreak control.

Though the total number of cases may be decreasing yearly in the EU, the articles published in this edition of *Eurosurveillance* indicate that hepatitis A is still an important public health issue, and highlight the need for increased awareness of both the risk of infection to the individual and the possibility of community outbreaks within a changing EU epidemiology.

As HAV vaccination is not included in universal immunisation schedules, the EU is likely to experience similar outbreaks in the future. This stresses the need to promote immunisation of all travellers to endemic areas to prevent return introduction and to develop evidence-based guidance for outbreak control strategies.

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Rapid communications

INCREASE IN HEPATITIS A CASES IN THE CZECH REPUBLIC IN 2008 – AN UPDATE

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In 2008, 1,616 cases of hepatitis A were reported in the Czech Republic, more than a 10-fold increase compared with the annual number of cases registered in 2003-2007. The infection was initially associated with injecting drug users, most probably by person-to-person contact or parenteral transmission, and in the second half of the year continued to spread among the general population with increased susceptibility.

Introduction

Since the end of May 2008, an increase in reported cases of hepatitis A virus (HAV) infection has been observed in the Czech Republic. From 1 January to 31 December 2008, a total of 1,616 laboratory-confirmed cases were reported. The objective of this paper is to provide basic information on hepatitis A morbidity and outbreak control measures taken by the Public Health Protection Authorities (PHPA) in the Czech Republic.

Methods

In the Czech Republic, hepatitis A is a reportable disease. The attending physician (most often the general practitioner) recommends quarantine of the patient with confirmed or suspected hepatitis A and reports the case to the respective PHPA without delay. The hospital infectious disease departments report admission of each patient with the indication of diagnosis at admission to the respective PHPA. Any patient quarantined or placed under medical

supervision with suspected hepatitis A is examined clinically, biochemically and by laboratory tests for the detection of diagnostic markers of HAV. In the Czech Republic, the laboratory tests include the screening of sera for the presence of specific antibodies against HAV (anti-HAV IgM).

Hepatitis A prevention in the Czech Republic is specified in the Guidelines of the Ministry of Health [1]. A confirmed case of hepatitis A is defined as a person who meets the clinical and laboratory criteria in accordance with the European Union (EU) case definition [2].

The confirmed cases of hepatitis A are reported by the respective PHPA to the national reporting system for infectious diseases EPIDAT. Identification data and standardised results of the epidemiological investigation and laboratory analyses are entered into the EPIDAT system.

Results

From 1 January to 31 December 2008, 1,616 laboratory-confirmed cases of hepatitis A were reported in the Czech Republic, i.e. 15.7 cases per 100,000 population. This is a 10.6 fold rise in comparison with the annual average number of cases reported in 2003 to 2007 (mean 153 cases, range 70 – 322 cases) (Figure 1).

FIGURE 1

Annual incidence rates of viral hepatitis A per 100,000 population, Czech Republic, 2003-2008

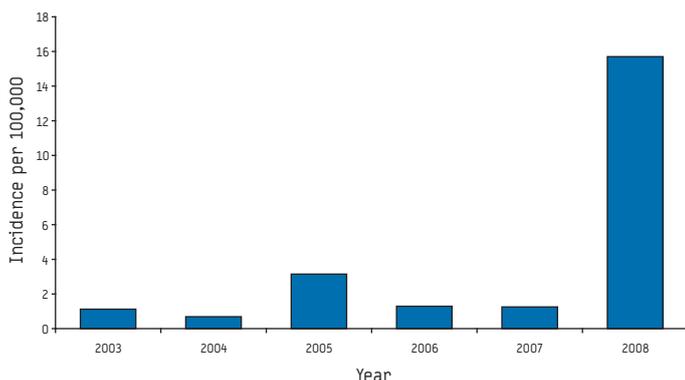
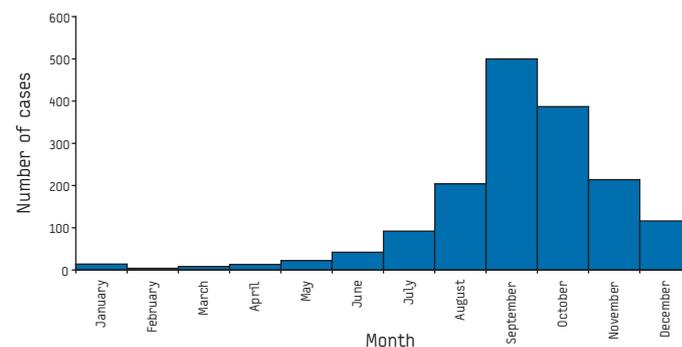


FIGURE 2

Cases of viral hepatitis A reported in the Czech Republic, in 2008, by month of onset (n=1,616)



A marked increase in hepatitis A cases had been observed since the end of May 2008 [3], with a total of 61 cases reported in the first five months of the year, compared to 1,555 cases in the period June to December 2008 (Figure 2).

Two cases were fatal. One was a 33-year-old non-vaccinated drug addict co-infected with hepatitis A, B and C and the other was a 75-year-old man vaccinated as a family contact one day prior to the onset of disease. The latter patient was hospitalised because of relapsed hepatitis. In accordance with the International Classification of Diseases (ICD 10) [4], the final diagnosis was B15.9: hepatitis A without hepatic coma.

The majority of cases were reported in the following three of the 14 administrative regions: Prague region (878 cases, i.e. 54.3% of the reported total), Central Bohemian region (206, i.e. 12.7%) and Olomouc region (147, i.e. 9.1%). In the remaining regions, sporadic cases and small, mostly family outbreaks were reported. The family outbreaks included 382 hepatitis A cases (23.6 % of the total). The absolute numbers of cases are shown in Figure 3.

FIGURE 3
Cases of viral hepatitis A in the Czech Republic, in 2008, by region (n=1,616)

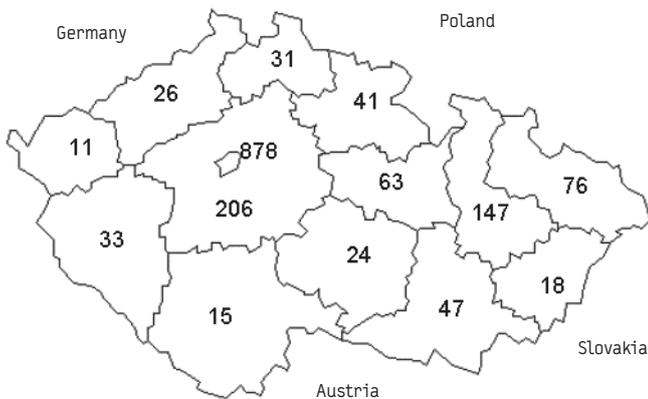
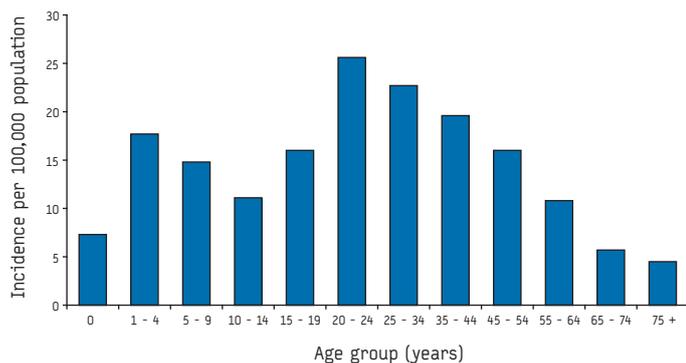


FIGURE 4
Cases of viral hepatitis A reported in the Czech Republic, in 2008, incidence rate per 100,000 population, by age (n=1,616)



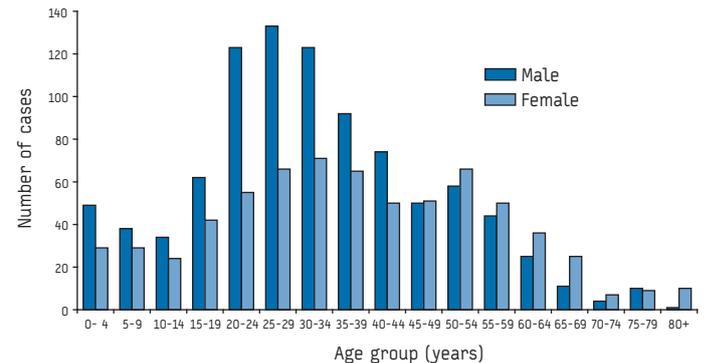
As for age distribution, most hepatitis A cases (82.7 %) were reported in patients aged 15 to 64 years. The most affected age group was that of 25-34 years (393 cases). The highest age-specific incidence rate was reported in the age group of 20-24 years (25.7 cases per 100,000 population). In children aged 0-14 years, 203 cases (12.3% of the total) were diagnosed (Figure 4). As expected, increase in hepatitis A cases in children was observed in September and October 2008 with the start of the new school year and the return of children to school and preschool communities.

Of the total of 1,616 cases of hepatitis A, 931 (57.6%) were reported in males and 685 (42.4%) in females. The greatest difference in sex distribution of cases was found in young adults, with up to 2.5 times more affected males than females (Figure 5).

At the very beginning, the increase in hepatitis A cases was significantly associated with injecting drug users (IDUs), with the highest contribution of the age group of 25-34 years, particularly in the administrative regions of Prague and Central Bohemia where epidemic outbreaks were reported. In the first weeks, IDUs accounted for 2/3 of the cases. HAV transmission in high-risk groups was due to sub-standard hygiene. In the second half of 2008, hepatitis A spread significantly among the adult general population and the proportion of cases in IDUs considerably decreased. In 2008, 226 hepatitis A cases (i.e. 14.0% of the total) were reported in IDUs. Altogether 421 (26.1%) cases were reported in persons considered to be at a higher risk of infection (homeless individuals, prisoners, drug users, alcoholics and persons engaging in high-risk sexual behaviour).

The number of imported cases of hepatitis A in 2008 was 68, about twice as high as reported annually during the last decade, but as a proportion of the total number of cases it was as low as 4.2%. The largest number of imported cases from a single country came from Egypt (20 cases), followed by Slovakia (9 cases), Greece and Croatia (5 cases per country), Tunisia (4 cases), Spain (3 cases), Ukraine, Turkey, France, Italy and Canary Islands (2 cases per country) and 10 other countries (single cases). None of the imported cases came from Latvia where a large outbreak has been ongoing [5,6].

FIGURE 5
Cases of viral hepatitis A reported in the Czech Republic, in 2008, by age group and sex (n=1,616)



Measures and recommendations

Standard outbreak control measures coordinated by the Ministry of Health continue to be taken. They include particularly isolation of patients, medical supervision of close contacts. Medical supervision that consisted in clinical and laboratory follow-up of contacts throughout the maximum incubation period was provided to more than 7,000 persons. Close contacts involved in epidemiologically significant activities (e.g. in food industry) have been instructed to stop such activities and to remain under enhanced surveillance for 50 days after the last contact with the hepatitis A patient. Other measures are disinfection and targeted vaccination in the focus of infection. Post-exposure prophylaxis with vaccine was provided to 7,519 known or probable contacts. The vaccination was fully covered by the state through the Ministry of Health. As many as 100 of the vaccinated contacts developed hepatitis A. These cases are currently analysed in detail from the point of view of the used vaccine, number of administered doses and interval between vaccination and onset of disease.

