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EDITORIAL

PRODUCTION OF EUROSURVEILLANCE TO BE SHARED WITH THE ECDC

Editorial team, Eurosurveillance editorial office

September 2005 marks a new stage in the continuing development of Eurosurveillance, as a special working relationship with the European Centre for Disease Prevention and Control (ECDC, http://www.ecdc.eu.int) is implemented. The ECDC has been mandated to publish a weekly epidemiological bulletin [1]. Eurosurveillance will draw on ten years of publishing experience to provide this service and be a platform for dissemination of scientific information from the ECDC.

Dr Karl Ekdahl, Strategic Advisor to the ECDC Director, joined the editorial team as an Associate Editor, and work has begun to integrate the contents of the Eurosurveillance website into the new ECDC website. A member of the editorial team in London is taking up a secondment to the ECDC offices in Sweden from 1st October 2005, where the daily intelligence briefings will become another source to inform the contents of Eurosurveillance [2]. The strengthened editorial team will introduce new features to build on the current publication format of news and short reports published weekly, and longer papers published monthly.

Through its weekly and monthly releases, Eurosurveillance has aimed to provide authoritative, peer-reviewed information on communicable diseases from a European perspective. Every country of the European Union (and three other countries, Norway, Bulgaria and Romania) is represented on the editorial board. Eurosurveillance has always published important news from the national communicable disease surveillance centres as quickly and accurately as possible, so that the readers – mainly public health and infectious disease professionals throughout Europe – have access to the information they need.

The new editorial collaboration between Paris, London and Stockholm will be a further example of European public health networking supported by DG-SANCO over the past decade

The first issue of Eurosurveillance was published in September 1995, and for the past ten years, the publication has been produced by an editorial team based at the Institut de Veille Sanitaire in France and the Health Protection Agency (formerly the Public Health Laboratory Service) in the United Kingdom. Eurosurveillance has been funded and supported throughout this time by the European Commission's Directorate-General for Health and Consumer Protection (DG-SANCO). The new editorial collaboration between Paris, London and Stockholm will be a further example of European public health networking supported by DG-SANCO over the past decade.

Note: An earlier version of this editorial was published online on 1 September 2002 (http://eurosurveillanceorg/ew/2005/050901.asp#2)

References

1. ECDC Programme of Work for 2005-2006. 4 February 2005. ECDC, Stockholm, Sweden (http://www.ecdc.eu.int/documents/pdf/ecdc_work_programme.pdf)
2. Coulombier D, Paget J, Meijer A, Ganter B. Highly pathogenic avian influenza reported to be spreading into western Russia. Eurosurveillance 2005; 10(8): 18/09/2005 (http://www.eurosurveillance.org/ew/2005/050818.asp#1)

EDITORIAL

VULNERABLE POPULATIONS: LESSONS LEARNT FROM THE SUMMER 2003 HEAT WAVES IN EUROPE

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What lessons can be learnt from the exceptionally long and severe heat wave experienced in Europe in 2003?

First, that these heat waves can be responsible for a dramatic excess mortality: certainly more than 50 000 excess deaths for Europe in August 2003. The consequences of the heat wave were probably underestimated in many countries, at least those based on the first estimates. This excess mortality affects vulnerable groups, particularly those who are old or ill. Identification of risk factors is a priority if the necessary prevention actions are to be implemented.

There is no doubt that age is one of the main risk factors, particularly for those over 75 or 80 years, but age-associated factors are also very important. Case-control studies carried out in France found that loss of autonomy and social isolation played a major role in the risk factors for the elderly, as did living directly below the roof of a building, in a heat island, particularly in cities.

These heat waves make us question the ways in which our societies are changing, and how we organise them. The main challenge for the future is the aging of the population, particularly the growing number of very old people, and how they live in our cities (in terms of housing and social integration) or in nursing homes (quality of healthcare and management).