Vaccination was also offered to IDUs and homeless persons in Prague and Central Bohemia; 2,002 were vaccinated of whom four developed hepatitis A. This vaccination can be characterised as combined pre- and post-exposure prophylaxis. The costs were covered by the respective PHPA. In addition, 7,900 children from the first classes of elementary schools in the Central Bohemian region were vaccinated, with no case of hepatitis A reported in this population. The expenses were covered by the Regional Authority of Central Bohemia.

In addition, PHPA issued information on hepatitis A for school facilities and general practitioners (GPs). Information for the general public has been available primarily at the websites of the National Institute of Public Health and Ministry of Health of the Czech Republic, regional PHPA and in the mass media. Active surveillance of viral hepatitis in the Czech Republic continues.

Conclusion

The European Centre for Disease Prevention and Control (ECDC) organised a technical meeting on hepatitis A held in Riga on 11 November 2008 with the participation of representatives from Latvia, Slovakia, Estonia, Germany, Italy, the Netherlands, United Kingdom and the Czech Republic. The conclusions drawn at the meeting are also relevant to the Czech Republic which is true particularly of the statement that hepatitis A outbreaks are associated with increase in the susceptible population with improved standard of hygiene as documented by higher numbers of hepatitis A cases not only in children and youth but also in adults. Other contributing factors are increase in imported cases coming from endemic countries and higher incidence of hepatitis A in IDUs and other individuals with high-risk behaviour. It was suggested that ECDC should recommend general immunisation against hepatitis A across the EU. The significance of post-exposure prophylaxis with vaccine included in the Guidelines of the Ministry of Health of the Czech Republic was discussed [1]. In a longer perspective, the implementation of serological surveys is considered important to determine susceptibility of the EU population to HAV infection. Results of serological surveys would provide background data for the development of the vaccination strategy guidelines.

HAV RNA sequencing and phylogenetic analysis of HAV isolates from outbreaks would be of relevance. In the Czech Republic, serum and stool samples are being collected in the most affected

areas. The kind offer of the National Institute of Public Health and Environment in Bilthoven, the Netherlands (RIVM) to analyse a part of samples and to provide the guidance for the completion of analyses in the National Reference Laboratory for Viral Hepatitis in the Czech Republic will be accepted.

Based on the available data, it is possible to exclude water- or food-borne and sexual transmission of HAV in the Czech Republic in 2008. The spread of hepatitis A in 2008 started among IDUs, most probably by person-to-person contact or parenteral transmission, and continued among other high-risk groups (homeless persons) in conditions of sub-standard hygiene. Subsequently, the infection spread among the general population with increased susceptibility. Higher susceptibility to HAV is likely to result from long-term low prevalence of hepatitis A.

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COMMUNITY-WIDE OUTBREAK OF HEPATITIS A IN LATVIA IN 2008 – AN UPDATE

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An outbreak of hepatitis A has been ongoing in Latvia with 2,817 confirmed cases reported between 20 November 2007 and 31 December 2008. Initially the spread of infection was due to transmission among drug users and other high-risk groups, as well as several outbreaks in Riga (affecting a school and a restaurant), but in the second half of the year led to a community-wide increase in the number of cases. Molecular analysis of 100 strains showed that 95 belonged to genotype IA, of which 89 were identical and six were single nucleotide variants of the same sequence.

Introduction

The Latvian Public Health Agency (PHA) updates through this article the information on epidemiological situation of hepatitis A in 2008 in Latvia. An increase in number of cases of hepatitis A has been observed since November 2007. A total of 2,817 confirmed cases of hepatitis A were notified between 20 November 2007 and 31 December 2008, and 419 suspected cases were still under investigation on 31 December 2008. The highest number of cases (678) was notified in October 2008. The distribution of confirmed and suspected cases of hepatitis A by month of onset is shown in Figure 1.

Methods

Hepatitis A is a disease under mandatory notification in Latvia. Clinicians should notify suspected and confirmed cases and

laboratories are required to report positive hepatitis A virus (HAV) results according to the European Union (EU) case definitions [1].

A probable case is defined as a person with a clinical picture compatible with hepatitis (discrete onset of symptoms and jaundice or elevated serum aminotransferase levels) and with an epidemiological link. A confirmed case is defined as any person meeting the clinical criteria and with serum IgM antibodies against hepatitis A virus (IgM anti-HAV) [1].

Upon receiving notification reports from clinicians or laboratories, all cases of hepatitis A are investigated by epidemiologists from the Public Health Agency (PHA) local branch.

To characterise the HAV circulating in the outbreak, 100 serum samples from the Latvian State Agency “Infectology Center of Latvia” were sent to the Dutch National Institute for Public Health and the Environment (Rijksinstituut voor Volksgezondheid en Milieu, RIVM) for genotyping.

Results of epidemiological investigations

The age of the cases ranged from five months to 86 years, with a median age of 31.7 years. The age and sex distribution of confirmed cases of hepatitis A is shown in Figure 2.

FIGURE 1

Number of reported cases of hepatitis A, by month of onset, Latvia, November 2007 - December 2008 (n=3,236)

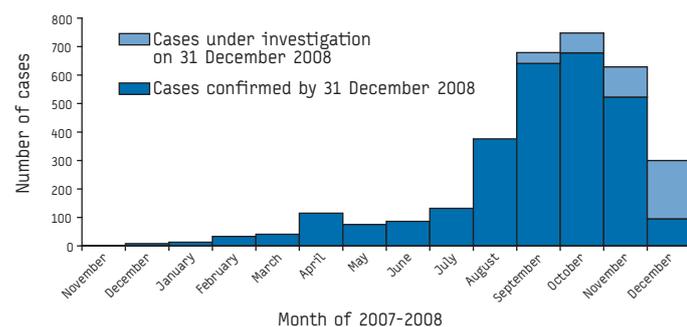


FIGURE 2

Age and sex distribution of confirmed cases of hepatitis A reported in Latvia from November 2007 to December 2008 (n=2,817)

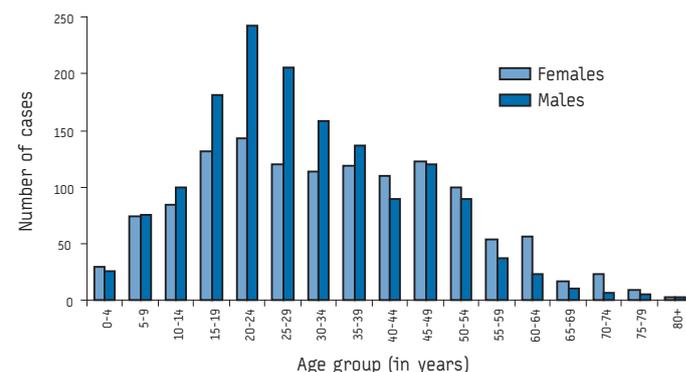


FIGURE 3

Number of cases of hepatitis A per 100,000 population, by age and sex, Latvia, November 2007 – December 2008

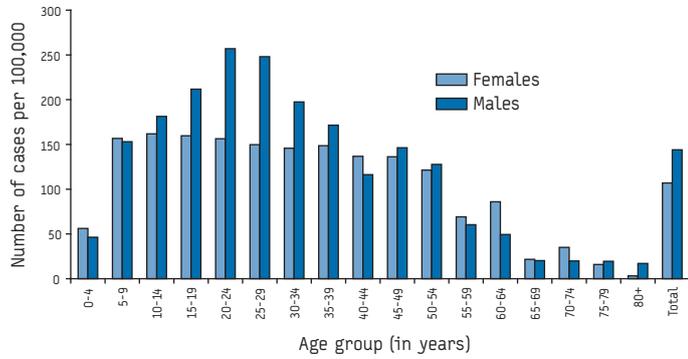


FIGURE 4

Cases of hepatitis A among drug users and the proportion of drug users among all hepatitis A cases, Latvia, November 2007 – December 2008 (n=191)

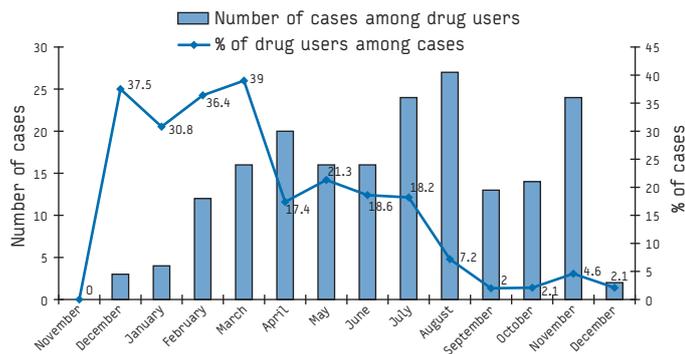


FIGURE 6

Number of death cases of hepatitis A, by age and sex, Latvia, November 2007 – December 2008 (n=17)

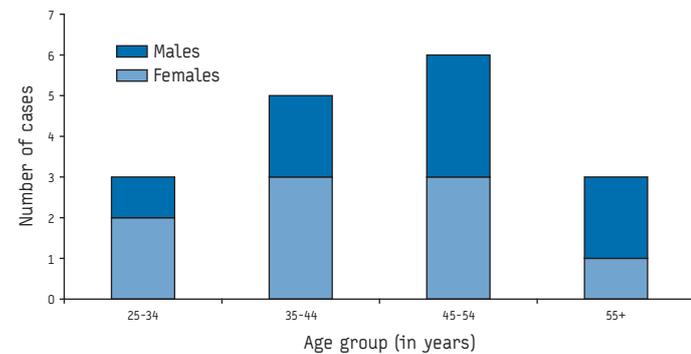
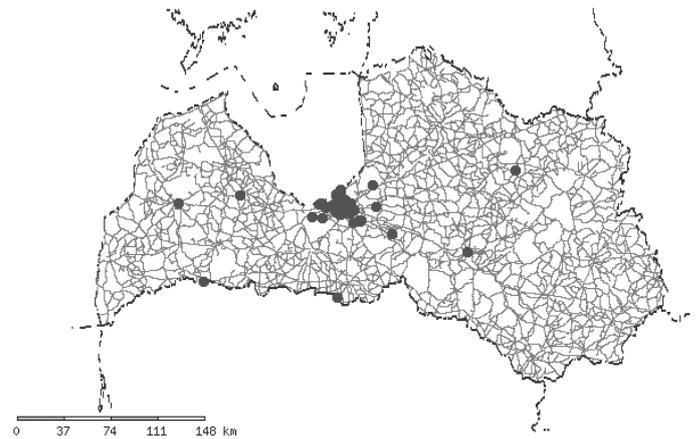