The main challenge for the future is the aging of the population, particularly the growing number of very old people

The next few decades will be marked by the convergence of three events that will transform the exceptional circumstances of 2003 into a recurrent risk that must be considered as a priority in our health policies.

These three events are population trends, air pollution and global warming.

- Population trends: as life expectancy increases, there will be increasing numbers of highly vulnerable people aged 80 years and over. The 25th International Population Conference, held in July in Tours (France), reported the human population is aging worldwide and that the proportion of those aged over 60 will double in the next 30 years. This aging trend is most marked in industrialised countries, particularly in Europe.
- Air pollution played an undeniable role in 2003. The respective roles of temperature and ozone in the excess mortality are difficult to assess [1]. The relationship between ozone pollution and excess mortality was estimated to be between 3% and 85% in nine French towns [2]. The reason for this high heterogeneity between towns remains unclear, and demands further study.
- Analysis of long term meteorological trends carried out in recent years underlines that global warming is a reality, and that more heat waves are highly likely to occur in the future.

It will no longer be possible for us to exclaim surprise at these climatic events and their consequences. We must reinforce policies for forecast, alert and prevention.

Nowadays, most European countries have implemented surveillance and alert systems. None of these systems can predict the occurrence of these events with any certainty, and the expected consequences of these heat waves, in terms of duration, intensity and populations affected, are difficult to estimate precisely. In other words, the positive predictive value of an increase in temperature versus mortality is low when analysing the historical series of heat waves and mortality. It is difficult to choose the sensitivity of the alert threshold. If the biometeorological indicators chosen are too high, this could result in inappropriate identification of risks linked to less severe heat waves. We should not rely totally on any alert system, whatever its sophistication.

The objective of the alert system must be to set up strengthened action and prevention measures, based on sound advice for vulnerable populations. Nevertheless, the uncertainties about the efficiency of these actions, launched just before or during threat of a climatic event, highlight the need to consider the problem in depth, so that we can prevent future risks, independently from any alert system.

This is why it is important to analyse the determinants of excess mortality during heat waves. It addresses our capacity to respond the needs of vulnerable persons: town planning needs to come up with solutions to reduce the effects of heat islands, and we ourselves need to strengthen social bonds with vulnerable people, particularly elderly and dependent people, and to improve the quality of the facilities and the skills of the staff who care for these people in hospitals and nursing homes.

Some may have fatalistically viewed the 2003 heat wave as a natural event whose effects were inescapable, but the epidemiological, environmental, and sociological study reveal the ways in which deficiencies in the care of these vulnerable populations and the lack of control in town planning increase the health risks linked to weather conditions.

Once again, surveillance programmes are invaluable for anticipating and managing those risks. A concerted action to deal with climatic risks at the European level is urgently needed.

References

1. Fischer P, Brunekreef B, Lebret E. Air pollution related deaths during the 2003 heat wave in the Netherlands. Atmos Environ (2.562) 38 [2004], pp. 1083-1085
2. Cassadou S, Chardon B, D'Helf M, Declercq C, Eilstein D, Fabre P, Filleul L, Jusot JF, Lefranc A, Le Tertre A, Medina S, Pascal L, Prouvost H. Vague de chaleur de l'été 2003 : relations entre température, pollution atmosphérique et mortalité dans neuf villes françaises. 2004 Rapport d'étude, InVS. (http://www.invs.sante.fr/publications/2004/psas9_070904/rapport.pdf)