FIGURE 5

Geographical distribution of reported cases of hepatitis A in Latvia, November 2007 – December 2008

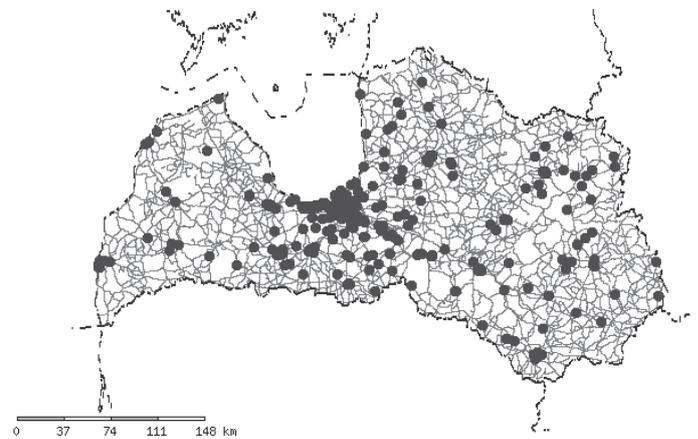
a) Cases reported between 20 November 2007 and 30 April 2008 (n=211)



b) Cases reported between 1 May and 31 August 2008 (n=669)



c) Cases reported between 1 September 2008 and 31 December 2008 (n=1,937)



Significant proportion of cases among adults could be explained by low hepatitis A infection activity in Latvia in recent years and absence of naturally acquired immunity in their childhood. The last biggest outbreak of hepatitis A occurred in 1988-1990 with almost 20,000 cases registered during three years. Since then the number of cases steadily declined and during the last 10 years was very low – an average of 100 cases per year. The lowest number of cases of hepatitis A (n=22) was registered in 2007, the year before the current epidemic.

The proportion of males amongst hepatitis A patients was 72% (range 66 to 73%) in the first six months of the epidemic (November 2007 - April 2008), and 52% in the following period (May - December 2008).

The overall male to female ratio was 1.15 to 1, with the highest rate of 1.55 to 1 in the age group 15 – 34 years.

The overall incidence rate per 100,000 population was 124. The incidence rate amongst males was about 1.35 times higher than amongst females (Figure 3)

The difference in infection risk between the sexes could be partly explained by significant number of cases among male drug users (DUs).

Hepatitis A in drug users

During the observation period, 191 drug users (of whom up to 90% were injecting drug users, IDUs) were notified as hepatitis A patients. The highest numbers were reported in July and August (23 and 27, respectively), but the proportion of drug users amongst all cases was highest in the beginning of the epidemic – up to 39%. The estimated number of problem drug users in Riga is 4,757. As the number of hepatitis A cases among DUs in Riga was 153, the incidence rate in this group could be as high as 3,216 cases per 100,000 in 2008.

Since September, the number of cases among DUs and, in particular, the proportion of DUs among all cases had declined. The reason for this is still unclear although one of the explanations may be that the epidemic in this group started earlier and therefore peaked and declined earlier compared to the outbreak in the general population.

Geographical distribution

The majority of cases of hepatitis A (2,132, 76%) occurred in inhabitants of Riga, 199 in the population of the wider Riga region, 88 cases in Jūrmala and the remaining cases were distributed

among other six cities and 23 districts in Latvia which reported between one and 66 cases each.

Clinical outcome

Of the 2,817 confirmed cases, there were 17 deaths (0.6%). 91% of cases of hepatitis A were treated in hospitals.

All death cases were registered in patients with underlying diseases and / or other risk factors (alcohol, drugs). An increase in mortality has been observed during the epidemic, ranging from 0 in the period of time November 2007- March 2008 to 0.77% in October – December 2008 (see Table 1).

There was no difference in mortality rates among cases of hepatitis A by sex.

Genotyping results

One hundred serum samples from Latvian patients were tested for the presence of HAV RNA. All samples were positive and were further processed for genotype analysis by sequencing of 460 nucleotides of the VP1/P2A region. Sequences were compared to each other and to sequences available in public databases. One of the 100 sequences was of genotype IB, with a maximum match of 99% with three sequences originating from North and West Africa. Four of the 100 sequences were of genotype IIIA. The four sequences were identical and have as nearest neighbors 20 sequences in the database that match at 99%. These sequences mostly have their origin in Pakistan.

By far the largest group of sequences from Latvian patients belonged to genotype IA. Of these 89 were identical, and six were single nucleotide variants of this sequence type. These 95 sequences represent the outbreak strain of Latvia 2008. In the databases only two strains were found with sequences matching at 99% or greater. Both were isolated from patients in the Netherlands in 2004 and were travel associated. In one case travel history involved Turkey.

For all three individual sequence types of the three genotypes there were many sequences matching at 98% with various regions of origin, several different transmission modes, and from an extended time period. Therefore, if sequence matching is used for epidemiological linking, sequences should be matching more than 99%

TABLE 1

Number and proportion of death cases in hepatitis A outbreak in Latvia, November 2007 – December 2008 (n=17)

Months	Number of cases	Number of deaths	% of deaths
November 2007 – March 2008	96	0	0
April – June	276	1	0.36
July – September	1,149	6	0.52
October – December	1,296	10	0.77
Total	2,817	17	0.6

TABLE 2

Genotype analysis of hepatitis A virus isolated from cases in Latvia, 2008 (n=100)

Genotype	Number of strains isolated from Latvian patients	>99% matching sequence (accession number)	Origin of closest match	Match quality and resolution
IA	95	DQ114859 DQ650789	Turkey	0 differences in 177 nucleotide overlap
IB	1	DQ387553 AY343701 DQ387553	Morocco Morocco Ghana	1 difference in 177 nucleotide overlap
IIIA	4	DQ387610 19 others	Pakistan	1 difference in 177 nucleotide overlap

Source: National Institute for Public Health and the Environment (RIVM), Bilthoven, the Netherlands

The single IB and the four IIIA strains were most likely introduced in Latvia by (returning) travelers, and spread to close contacts if at all. This is a pattern that can be seen in many European countries with a low level of hepatitis A endemicity. The IA strain that caused the outbreak may also have been introduced by a traveler but more importantly it was introduced into a group, in which it could spread more widely than just close contacts, thereby causing an outbreak.

Control measures

With the aim to contain the epidemic, the following measures have been implemented:

All cases of hepatitis A have been investigated by epidemiologists of the relevant local branches of "Public Health Agency". Family doctors have been informed about contacts. Control measures, such as medical observation of contacts and increasing of hygiene and restriction of contacts between children from different groups, have been implemented at places at risk – children establishments, food enterprises, as well as workplaces and households where two and more cases of hepatitis A were registered.

Monitoring of cases of hepatitis A has been enhanced - weekly and, if necessary, daily data are available at the national and local levels. Monitoring data are published on PHA website.

Detailed recommendations for different target groups (staff of food enterprises, children establishments, and general public) have been developed and distributed to different institutions at national and local levels. Recommendations had already been available on the PHA website. Survey data indicated that in October, PHA recommendations were available in 98% of schools.

Lectures for different targets groups (health professionals association, school nurses, family doctors etc.) have been provided.

A special poster-sticker to stress the importance of hand washing has been developed and distributed to schools.

A special survey to identify risk factors for hepatitis A has been performed by PHA in schools. Local governments and administration of the schools were informed about the results of the survey, its conclusions and recommendations.

Intensive collaboration with mass media has been in place. PHA press releases on hepatitis A situation and recommendations have been developed and distributed weekly. Only in November there were 53 publications on hepatitis A in national and local mass media, and 13 interviews on this topic on TV and 17 on the radio.

Although vaccination against hepatitis A has not been provided free of charge, vaccination has been recommended to risk groups and contacts. A significant increase in the number of people vaccinated against hepatitis A has been observed since September 2008 corresponding to the spread of the epidemic.

Conclusion

The ongoing outbreak of hepatitis A in Latvia has not yet been fully understood, but a few working hypotheses may explain the spread of the epidemic. The increase in the number of cases in the beginning of 2008 can be related to the initial spread of infection among DUs and persons with low income level living in substandard hygienic conditions, as well as to several outbreaks (a school in Riga, a restaurant in Riga [2,3]). Increased circulation of the virus in highly susceptible population led, in the second part of the year, to a community-wide increase in the number of cases that demonstrated the typical seasonal activity of hepatitis A usual for endemic years in the past. The modes of transmission involved vary, including person-to-person transmission, contaminated food, and, possibly, swimming in bathing waters in summer.

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TABLE 3

Number of vaccinations against hepatitis A in Latvia, 2006-2008

Year	Month	Number of vaccinated with the first dose of vaccine
2006	January – December	1,815
2007	January – December	2,912
2008	January	292
	February	383
	March	247
	April	309
	May	415
	June	301
	July	187
	August	357
	September	1,054
	October	1,754
	November	1,631
	December	1,950
	January – December	8,880

Source: Monthly statistical data provided by clinicians

Rapid communications

HEPATITIS A OUTBREAK IN A ROMA VILLAGE IN EASTERN SLOVAKIA, AUGUST-NOVEMBER 2008

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We describe an outbreak of hepatitis A in Lomnička, a village in the eastern part of Slovakia. The outbreak was limited to the village and did not spread either to other districts of Slovakia or to the neighbouring countries. The number of cases reported from 28 August to 30 November 2008 was 298. All cases but one occurred in the Roma population. The outbreak was associated with low socio-economic conditions which facilitated person-to-person transmission. No common source of the outbreak was verified.

Background

In Slovakia, hepatitis A is a mandatorily notifiable disease [1]. The national surveillance is coordinated by the Chief Public Health Officer of the Slovak Republic who is the head of the Public Health Authority of the Slovak Republic (PHA SR), an institution in charge of 36 Regional Public Health Authorities (RPHAs) covering 79 districts of the country.

The case classification is in accordance with the European Union (EU) case definition of hepatitis A [2].

Physicians and laboratory microbiologists are liable to report any confirmed or suspected case of acute viral hepatitis A to the epidemiologist of territorially relevant RPHA. Data from all regions are then collected in the National Central Register. The Epidemiological Information System (EPIS) is used for the purpose of data reporting, collecting, processing and analysing. It is a real

time system and thus new data about either sporadic cases or outbreaks can be evaluated every day.

The population of Slovakia was around 5.4 million as of 30 June 2008 [3]. According to the official population census, in 2001, the number of Roma inhabitants was 260,605. However, this seems to be an underestimate and the actual proportion of the Roma population is likely to be much higher. According to the World Bank study published in 2003, there were almost half a million Roma living in Slovakia [4]. The majority (about 57%) of the Roma population lives in eastern Slovakia.

Hepatitis A in Slovakia

The overall incidence of hepatitis A in Slovakia has shown a constantly decreasing trend in the last decades. The rates declined from more than 50 cases per 100,000 population in 1988 to the lowest ever recorded incidence of 7 cases per 100,000 in 2007. However, peaks of incidence have occurred in periodical intervals (every few years) since 1988, probably due to increasing numbers of non-immune children. Each peak, however, has represented a lower incidence than the previous one (Figure 1).

In recent years, mostly sporadic cases and rare small outbreaks have been reported. The outbreaks often affected the Roma population and were associated with low hygienic conditions and person-to-person transmission.

FIGURE 1

Incidence rates of hepatitis A per 100,000 population, Slovakia, 1988 – 2008 (as of 30 November 2008)

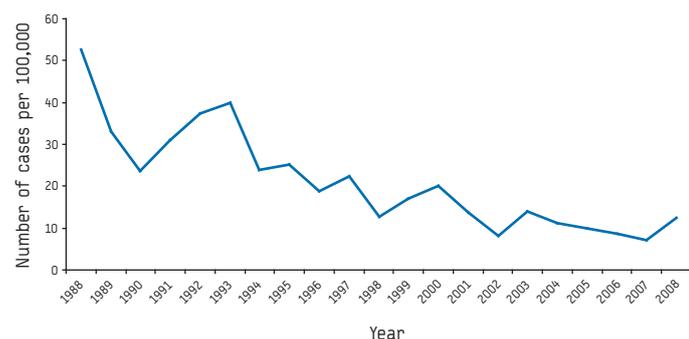
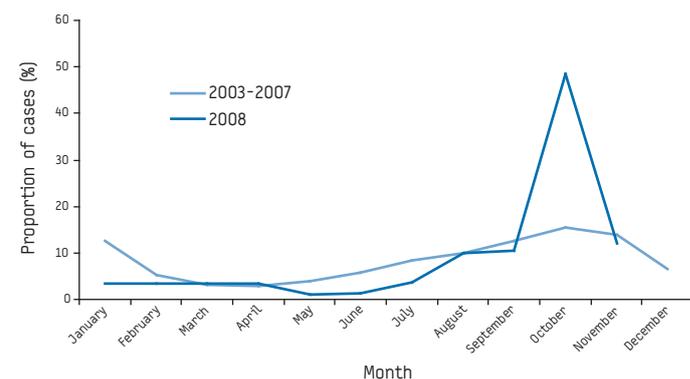


FIGURE 2

Seasonality of hepatitis A in Slovakia, 2003-2007 and January - November 2008



In 2008, a total of 667 cases of hepatitis A (incidence of 12.4 per 100,000 population) have been reported to the EPIS database, as of 30 November 2008. This includes nine outbreaks involving 485 cases.

The seasonal distribution of cases of hepatitis A in 2008 shows a typical pattern observed also in the previous years, with the highest proportion of cases reported in September, October and November (Figure 2).

The notification reports include information on whether the case is associated with "low" or "normal" hygienic standard. In 2008, 536 cases were recorded as "low hygienic standard" (80% of the total, incidence of 107.2 per 100,000 population) and 131 as normal hygienic standard (incidence of 2.7 per 100,000 population). Although the reports do not contain data on the ethnic origin of the cases, on the basis of available evidence, the Slovak public health authorities generally consider cases recorded with "low hygienic standard" to have occurred in the Roma population, reflecting the poor living conditions of this group.

Among the 131 hepatitis cases reported in 2008 and associated with "normal hygienic standard" (thus assumed to have occurred in the majority population), 14 were imported cases: nine from the Czech Republic, three from Egypt, one from Madagascar and one from Tunisia.

As many as 495 of the 667 cases reported in 2008 (74%) occurred in children below the age of 10 years, and the age-specific incidence rate was highest in this group. This can be linked with the fact that most cases were assumed to have occurred in the Roma population where children are exposed to the hepatitis A virus (HAV) at an early age, due to poor socio-economic living conditions.

The geographical distribution of cases reported in 2008 shows the highest incidence rates in two districts: Stará Ľubovňa with 720 cases per 100,000 population and Bardejov with 110 cases per 100,000 population, in comparison with the average incidence rate of 12 cases per 100,000 population for the whole country (Figure 3). The two most affected districts are situated in the Prešov region which has the highest density of the Roma population in Slovakia. Also, four of the nine outbreaks reported in 2008 occurred in these

two districts. The largest one involving 298 cases occurred in the village of Lomnička, district Stará Ľubovňa.

Hepatitis A outbreak in the village of Lomnička

Lomnička is a small village with population of 2,044 situated in the north-east of Slovakia, in the district Stará Ľubovňa. Almost all (2,034, more than 99%) inhabitants of the village are Roma, and close to 60% are below the age of 18 years.

The sanitation and living conditions in the village are very poor. There is access to running water service but the supply is often stopped in households that do not pay the fees. Waste and sewage water disposal is inadequate.

The first case in the outbreak was hospitalised on 27 August 2008, followed by further eight hospitalised in the next two days. An interval with none or very few cases was followed by an explosive wave with the peak on 17 October 2008 (26 cases hospitalised in a day). After that the occurrence of new cases gradually declined with none or single cases reported from 14 to 30 November 2008.

In all, 298 cases of hepatitis A, all of them hospitalised, were reported from the village of Lomnička between 27 August and 30 November 2008 (Figure 4). The most affected were children below 10 years of age. Of the cases, 148 were below 6 years of age, 142 were between 6 and 10 years old, seven were in the age group of 11-18 years, and only one was adult.

Control measures

The outbreak was officially declared on 28 August 2008, when the first four cases of hepatitis A occurred. Control measures were launched within 24 hours.

Control measures were carried out by the PHA SR and RPHA Stará Ľubovňa. The response action was coordinated by the Chief Public Health Officer and the PHA SR. He also called the regional anti-epidemic committee and the crisis committee, who announced an emergency situation in the district Stará Ľubovňa on 15 October 2008. This allowed potential restriction of movement of inhabitants to avoid spread of infection. The emergency situation was ceased on 22 October 2008. A temporal outpatient clinic was established in the village. The chief hygienist ordered to reprofile the hospital beds in the district of Stará Ľubovňa as well as in neighbouring

FIGURE 3
Incidence rates of hepatitis A per 100,000 population, by region, Slovakia, 2008

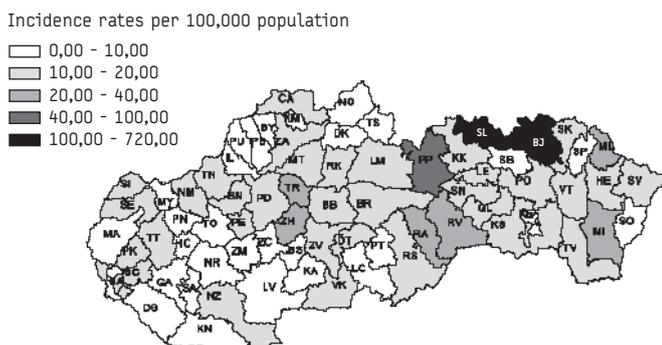
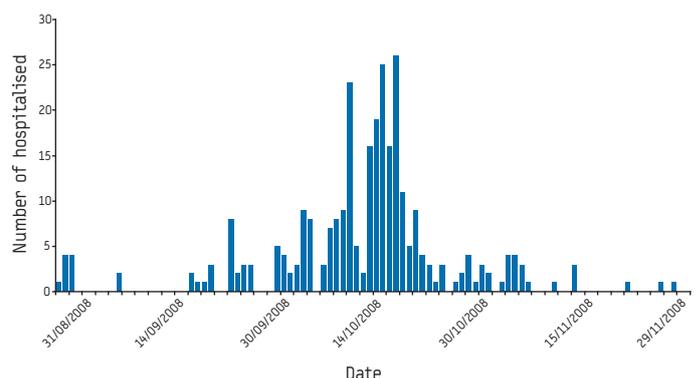


FIGURE 4
Number of hospitalised cases of hepatitis A in Lomnička village, Slovakia, 27 August – 30 November 2008 (n=298)



districts to make them ready to receive more hepatitis A patients. The EPIS served as a very good communication tool for public health professionals, medical doctors and the general public [5].

Standard control measures to be applied in the foci of hepatitis A infection [6] were implemented - hospitalisation and treatment, contact tracing, medical supervision and disinfection. To prevent further spread of infection, control measures were implemented also in the food facilities, in the kindergarten, and in the primary and secondary school. Furthermore, water tanks as source of drinking water were provided.

Post-exposure and preventive vaccination was also administered. On 6 September, the day after two hepatitis A cases were reported in children attending the local kindergarten, mass vaccination started including family members of cases and children below 15 years of age attending the kindergarten and the elementary school in the village. As the next step, vaccine was provided to all young people up to 18 years of age and health professionals. In the end, the inhabitants of the neighbouring village of Podolinec were vaccinated. As of 30 November 2008, 1,814 children (almost 80% of all children below 15 years of age) and 742 adults have been vaccinated in the district.

Information on hepatitis A was disseminated via newspapers, radio and television. Educational leaflets on hepatitis A were distributed in public places (kindergarten, primary and secondary school, hospital, outpatient clinic, post office). Information was also available at the websites of the PHA SR and the RPHA of Stará Ľubovňa.

Conclusion

The outbreak of hepatitis A described in this paper was limited to one village. Since the end of November no further cases have been reported from the area. Considering the incubation period (max. 50 days), this shows that the control measures have proven effective and the outbreak has been contained. Nevertheless, this example shows that outbreaks of hepatitis A can affect relatively large number of people, particularly in susceptible populations.

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Rapid communications

CLUSTER OF CASES OF HEPATITIS A WITH A TRAVEL HISTORY TO EGYPT, SEPTEMBER-NOVEMBER 2008, FRANCE

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Since September 2008, 26 cases of hepatitis A with a history of travel to Egypt have been reported in France. Investigations indicate that a common source of contamination linked to Nile river cruises is the most likely explanation of the increase in the number of cases reported in France as well as in several other European Union countries.

Introduction

In France, hepatitis A is a mandatorily reportable disease defined by the presence of immunoglobulin M antibodies to hepatitis A virus (IgM anti-HAV) in the serum. From 1 September to 2 October 2008, 11 cases of hepatitis A with a travel history to Egypt (within two to six weeks prior to symptom onset) were notified by eight district health departments. This number was higher than observed in previous years: in 2006 five cases and in 2007 two cases with a history of travel to Egypt were notified for the period September to October.

An investigation was undertaken to identify the source of infection and implement appropriate measures.

Methods

A case was defined as any person with IgM anti-HAV who had stayed in Egypt between 2 to 6 weeks prior to symptom onset. All cases notified since 1 September 2008 were interviewed by telephone using a standardised questionnaire. Data were collected on age, sex, date of symptom onset, symptoms (jaundice, asthenia, anorexia, vomiting, fever), date of jaundice onset, date of IgM anti-HAV test result, hospitalisation, dates of travel to Egypt, type of travel (with a group or individual), description of the travel (Nile cruise, name of the ship, stay in hotel, name of the hotel), food consumption (raw vegetables, unpeeled fresh fruits, fresh fruit juices, ice creams, seafood, unbottled water, beverages with ice cubes) and vaccination against hepatitis A.