EDITORIAL

THE 2003 EUROPEAN HEAT WAVES

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The current issue of Eurosurveillance updates and provides additional context to the report in early 2004 of an estimated 22 080 excess deaths in England and Wales, France, Italy and Portugal during and immediately after the heat waves of the summer of 2003 [1]. While estimates for England and Wales [2], France [3], and Portugal [4], are largely unchanged from those reported earlier, to these should be added 6595-8648 excess deaths in Spain [5], of which approximately 54% or 3574-4687 occurred in August, and 1400-2200 in the Netherlands [6], of which an estimated 500 occurred during the heat wave of 31 July-13 August. Data for Italy, provided here for the cities of Bologna, Milan, Rome, and Turin, are compatible with the earlier estimate that 3134 excess deaths occurred in the 21 Italian regional capitals during the period 1 June-15 August [1,7]; the Italian National Institute of Statistics however, reported an excess of 19 780 deaths country-wide during June-September 2003 as compared to 2002 [8]. Reports elsewhere indicate that approximately 1250 heat-related deaths occurred in Belgium during the summer of 2003 [9], that there were 975 excess deaths during June-August in Switzerland [10] and 1410 during the period August 1-24 in Baden-Württemberg, Germany [11]. At this point, it seems reasonable to speculate that with evidence of heat wave-associated deaths beyond England and Wales, France, Italy, and Portugal, the previously published estimate of 22 080 early August excess deaths should be revised upward by at least 50% for all of western Europe, and by 100% or more if heat events that occurred during June and July 2003 are also taken into account.

The task ahead is to build coordinated, sustained national and local programmes to reduce the vulnerability of the population to extreme heat

Contributors employed a variety of methods to estimate the number of excess deaths during and just after the 2003 heat episodes and to relate daily death counts to weather, to concentrations of air pollutants, and to demographic and social characteristics. Indeed, the varying emphases and methods demonstrated by the six national contributors provide complementary evidence of what happened in 2003, and to whom. While the absence of uniform methods does limit between-country comparisons of the health impact of the 2003 heat waves, these reports taken together suggest that weather alone does not explain the varying tolls of excess death within and between countries.

All six reports demonstrate that the mortality impact of the 2003 heat wave was greatest on the very old: for example, excess mortality in France was estimated at 20% for those aged 45-74 years, at 70% for the 75-94 year age group, and at 120% for people over 94 years [3]. There was no evidence of excess mortality in infants and children in any of the six reports. Among the elderly in France, Portugal and Italy, the three countries which stratified deaths by sex, rates were higher in females [3,4,7]. The strength of the age effect and the direction of the sex effect differ from those described for the 1995 heat wave in Chicago, United States [12], and indeed from those of the 1981 heat wave in Portugal [13]. Also rather unexpected is the observation from Spain that mortality impacts were more pronounced in rural villages than in the provincial capitals [5]; heat wave deaths are generally assumed to be an urban phenomenon, related in part to endogenous production of heat by city-based buildings, traffic, and factories, and to heat retention by inner city asphalt and concrete [14].

Investigators in Rome and Turin calculated rates of excess death as a function of socioeconomic level. They report that the greatest excess was in people living in areas of the lowest socioeconomic level, and suggest that finding may be upwardly biased, due in part to the phenomenon that those who have the means to do so leave Italian cities in summer, leading to an overestimate of the denominator for economically advantaged elderly people resident in the city in summer [7].

It has been observed that few deaths during heat waves are declared to be due to hyperthermia, heatstroke and other classic heat illnesses [15]. Reports from both France and Portugal observe that in 2003, deaths certified as caused by ambient heat constituted an important proportion of the death excess [3,4]; in France, 2852 of 11 891 (24%) excess deaths among people over 74 years were medically certified as directly heat-related.

Assessment of deaths per day offers speculative evidence for the effect of heat wave severity and duration on excess mortality. In the Netherlands [6], deaths per week vary with average weekly maximum temperature over the entire temperature range. In Milan [7] and in Spain [5], heat events of shorter duration earlier in the summer show a moderate death excess, compared with the deep and prolonged mortality spikes associated with the 10 day August heat event. In Paris, the daily death record shows that excess deaths are apparent within 1-2 days of rising August temperatures, crescendo during the unrelenting heat of 2-12 August, drop as temperatures fall, and reach baseline levels by 19 August [3]. Taken together, these graphs of deaths per day suggest that the lag time from extreme heat to excess death is around 1-2 days, and that cumulative mortality effects occur when hot weather is prolonged.