Sera from 11 hepatitis A cases who had travelled to Egypt and had positive results of IgM anti-HAV detected between 13 September and 23 October 2008 were analysed at the National Reference Centre for HAV. Phylogenetic analysis of HAV sequences was performed as described elsewhere [1]. For comparison, eight sequences from patients infected by HAV genotype IB who had travelled to countries other than Egypt were included in the analysis. We also included two strains involved in Belgian HAV cases with a travel history to Egypt in 2008 [2].

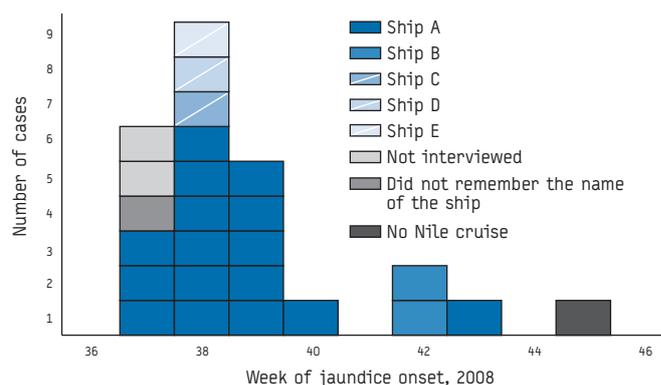
Results

As of 9 January 2009, 26 cases were notified and 24 were interviewed. Among the 26 cases, 13 (50%) were men, and the age of the cases ranged from 10 to 65 years (mean age 32.8 years). Of the 26 patients, 25 (96%) had jaundice (Figure 1) and 17 (65%) were hospitalised. None died. None had been vaccinated against hepatitis A.

Of the 24 patients interviewed, 20 had travelled to Egypt in August, two in September and two in October. The length of their stay ranged from one to two weeks; 23 had participated in an organised tour to Egypt.

All cases except one had gone on a cruise on the river Nile and 15 had stayed in a hotel. Among the 24 cases, nine participated in a cruise only, 14 had gone on a cruise and stayed in a hotel and one had stayed in a hotel only. In 12 out of the 14 cases who stayed both on a ship and in a hotel, the stay at the hotel occurred after the cruise on the Nile.

FIGURE 1
Distribution of cases of hepatitis A with a history of travel in Egypt, by week of jaundice onset, September-November 2008, France (n=25)



Among the 23 cases who had gone on a cruise, 16 (70%) sailed on ship A, two on ship B, three on three different ships (C,D,E) and two did not remember the name of the ship (Figure 1).

Among the 16 cases who sailed on ship A, 11 (69%) travelled from 9 to 16 August and five from 16 to 24 August. The dates of the cruise on ship B were the same for both cases (6 to 13 September). The port of departure and arrival was Luxor for both ships.

Among the nine cases who participated in a cruise only, seven (78%) named ship A, one ship B and one did not remember the name of the ship.

Among the 15 cases with a stay in a hotel, 10 stayed in Hurghada (nine in the same hotel). The remaining five cases stayed in five different hotels in two different towns, Marsa Alam and Cairo. Twelve cases stayed in these hotels in August (11-30), one in September and two in October.

Cases reported consumption of the following food items during their stay in Egypt: raw vegetables (12/23, 52%), unpeeled fresh fruits (12/24, 50%), fresh fruit juices (8/24, 33%), seafood (1/24, 44%). None had ice cream, three (3/23, 13%) drank unbottled water and five (5/21, 24%) had beverages with ice cubes.

Molecular analysis of sera from 11 cases showed they had been infected by HAV genotype IB. A cluster of 10 sequences was

identified in the phylogenetic tree (strain 1) (Figure 2). These 10 sequences were identical over the 440 base-pair fragment analyzed. This cluster also contained the Belgian sequence 2008-Egypt-BEL-1 involved in HAV cases who also travelled to Egypt. All 10 patients have made a cruise on the Nile, though in different ships (six on ship A, one on ship B, one on ship C, one on ship D, one on ship E). The eleventh sequence was from a 12-year-old patient and differed from strain 1 by 7 nucleotides (strain 2) and was also different from 2008-Egypt-BEL-2, the second strain identified by our Belgian colleagues in patients returning from Egypt. IB strains from patients who had travelled in West Africa, South America or others countries in Northern Africa (n=8), were different from strain 1 and strain 2.

Discussion

In October 2008, an increase in cases of hepatitis A who had travelled in Egypt was observed compared to 2006 and 2007 surveillance data. The majority of cases had travelled to Egypt in August 2008 and had gone on a cruise on the Nile river. Among these, more than half had sailed on the same ship (ship A) during two different periods in August. Moreover, three quarters of the cases who only participated in a cruise during their stay in Egypt had travelled on ship A.

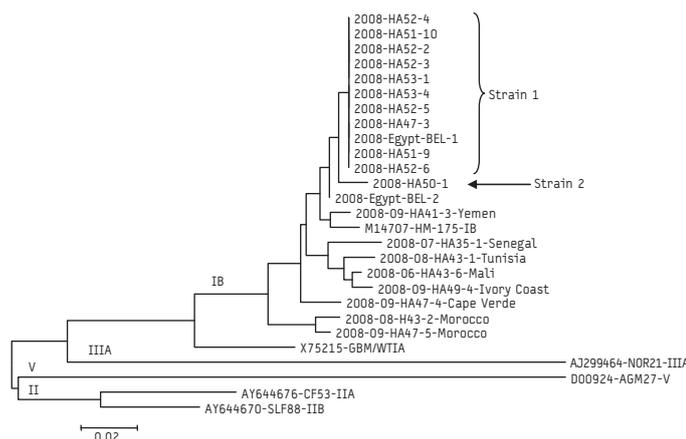
On 15 October 2008 France issued a message via the Early Warning and Response System (EWRS). Several European Union (EU) countries (Belgium, Germany, Ireland, Poland) reported single or clustered hepatitis A cases after cruises on the Nile river. None of the cases in these countries named the ships involved in the French investigation.

The excess of French hepatitis A cases may be explained by an exposure on ship A. However, the occurrence of cases who had travelled on others ships suggests that exposure to HAV infection was not limited to ship A, and a common source of contamination cannot be excluded (e.g. supplies to the ships, common stop-over). The genetic relatedness of the HAV sequence for all cases who had sailed on a cruise ship, regardless of the ship, supports this latter hypothesis. Several sources of contamination should be considered: consumption of foods or drinks on board of the ships or during stop-over contaminated by different food handlers excreting the virus, contaminated common supplies for the ships, baths in the ship swimming pool or in the Nile river.

Investigation limited to interview information was transmitted to the Egyptian health authorities. Hepatitis A is endemic in Egypt but we are not aware of an increase in the number of hepatitis A cases which could have contributed to an increase of contamination of food or water. The fact that other EU countries reported cases of hepatitis A among travellers who had been on cruises on the Nile river indicates that transmission of hepatitis A on board of ships involved in such cruises may be a relatively widespread problem. It is noteworthy that the main epidemic strains involved in French and Belgian cases are closely related. It is also likely that national surveillance systems in the EU have missed cases related to this exposure.

The French vaccination guidelines recommend hepatitis A vaccination for persons travelling in endemic area such as Egypt. This recommendation is often not followed; in 2007, 40% of hepatitis A cases reported in the surveillance system were imported [3]. Due to this outbreak, information on hepatitis A vaccination

FIGURE 2
Phylogenetic analysis of hepatitis A virus (HAV) strains from patients who had travelled to Egypt, September-November 2008, based on the sequences of the VP1-2PA junction of the HAV genome



Genotype and subtype are indicated for each branch. Reference sequences from GenBank are: genotype IA strain (X75215, GBM/WT), genotype IB strain (M14707, HM-175), genotype IIB (AY644670-SLF88), genotype IIA (AY644676, CF53), genotype IIIA (AJ299464, NOR21), and genotype V (D00924, AGM27). IB sequences from eight patients who had travelled to countries other than Egypt are: 2008-09-HA41-3-Yemen; 2008-07-HA35-1-Senegal; 2008-08-HA43-1-Tunisia; 2008-06-HA43-6-Mali; 2008-09-HA49-4-Ivory Coast; 2008-09-HA47-4-Cape Verde; 2008-08-HA43-2-Morocco; 2008-09-HA47-5-Morocco. The outbreak strains found in Belgium are: 2008-Egypt-BEL-1; 2008-Egypt-BEL-2. A cluster of 10 sequences from the French outbreak is identified as "strain 1", and included the Belgian sequence 2008-Egypt-BEL-1.

was reinforced in public vaccination centres for travellers and in travel companies in France.

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Rapid communications

CLUSTER OF HEPATITIS A CASES AMONG TRAVELLERS RETURNING FROM EGYPT, BELGIUM, SEPTEMBER THROUGH NOVEMBER 2008

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Following a European alert by France, we detected a hepatitis A cluster in Belgian travellers returning from Egypt. Our investigation supports the hypothesis of a common source outbreak, linked to Nile river cruises. The outbreak also suggests the need to consider an intensification of the vaccination policy for travellers to hepatitis A endemic countries.

Introduction

Following the French notification in the Early Warning and Response System (EWRS) on 15 October 2008 about an increase of hepatitis A cases in travellers returning from Egypt and possibly related to cruises on the Nile, the Belgian health authorities were alerted in order to verify whether a similar increase had been observed in Belgium. The infectious disease control units, which are organised by region in Belgium and to whom mandatory notification of each hepatitis A case has to be sent by both physicians and clinical laboratories, analysed their data. At the same time their teams at the level of the provinces were asked to actively investigate each notified case for a potential link to travel in Egypt.

Hepatitis A virus (HAV), a single stranded RNA virus, is mainly transmitted by the faecal-oral route, either by person-to-person contact or by ingestion of contaminated food or water [1]. Only 2-3% of reported cases are identified as part of recognised foodborne outbreaks, though a considerable percentage of sporadic cases might actually be foodborne [2,3]. A large outbreak of hepatitis A among travellers to Egypt in 2004 has been described to be associated with the consumption of orange juice [4]. Hepatitis A is endemic in Egypt and import of hepatitis A from endemic countries is common in Belgium, as it was the case in at least 14% of the hepatitis A notifications in Flanders in 2008. Over the last twenty years the prevalence of hepatitis A in Belgium shifted from intermediate to low, which makes the population more prone to clusters or outbreaks. International and Belgian travel medicine guidelines recommend hepatitis A vaccination of travellers to hepatitis A endemic countries [1].

Methods

A confirmed case was defined as a clinically compatible case with IgM hepatitis A serology, with disease onset between 1 September and 30 November 2008 and with a history of travel to Egypt between 2 to 6 weeks prior to symptom onset.

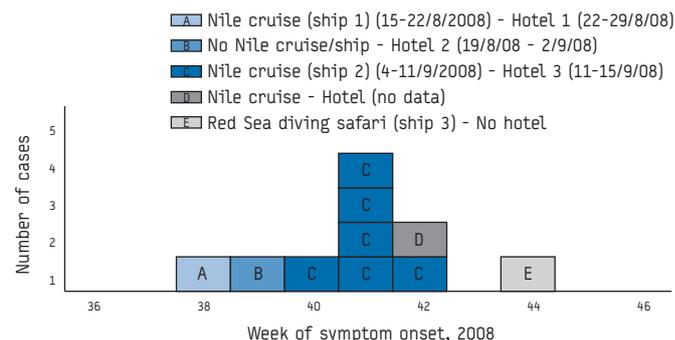
A limited epidemiological investigation was performed in order to verify a possible link between the Belgian cases and the possible sources (cruise ships), mentioned by name in the French alert. Data collection was done by telephone interview with the cases and their physicians. We collected information about age, sex, diagnostics, vaccination against hepatitis A, date of symptom onset, dates of travel and places of stay such as hotels and ships.

A virological analysis has been performed by the National Center of Viral Hepatitis (Scientific Institute for Public Health, Brussels). The HAV outbreak strain was characterised by sequencing a 350bp region, within the variable VP1/2PA junction of the HAV genome [5].

Results

At the time of the European alert, two cases of hepatitis A, suspected to be related to recent travel to Egypt, had been notified since 1 September 2008. By 30 November 2008, a total of 10 laboratory-confirmed cases of hepatitis A infection, with disease onset since 1 September and a history of recent travel to Egypt, had been registered (Figure 1). The median age of the cases was 41 years (range 23-59 years) and the male/female ratio was 3/7.

FIGURE 1
Distribution of cases of hepatitis A with travel in Egypt, by week of symptom onset, September-November 2008, Belgium (n=10)



One patient required hospitalisation but none died. None of the cases had been vaccinated against hepatitis A. They were living in four different provinces.

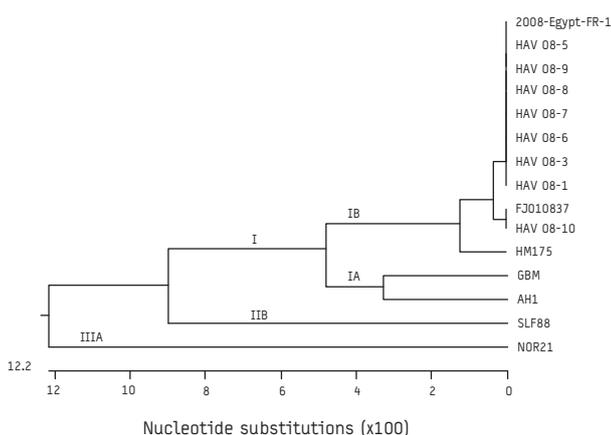
Eight cases had been travelling on a Nile cruise and one on a Red Sea diving safari. Those who took a Nile cruise had done this in combination with a hotel stay. At least three different ships and three different hotel accommodations were mentioned in the travel histories of the cases. However, none of these ships or hotels had been mentioned in the French alert and a bilateral contact by email with the French authorities did not reveal any common name.

One cruise ship was mentioned by six of the 10 Belgian cases. Although they had been travelling together, only two of them (friends who had been lodged in the same cabin on the ship) were aware of their common infection.

Virological analysis was performed on eight (not case D and E on figure 1) out of the ten confirmed cases. Phylogenetic analysis revealed that the HAV strains belonged to genotype IB, and were closely related to the Egyptian isolate (FJ010837). Among the eight patients, seven carried the same strain and the other one differed in only two nucleotides. The outbreak strain identified in France among ten patients who had travelled to Egypt (2008-Egypt-FR-1) showed 100% homology with the seven HAV sequences (HAV 08-1, HAV08-3, HAV08-5, HAV08-6, HAV08-7, HAV08-8, HAV08-9) (Figure 2).

FIGURE 2

Phylogenetic tree of the outbreak strains (HAV 08-1, HAV08-3, HAV08-5, HAV08-6, HAV08-7, HAV08-8, HAV08-9, HAV08-10) circulating in the Belgian travellers returning from Egypt, based on the 350bp region within the VP1-2PA junction of the HAV genome



The phylogenetic tree was generated using the MegAlign program (DNASTAR) by the CLUSTAL method, and the branch length represents the evolutionary distance expressed as the number of base substitutions per site. Genotype and subtype are indicated for each branch. Sequences from Genbank included: genotype IA strain (AH1, AB020564), genotype IA strain (GBM, X75214), genotype IB strain (HM175, M59808), genotype IIB (SLF88, AY644670), genotype IIIA (NOR21, M66695), and an Egyptian isolate strain (FJ010837). Among the eight patients, seven carried the same strain and the last one differed in only two nucleotides. The outbreak strain identified in France among ten patients who had travelled to Egypt (2008-Egypt-FR-1) was included in the analysis.

Discussion

A cluster of hepatitis A cases, related to travel in Egypt, has been identified in a group of Belgian travellers. Only active inquiry, prompted by the French EWRS alert, led to the identification of this cluster, indicating that similar hepatitis A clusters may often go undetected. As our findings come together with similar reports from France and Germany, a possible common source in Egypt, though not identified, cannot be discarded. The similarity of virological sequence analysis between cases in France and Belgium supports this hypothesis. Though travel medicine guidelines recommend hepatitis A vaccination of travellers to hepatitis A endemic countries, all of the identified cases were unvaccinated. In this perspective, and taking into account the increasing susceptibility of our population to hepatitis A, an intensification of the hepatitis A vaccination policy should be considered.

Acknowledgements

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Rapid communications

CLUSTER OF HEPATITIS A CASES AMONG TRAVELLERS RETURNING FROM EGYPT, GERMANY, SEPTEMBER THROUGH NOVEMBER 2008

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From September to November 2008, 34 cases of hepatitis A imported from Egypt were reported to the German public health authorities. Investigations point to a continuing common source of infection, most likely linked to Nile river cruises. The patients affected had not been vaccinated, which emphasises the need for more effective travel advice before trips to hepatitis A endemic countries.

Introduction

On 15 October 2008, the French Institute for Public Health Surveillance (Institut de veille sanitaire, InVS) issued a warning to the European Union member states via the Early Warning and Response System (EWRS) about a detected increase of hepatitis A cases with date of onset from 8 September onwards, and a history of travel to Egypt in August 2008. All cases had been on Nile river cruises, more than half on the same cruise ship. An association of hepatitis A infection with a Nile river cruise was therefore suspected. In following weeks, Ireland, Belgium and Poland also reported single cases or clusters of hepatitis A infections with history of Nile river cruises but on other ships than the majority of the French cases.

Hepatitis A (typical symptoms plus laboratory confirmation of acute infection) is mandatorily notifiable in Germany. At the time the warning was issued, a total of 10 cases of hepatitis A with date of onset from 1 September 2008 had been notified to German health authorities after travelling to Egypt. And further cases kept coming in. This compared to a mean of three cases (range 2-4) during the same time period in the previous three years.

Methods

The observed increase in case numbers prompted an investigation of all hepatitis A cases with date of onset from 1 September 2008 and travel to Egypt 15-50 days prior to symptom onset (case definition). In an email we asked local and state health authorities to obtain information on travel itineraries from the patients, including names of hotels and Nile cruise ships and dates of stay(s). This information was to be reported to the Robert Koch Institute, the German national public health institute.

Results

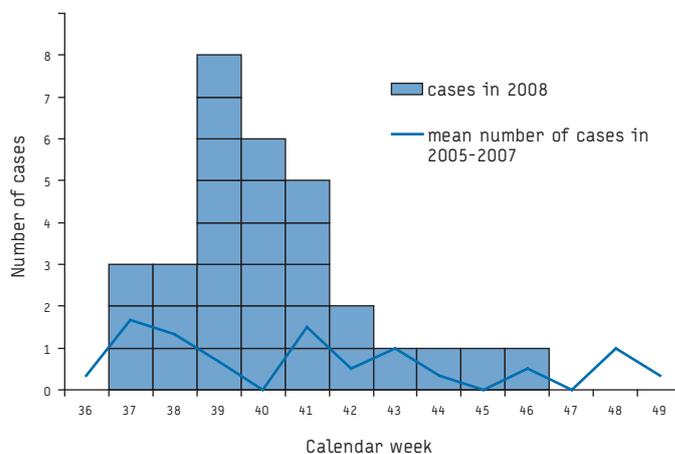
By 2 December, 2008, a total of 34 laboratory-confirmed symptomatic infections meeting the case definition were notified to

the German public health authorities (Figure 1). For three cases the exact date of onset was unknown but was later than 1 September. They are therefore not shown in figure 1. Weekly case numbers exceeded the mean case numbers notified in the three preceding years.

The mean age of cases was 40.1 years (range 11-69), and 20 (59%) were female. No case had been vaccinated against hepatitis A, 20 (59%) required hospitalisation, nobody died. Cases were from all across Germany.

Of the 34 cases, only four (14%) had not gone on a Nile cruise. For the others, the following information is indicated in Figure 2, if available: cruise ships, hotels, dates of travel and of symptom onset. Periods of stay on individual ships appear grouped in time. None had been on the ships implicated by French cases or by cases from other member states. In addition to cruise ships, many cases had also stayed in hotels in Hurgada, but named hotels varied much more than cruise ships.

FIGURE 1
Hepatitis A cases imported from Egypt to Germany, week 36-49 of 2008 (n=31)



Data as of 2 December 2008

Discussion

In summary, from September to November 2008 there was an increase in hepatitis A cases imported from Egypt to Germany. Whereas cases stayed in a plethora of hotels, some Nile cruise ships were named repeatedly, and cases' travel on them appeared to cluster in time.

To explain the excess of cases in Germany and elsewhere, a group of ships must have facilitated hepatitis A infections in tourists. The epidemic curve suggests a continuing common source rather than a point common source. Possible sources of infection might be contaminated food consumed onboard obtained from a common food catering company, contaminated tap water supplies for the ships' bunkers, or a common exposure on shore (e.g. a restaurant where tourist groups from various ships are being taken during day trips). As all of these ships continuously travel up and down a short stretch of the river (Aswan to Luxor and back) with standard must-see stops along the way, the cases possibly shared an exposure on land, which only intense additional study could reveal.

Both the long incubation period of hepatitis A (15-50 days) and long delays in collecting information on the individual cases precluded any rapid intervention on location.

International travel medicine guidelines and the German standing committee on vaccinations (STIKO) recommend hepatitis A vaccination for persons travelling to countries in which hepatitis A is endemic such as Egypt. Some health insurance companies reimburse the cost of the vaccination. In 2004 a large outbreak of hepatitis A among European tourists centred on a hotel in Hurghada [1], demonstrated that also package tourists ought to follow vaccination advice. Since then travel companies in Germany have become more active in recommending hepatitis A vaccinations to travellers to Egypt. Despite this, all cases described here were unvaccinated, emphasising the need for more effective travel advice before trips to hepatitis A endemic countries.