Between-city comparisons offer insight into the influence on deaths during heat waves of air pollution, population adaptation, and community preparedness. In Portugal, August forest fires led to a reported 18 accidental casualties [4]: presumably the attendant air pollution may also have had an impact on short-term mortality. Coincident to the high temperatures, elevated concentrations of ground-level ozone and PM10 were recorded in London and the south east of England, those areas of England and Wales where excess mortality was most in evidence [2]. In France, varying concentrations of ground-level ozone in cities subject to differing meteorological circumstances has allowed investigators to assess the joint effects of ozone and heat: these appear to be additive; while the apportionment of deaths to heat versus ozone differed markedly between cities, it appears that for France overall, during

the period 3-17 August 2003, heat had the preponderant impact on mortality [16]. French contributors suggest that Marseille's experience of a heat wave in 1983 and the existence there of a risk management plan for hospitals and a public communication strategy may have led to a death excess in that city of only 26%, compared with 53% for Nice (although the proportion of the very old in Nice is somewhat larger than in Marseille) [3].

Are those who die during heat waves already near death, with extreme heat advancing the date of their demise by only a few days to weeks, and thus creating a compensatory deficit in expected deaths during the days following the heat event? US investigators have suggested so [17], and the very high rates of excess death in Europe during 2003 among the very old tends to support that concept. However, while deaths for all agesin England and Wales declined by 4% between 24-29 August when compared with expected numbers, there was no evidence of mortality displacement in France or Spain, neither during late August, nor during September, October, and November [2,3,5].

Related to this notion of mortality displacement by heat waves is the hypothesis advanced by contributors from Spain that excess 2003 summer mortality may relate in part to the lower than expected level of mortality there during the winter of 2002-2003, leading to a larger than expected pool of people in fragile health by summer 2003 [5]. Italian contributors suggest that the lower levels of excess mortality in Rome during the August heat wave, compared with two earlier episodes in June and July, may be attributable to a reduction by late summer of the pool of susceptible persons [7].

Taken together, the six articles presented here offer a quantitative overview of the short-term effects on mortality of prolonged extreme heat in Europe, a meteorological phenomenon likely to become more frequent towards the mid twenty-first century [18]. The experience of 2003 shows that those most likely to die of the heat are the old, the chronically ill, and the isolated. Both northern and southern Europe are at risk.

Still, there may be good news amidst these descriptions of catastrophe. The Netherlands has seen a decline in the influence of heat on mortality when the 1950s are compared with the 1970s or 1990s [6]. Recent community and/or institutional experience with extreme heat may lead, as in Marseille, to a dampening of the impact of subsequent heat waves [3]. And, in contrast to the situation in Portugal in 1981 and 1991, the official alerts and interventions deployed there in 2003 may in part explain a relative reduction in the impact of extreme heat on mortality [4]. Perhaps most important, national plans for hot weather preparedness and response have been implemented or refined in five of the six contributing countries since 2003.

The task ahead is to build coordinated, sustained national and local programmes to reduce the vulnerability of the population to extreme heat. This involves pre-event planning and effective during-event intervention. While research is needed to guide these programmes, surveillance, such as that described in this issue, can monitor the effectiveness of our efforts and pinpoint the evolution of vulnerabilities.

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References

1. Kovats S, Wolf T, Menne B. Heatwave of August 2003 in Europe: provisional estimates of the impact on mortality. Eurosurveillance Weekly. 11 March 2004; 8(11). http://www.eurosurveillance.org/ew/2004/040311.asp
2. Johnson H, Kovats RS, McGregor G, Stedman J, Gibbs M, Walton H. The impact of the 2003 heatwave on daily mortality in England and Wales and the use of rapid weekly mortality estimates. Euro Surveill. 2005; 10(7/8).
3. Pirard P, Vandentorren S, Pascal M, Laaidi K, Ledrans M. Summary of the mortality impact assessment of the 2003 heatwave in France. Euro Surveill. 2005; 10(7/8).
4. Nogueira PJ, Falcão JM, Contreiras MT, Paixão E, Brandão J, Batista I. Mortality in Portugal associated with the heatwave of August 2003: Early estimation of effect, using a rapid method. Euro Surveill. 2005; 10(7/8).
5. Simón F, Lopez-Abente G, Ballester E, Martínez F. Mortality in Spain during the heatwaves of summer 2003. Euro Surveill. 2005; 10(7/8).
6. Garssen J, Harmsen C, de Beer J. The effect of the summer 2003 heatwave on mortality in the Netherlands. Euro Surveill. 2005; 10(7/8).
7. Michelozzi P, de Donato F, Bisanti L, Russo A, Cadum E, DeMaria M, D'Ovidio M, Costa G, Perucci CA. The impact of the summer 2003 heatwaves on mortality in four Italian cities. Euro Surveill. 2005; 10(7/8).
8. Istituto Nazionale di Statistica (ISTAT), 2004: Bilancio demografico nazionale. Anno 2003. Roma. Comunicato Stampa Popolazione. http://www.istat.it/salastampa/comunicati/in_calendario/bildem/20040715_01/testointegrale.pdf.
9. Sartor F. La surmortalité en Belgique au cours de l'été 2003. Section de l'épidémiologie, juin 2004; Bruxelles, Institut Scientifique de Santé Publique, IPH/Epi Reports n° 2004-009, D/2004/2505/17.
10. Grize, L, Huss A, Thommen O, Schindler C, Braun-Fahrländer C. Heat wave 2003 and mortality in Switzerland. Swiss Med Wkly. 2005; 135:200-205.
11. Sozialministerium Baden-Wuerttemberg, 2004: Gesundheitliche Auswirkungen der Hitzewelle im August 2003. Stuttgart. Sozialministerium Baden-Wuerttemberg.
12. Whitman S, Good G, Donoghue ER, Benbow N, Shou W, Mou S. Mortality in Chicago attributed to the July 1995 heat wave. Am J Public Health. 1997; 87:1515-8.
13. Garcia AC, Nogueira PJ, Falcão JM. Onda de calor de Junho de 1981 em Portugal: efeitos na mortalidade. Revista Portuguesa de Saude Publica. 1999; Volume tematico I: 67-77.
14. Buechley RW, Van Bruggen J, Truppi LE. Heat island equals death island? Environ Res. 1972; 5:85-92.
15. Shen T, Howe HL, Alo C, Moolenaar RL. Toward a broader definition of heat-related death: comparison of mortality estimates from medical examiners' classification with those from total death differentials during the July 1995 heat wave in Chicago, Illinois. Am J Forensic Med Pathol. 1998;19:113-8.
16. Cassadou S, Chardon B, D'Helf M, et al. Vague de chaleur de l'été 2003: relations entre température, pollution atmosphérique, et mortalité dans neuf villes françaises. 2004 Rapport d'étude, InVS.
17. Braga AL, Zanobetti A, Schwartz J. The time course of weather-related deaths. Epidemiology. 2001;12:662-7.
18. Beniston, M. The 2003 heat wave in Europe: A shape of things to come? An analysis based on Swiss climatological data and model simulations. Geophys Res Lett. 2004; 31: 2022-2026.