Acknowledgements

The authors thank the colleagues at the local and the state health authorities for collecting all information on the cases.

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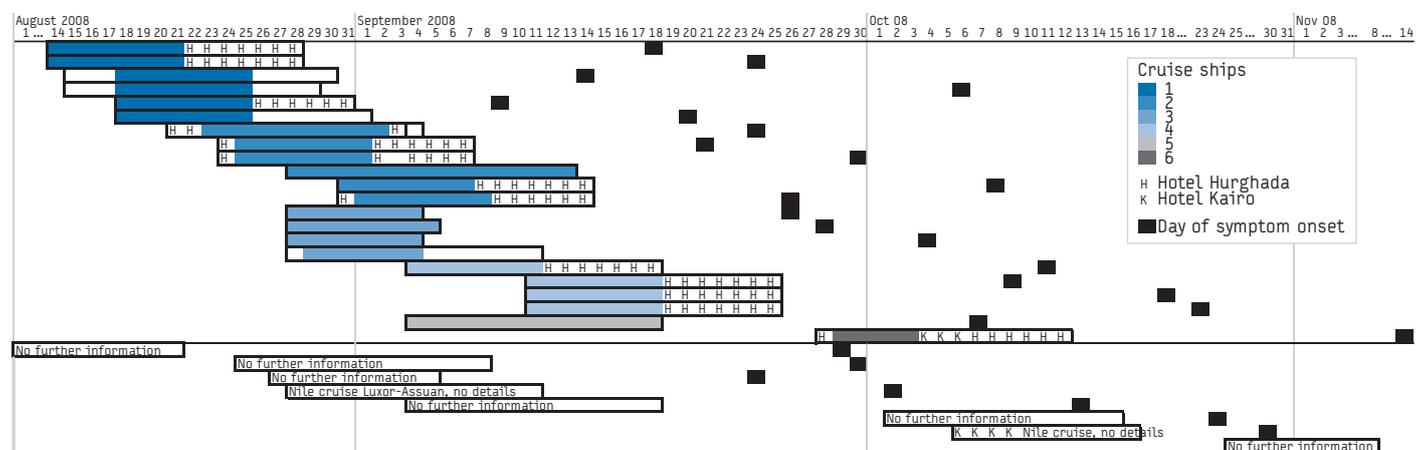
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FIGURE 2

Hepatitis A cases post travel to Egypt, Germany, September-November 2008 (n=30 cases with known date of travel)



Data as of 2 December 2008
 Each line represents one case
 Coloured boxes represent stays on Nile cruise ships and in hotels

ZOONOTIC INFECTIONS IN EUROPE IN 2007: A SUMMARY OF THE EFSA-ECDC ANNUAL REPORT

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The European Food Safety Authority and the European Centre for Disease Prevention and Control have just published their Community Zoonoses Report for 2007, analysing the occurrence of infectious diseases transmittable from animals to humans. *Campylobacter* infections still topped the list of zoonotic diseases in the European Union and the number of *Salmonella* infections in humans decreased for the fourth year in a row. Cases of listeriosis remained at the same level as in 2006, but due to the severity of the disease, more studies on transmission routes are warranted. The report highlights the importance of continued co-operation between veterinarians and public health specialists, both at the EU level and within Member States.

Introduction

The 2007 annual Community Summary Report by the European Food Safety Authority (EFSA) and the European Centre for Disease Prevention and Control (ECDC) was released this week with the latest trends and figures on the occurrence of zoonoses and zoonotic agents in humans, animals and foodstuffs in the 27 European Union (EU) Member States and the four European Free Trade Association (EFTA) countries (Iceland, Liechtenstein, Norway and Switzerland) [1].

Zoonoses are infections and diseases that are transmissible between animals and humans. The infection can be acquired directly from animals, through the ingestion of contaminated food, or from other environmental sources. The severity of these diseases in humans can vary from mild symptoms to life-threatening conditions.

In order to prevent and control zoonoses, it is important to identify which animals and foodstuffs are the main sources of infections. For this purpose and to monitor the progress on food safety in the European Union, information aimed at protecting human health is collected and analysed from all European Union Member States according to the Zoonoses Directive 2003/99/EC [2].

Assisted by its Zoonoses Collaboration Centre, EFSA and ECDC jointly analysed the data, and the main findings are presented in this article. The trends described below include only EU Member States.

Main zoonoses trends in 2007

Campylobacter

In 2007, as in the previous two years, campylobacteriosis was the most commonly reported zoonotic disease in humans in the EU, with 200,507 confirmed cases reported. This was a 12% overall increase compared to 2006 (including the new Member States Bulgaria and Romania for 2006 to facilitate comparison) with most Member States reporting an increase, some as high as 27%, compared to 2006.

In foodstuffs, *Campylobacter* was most commonly detected in fresh broiler (poultry) meat where on average 26.0% of samples were found positive at the EU level. *Campylobacter* was also frequently found in animals and most often in poultry flocks and pigs. In the broiler flocks tested in the EU, 25.2% were positive for *Campylobacter*. Although a high prevalence (56.1%) was also reported in pig herds, *Campylobacter* rates in pig (and bovine) meat typically decrease sharply following slaughter and remain low at retail.

Salmonella

Salmonellosis was the second most commonly reported zoonotic infection in the EU in 2007, with 151,995 human cases and a statistically significant decreasing trend in the notification rate in the EU over the past four years. A seasonal peak in the number of cases during late summer and autumn was generally observed in all Member States, though *S. Enteritidis* exhibited a much more prominent peak than the other serovars.

In food, *Salmonella* was most commonly found in fresh broiler meat and in pig meat, where 5.5% and 1.1% of samples, respectively, were found positive. The bacterium was very rarely detected in vegetables and fruit or in dairy products (although outbreaks involving such vehicles are known to occur).

In animals, *Salmonella* was most frequently detected in poultry flocks but at lower levels than *Campylobacter*. A total of 4.3% of the tested laying hen flocks were found infected in the reporting Member States in 2007, slightly more than in the two previous years. For broilers, the observed proportion of *Salmonella*-positive flocks in 2007 remained approximately at the same level as in 2006 (3.7% versus 3.4%) in Member States with control or monitoring programmes. Of the tested flocks of turkeys, ducks and geese, 7.8%, 10.6% and 9.3%, respectively, of the flocks were reported infected. 2007 was the first year when Member States implemented

new *Salmonella* control programmes in breeding flocks of fowl, and already 15 Member States reported prevalences that were below the *Salmonella* target for these flocks (1%) that is to be met by the end of 2009.

Listeria

The number of confirmed cases of listeriosis was 1,558 in 2007, thus remaining at the same level as in 2006. Listeriosis is an important food-borne zoonosis due to the severity of the disease and high mortality. A high case-fatality rate of 20% was reported in 2007 among the cases for whom the information was available, affecting the elderly in particular. Young children, especially newborns, had the second highest notification rate after the group of over 65 year-olds. The risk groups for listeriosis are the elderly, immunocompromised individuals, pregnant women and neonates younger than four weeks [3].

Ready-to-eat foods, i.e. food that is not cooked before consumption, is the most important source of human listeriosis infections. However, the proportion of food samples exceeding the legal safety limit in 2007 (100 cfu/g) was very low in ready-to-eat foods, and was most often reported in smoked fish, ready-to-eat meat products and various types of cheese.

Vero-toxin producing E. coli (VTEC)

A total of 2,905 confirmed cases of VTEC were reported in 2007, representing a 13.5% decrease compared to 2006. The notification rate was highest in children aged 0 to 4 years, and this group also accounted for almost 60% of the 103 reported cases with haemolytic uraemic syndrome (HUS). The HUS cases were mainly associated with infections with VTEC serogroup O157.

The data from the animal sector indicated that VTEC was mainly detected in cattle and cattle products such as beef. However, the reported occurrence of VTEC bacteria in foods was generally low, and has remained relatively constant between 2005 and 2007.

Yersinia

The number of confirmed cases of yersiniosis in humans decreased somewhat from 8,979 in 2006 to 8,792 in 2007. In animals, *Yersinia* bacteria were found mainly in pigs, and at the EU level an average of 2.0% of the tested pig meat samples were reported positive for *Y. enterocolitica*.

Trends in other zoonoses

EU Member States that are not free of bovine tuberculosis and receive Community co-financing for their eradication programmes [4], reported a statistically significant decreasing trend in the prevalence of bovine tuberculosis. Non-co-financed Member States reported a decreasing prevalence or a prevalence at the same level as in 2006. Reported human cases of tuberculosis due to *Mycobacterium bovis* (120 cases) in the EU remained similar to the levels in previous years. The detection of *M. bovis* in domestic animals other than cattle, as well as in wildlife and zoo animals, indicates that these animal species can serve as a reservoir of bovine tuberculosis.

The prevalence of bovine brucellosis in cattle herds remained largely unchanged in the EU compared to 2006, whereas the prevalence of brucellosis in sheep and goats seemed to be decreasing. The number of notifications of brucellosis cases in humans in 2007 decreased as well, with 542 confirmed reported cases compared to 752 in 2006. Herds infected with brucellosis as well as consumption of cheese appeared to be important sources

of human infections in Member States that are not free of animal brucellosis.

The two parasitic zoonoses, trichinellosis and echinococcosis, caused 779 and 834 human cases, respectively. Both were found in farm animals and wildlife in the EU, and wildlife appears to be the major reservoir of these parasites.

In 2007, three fatal cases of rabies were reported in humans. However, the infection originated in endemic areas outside of the EU [e.g. 5]. In domestic and wild animals, the majority of rabies infections were reported from the Baltic and some eastern Member States where foxes and raccoon dogs account for more than 75% of positive samples. Three Member States reported a marked decrease in the number of rabies cases in wildlife, most likely due to successful vaccination programmes.

Conclusions

In 2007, as in previous years, campylobacteriosis and salmonellosis were the most commonly reported zoonotic infections in humans in the EU. Nevertheless, it is reassuring that the declining trend of salmonellosis continued, most likely as a result of the intensified control of *Salmonella* in animal populations, in particular in poultry, and better hygiene throughout the food chain. Similarly, it is anticipated that the baseline survey on *Campylobacter* in live broilers and broiler carcasses carried out in EU Member States in 2008 will enable the European Commission and Member States to identify control options that could reduce *Campylobacter* in animals and reverse the upward trend in human *Campylobacter* infections.

The high proportion of deaths amongst older people as a result of *Listeria* infection and the high proportion of newborn babies among listeriosis cases is of particular concern. ECDC is therefore working closely with EFSA to find out more about the transmission of *Listeria* and possible prevention measures that could reduce the number of cases and deaths.