MORTALITY IN PORTUGAL ASSOCIATED WITH THE HEAT WAVE OF AUGUST 2003: EARLY ESTIMATION OF EFFECT, USING A RAPID METHOD

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During the first two weeks of August 2003, Portugal was affected by a severe heat wave.
Following the identification in Portugal of the influence of heat waves on mortality in 1981 and 1991 (estimated excess of about 1900 and 1000 deaths respectively), the Observatório Nacional de Saúde (ONSA) - Instituto Nacional de Saúde Dr. Ricardo Jorge, together with the Vigilância Previsão e Informação - Instituto de Meteorologia, created a surveillance system called ÍCARO, which has been in operation since 1999. ÍCARO identifies heat waves with potential influence on mortality [1].
Before the end of the 2003 heat wave, ONSA had produced a preliminary estimate of its effect on mortality. The results based on daily number of deaths from 1 June to 12 August 2003 were presented within 4 working days. Data was gathered from 31 National Civil registrars, covering the district capitals of all 18 districts of mainland Portugal, and representing approximately 40% of the mainland's mortality.
The number of deaths registered in the period 30 July to 12 August was compared with the ones registered during 3 comparison periods (of 2003): 1-14 July, 1-28 July, and 15-28 July. 15-28 July, the period best resembling the heat wave in time and characteristics, produced an estimation of 37.7% higher mortality rate then the value expected under normal temperature conditions. From this value, an estimate of 1316 death excess was obtained for mainland Portugal.
The main purpose of this article is to present the method used to identify and assess the occurrence of an effect (excess mortality) during the heat wave of summer 2003.

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Key words: Heat wave, Portugal

Introduction

Heat waves are known to affect mortality rates. Severe heat wave effects in the United States have been described for the cities of St Louis (1966) [2], St Louis and Kansas City (1980) [3], Philadelphia (1993) [4] and Chicago (1995) [5].

The effects of heat waves appear to be important in Portugal. Portuguese heat wave episodes and their consequences are currently well documented [6-8].

Severe heat wave effects on mortality in June 1981 were acknowledged, initially in the concelho (small administrative unit) of Cascais within the district of Lisbon, and an estimation of excess of deaths prepared for the entire district of Lisbon was presented later (1988) [6]. In 1998, a study based on national mortality data, carried out by the Observatório Nacional de Saúde (National Observatory of Health, ONSA), estimated the number of heat wave related deaths nationwide at about 1900 [7].

In July 1991, Portugal was struck by another heat wave. Again, its effects on mortality were studied and a nationwide estimate of 1000 excess deaths was made [8].

Given the impact of the two previous heat waves, in 1999 ONSA created ÍCARO (standing for 'Importância do CAlor: Repercussão sobre os Óbitos', which means 'the importance of heat and its repercussions on mortality'), a system, which sought to conceive and operate an alert system for heat waves that influence mortality; and to study the characteristics and effects of heat waves [1]. The result of a joint action between ONSA and of the Centro de Vigilância, Previsão e Informação (the Insitute of Meteorology's Surveillance, Forecast and Information Service), this system generates the ÍCARO index, calculated and reported to other institutions, daily between 15 May and 30 September each year. This index indicates the possibility of occurrence of heat waves, with probable influence on mortality for the region of Lisbon, with an anticipation of 3 days (further details are available in 'Fontes de informação', 'ÍCARO' at www.onsa.pt).

In the summer of 2003, between 29 July and 13 August. all districts in Portugal experienced unusually high temperatures. At least 8 of the 18 mainland Portuguese districts had daily maximum temperatures above 32°C during all this period. Four districts, corresponding to the non-coastal interior of Portugal, had daily maximum temperatures above 35°C during the entire period.

When records going back to 1980 were consulted, it was seen that, for the first time during this period, 15 out of the 16 days between 29 July and 13 August had maximum temperatures above 32°C in the district of Lisbon, including a noteworthy consecutive run of 10 days of such high temperatures. A 5 day run of temperatures above 35°C was also recorded for the first time since 1980.

On 12 August 2003, while the heat wave was still happening, ONSA designed a preliminary study that aimed to assess the influence of the heat wave on mortality in the general population. Results were preliminary, because it was not yet possible to consider the full effect of the heat wave at this time.

Methods

Mortality data

Mortality data were obtained from the 31 national civil registrars covering all the district capitals of mainland (continental Portugal), and representing approximately 41.5% of overall mortality. The daily number of deaths registered from 1 June to 12 August was requested on 12 August, and obtained by 19 August.

Period of time studied

The reference period used for the death toll was 14 days, comprising data from 30 July (the first day of the heat wave +1 day for the death registration delay) and 12 August.