The report shows that zoonoses have a considerable impact on human health and contribute to the overall burden of infectious diseases in humans. The continued surveillance of zoonotic diseases and agents as well as measures aimed at preventing and controlling them remain of importance in the EU.

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START OF THE INFLUENZA SEASON 2008-9 IN EUROPE - INCREASING INFLUENZA ACTIVITY MOVING FROM WEST TO EAST DOMINATED BY A(H3N2)

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The influenza season 2008-9 started in week 49 of 2008 and is so far characterised by influenza virus type A subtype H3N2. Isolates of this subtype that were tested proved susceptible to neuraminidase inhibitors, but resistant to M2 inhibitors. The circulating A(H3N2) viruses are antigenically similar to the component in the current northern hemisphere influenza vaccine.

This report describes the epidemiological and virological characteristics of seasonal influenza at the start of the influenza season 2008-9 in Europe. Linked clinical and virological surveillance of seasonal influenza in Europe is carried out between October and May (week 40 of one year and week 20 of the following year) by networks of sentinel physicians (mainly general practitioners). Clinical surveillance includes recording of episodes of influenza-like illness (ILI) and/or acute respiratory infections (ARI) and comparison with baseline levels usually seen outside of the surveillance season. Influenza activity is defined according to two main indicators: intensity and geographical spread [1]. Intensity is scaled based on the consultation rates per week as compared to historical data in each country. The start of increased influenza activity is defined as the week of first occurrence of medium intensity. Geographical spread indicates the spatial distribution of influenza activity in each country and ranges between no activity and widespread activity. Clinical specimens for virological confirmation are collected from the sentinel population, and virological data are also reported based on non-sentinel sources of virus detection, e.g. hospital outpatients. In addition, viruses are used for antigenic and genetic characterisation and antiviral resistance testing.

Results

Epidemiology

A number of European countries reported primary care consultation rates for ILI or ARI above their baseline levels towards the end of 2008. Increased influenza activity was initially reported in Malta in week 48, after that in Ireland, Northern Ireland (United

Kingdom (UK)) and Portugal in week 49, in England (UK) in week 50, in Austria and Spain in week 51, in Denmark, France, Italy, Scotland (UK) and Sweden in week 52 of 2008, and in many other European countries since the first week of 2009 (Table 1).

By week 2 of 2009, high intensity influenza activity has been reported in Portugal, Ireland and Switzerland and the number of countries reporting medium intensity activity since the start of the influenza season has increased to 23 (Table 1). Consultation rates have increased in a number of eastern European countries (Czech Republic, Estonia, Hungary, Latvia, Lithuania, Serbia, Slovakia and Romania), but the levels of influenza activity in these countries remain below their respective baseline level thresholds. Portugal has already passed peak influenza activity as clinical consultation rates for Portugal have decreased since week 52 of 2008 and the activity indicator has returned from high to medium activity (Table 1).

Virology

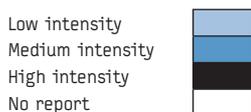
The proportion of sentinel respiratory specimens positive for influenza continued to increase over the past weeks and has reached 39.7% in week 2 of 2009. A total of 5,693 laboratory-confirmed cases of influenza infection from sentinel and non-sentinel sources have been detected across Europe since the start of the 2008-9 season. Of these, 5,474 were influenza type A (2,128 subtype H3, 141 subtype H1, 3,205 not subtyped) and 219 were type B (Figure).

Of the influenza viruses detected up to week 2 of 2009, 374 were antigenically and/or genetically characterised: 321 were reported as A/Brisbane/10/2007(H3N2)-like, 32 as A/Brisbane/59/2007(H1N1)-like, 14 as B/Malaysia/2506/2004-like (B/Victoria/2/87 lineage) and seven as B/Florida/4/2006-like (B/Yamagata/16/88 lineage). This indicates that both lineages of influenza B are currently circulating at low levels in Europe. The circulating influenza A and B/Yamagata lineage viruses are

TABLE 1

Spread of influenza across Europe* as measured by level of influenza activity, influenza season 2008-9

Country	Intensity by week							
	2008						2009	
	47	48	49	50	51	52	1	2
Ireland								
Portugal								
Spain								
England								
Northern Ireland								
Scotland								
Wales								
France								
Belgium								
Netherlands								
Luxembourg								
Switzerland								
Germany								
Denmark								
Norway								
Italy								
Austria								
Malta								
Slovenia								
Sweden								
Czech Republic								
Slovakia								
Hungary								
Poland								
Serbia								
Greece								
Lithuania								
Bulgaria								
Latvia								
Romania								
Estonia								
Finland								
Cyprus								



* Countries ordered by longitude of data providers

similar to the A(H1N1), A(H3N2) and B components in the current influenza vaccine recommended by the World Health Organization (WHO) [2].

Antiviral susceptibility

Antiviral susceptibility data for neuraminidase inhibitor drugs (oseltamivir and zanamivir) and M2 inhibitors (amantadine and rimantadine) is limited to analyses of isolates from five countries which experienced early influenza activity (Italy, Norway, Spain, Sweden and the UK) (Table 2).

Data were obtained by both genotypic and phenotypic methods. Drug susceptibility patterns vary with influenza type and subtype. Circulating A(H3N2) viruses in all countries were sensitive to neuraminidase inhibitors, but resistant to M2 inhibitors. A limited number of A(H1N1) viruses has been identified in Europe this season (141/2,269; 6.2% of influenza A viruses typed/subtyped up to week 2/2009). Over 95% of the A(H1N1) isolates tested in four different countries (Norway, Spain, Sweden and the UK) were resistant to oseltamivir, but retained sensitivity to zanamivir, and all of them were sensitive to the M2 inhibitors. The few influenza B isolates that were analysed retained sensitivity to oseltamivir and zanamivir.

Discussion

Experience from previous influenza seasons suggests that it is most likely, though not inevitable, that the annual epidemics will now intensify in the countries in the east and north of Europe [3]. The final virological picture may change because typing and subtyping data are based on specimens from a limited number of sites and countries at this point in the season. In addition, type B influenza viruses are generally detected in the second half of the influenza season. A comparison can be made with the situation in other countries in the northern hemisphere such as the United States (US). They are experiencing a season with a predominance of A(H1N1) viruses resistant to oseltamivir but sensitive to zanamivir [4]. The different patterns observed in Europe and the US may have arisen due to differences in population immunity, since the preceding 2007-8 season had been dominated by A(H1N1) viruses in Europe but by A(H3N2) viruses in the US. The European Centre for Disease Prevention and Control (ECDC) issued a technical opinion and press release on 8 January stressing the importance of immunising people in risk groups as well as health care workers [5]. This was partly done to address the fact that immunisation coverage is known to be lower in older people particularly in the east of Europe [6].

TABLE 2

Antiviral resistance detected in influenza viruses in Europe, influenza season 2008-9

Virus type and subtype	Resistance to neuraminidase inhibitors				Resistance to M2 inhibitors	
	Oseltamivir		Zanamivir		Isolates tested	Resistant n (%)
	Isolates tested	Resistant n (%)	Isolates tested	Resistant n (%)		
A(H3N2)	93	0	93	0	88	88/(100)
A(H1N1)	52	51/(98)	52	0	23	0
B	3	0	3	0	n.a.	n.a.

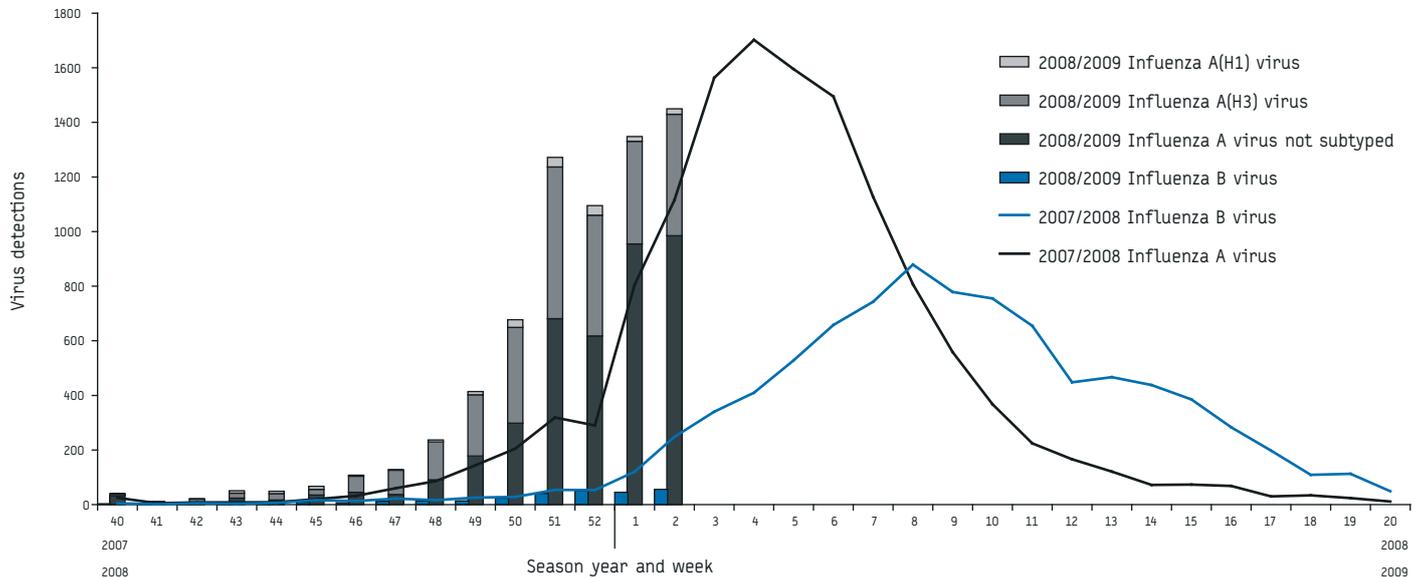
n.a. = not applicable as M2 inhibitors do not act on influenza B viruses.

Acknowledgements

The European Influenza Surveillance Scheme in Europe (EISS) formed the basis for monitoring the spread of influenza virus strains and their epidemiological impact in Europe from 1996 onwards in collaboration with the WHO Collaborating Centre in London (UK) [7]. From this season, the system continues under the European Centre for Disease Prevention and Control (ECDC) who finances the ongoing virological laboratory network coordination by the CNRL co-ordinating team. All 27 European union (EU) countries, Norway, Serbia and Switzerland have participated in the surveillance scheme which publishes an update of influenza activity in Europe online every Friday at <http://www.eiss.org> [8] and on the ECDC home page (www.ecdc.europa.eu). The whole feeds into the WHO's Global Influenza Surveillance Network (GISN; <http://www.who.int/csr/disease/influenza/surveillance/en/>).

FIGURE

Influenza virus detections in the influenza seasons 2007-8 and 2008-9, by week and virus type/subtype*



* 96% of influenza A viruses in the 2007-8 season were A(H1N1) for Europe as a whole.

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