Expected number of deaths

The expected number of deaths (E) if the heat wave had not occurred was calculated using three periods within July 2003 (for comparison purposes): 15-28 July; 1-14 July; and 1-28 July, all excluding heat wave-influenced days.

The product of 14 days multiplied by the average daily number of deaths registered for each of the three reference periods was used for the calculation of E, generating three expected death estimates.

Comparison of the expected and observed number of deaths

The number of deaths registered in each one of the national civil registrars was summed, constituting the total number of deaths observed (O).

The excess of deaths caused by the heat wave was calculated by the difference O–E, for each of the 3 different E values. These differences represent the number of heat wave-related deaths, for each of the comparison periods. p = (O–E) / E = 1 – O/E = 1 – r represents the proportion of the excess of deaths in relation to the expected deaths.

Estimation of the total excess of deaths related to the heat wave in mainland Portugal

The total number of deaths related to the heat wave was estimated by

p x ECont in which

ECont = 3486, the number of expected deaths, in the reference period, in the mainland and was calculated by the product of 14 days and 249 deaths. This last number is the daily average number of deaths in the same period as the heat wave in mainland Portugal in 2001 (the most recent mortality data available from ONSA).

Confidence interval estimates

Excess mortality 95% confidence limits (E_{Low} ; E_{Upp}) for each comparison period were obtained from the 95% confidence for the O/E ratio (rLow ; rUpp) calculated by the 'exact method' described by Silcocks that uses the relation between the Beta and Binomial distributions [11].

$E_{Low} = (r_{Low} - 1) \times 3486$ and $E_{Upp} = (r_{Upp} - 1) \times 3486$.

Results

The total number of deaths registered between 30 July and 12 August was 1966. The daily average number was calculated as 140.4 [TABLE 1].

TABLE 1

Total and daily average number of deaths registered in participant civil Registrars' offices during the period of the heatwave for all 3 comparison periods, Portugal, 2003

	Heatwave period 30 July - 18 August	Period 15-28 July	Period 1-14 July	Period 1-28 July
Total no. of deaths	1966	1427	1454	2881
Daily average no.	140.4	101.9	103.9	102.9

TABLE 2

Number of expected deaths, excess of deaths and proportion of the expected deaths, in the period of the heatwave, in the counties of participant civil Registration Offices, according to the used reference periods, Portugal, 2003

	Deaths expected in the heatwave period (30 July-12 August)		
	Period 15-28 July	Period 1-14 July	Period 1-28 July
No. of expected deaths (E)	1427	1454	1440.5
Excess of deaths (Observed-Expected) (O-E)	539	512	525.5
p = (O-E) / E	0.377715	0.352132	0.364804
(95% CI)	(0.286-0.476)	(0.262-0.448)	(0.275-0.462)

The excess deaths estimates varied slightly for the three comparison periods used [TABLE 2].

The estimation of excess of deaths within the selected concelhos and during the period of the heat wave studied, amounted in 539 deaths, when the last 14 days prior to the heat wave are used as a comparison period. When compared with number of deaths registered during the first two weeks of July, the same estimate results in an excess death toll of 512.

The estimated excess of deaths, using the period 15-28 July for comparison, represents a heat-related death toll raise of about 37.8%.

Estimates of the total number of heat wave related deaths within the mainland

Using for comparison the period of two weeks that preceded the heat wave (15-28 July), an excess of about 1316 deaths was estimated [TABLE 3].Although the 3 reference periods provide similar estimates, as presented in table 3, the estimate using the period 15-28 July should be the most accurate, given its proximity to the first day of the heat wave.

TABLE 3

Estimates for the total number and 95% confidence intervals of heatwave related deaths in the mainland, according to the reference periods used, Portugal, 2003

	Period of the heatwave (30 July – 12 August 2003)		
	Period 15-28 July	Period 1-14 July	Period 1-28 July
Total no. of heatwave related deaths	1316.7	1227.5	1271.7
(95% CI)	(998.0-1659.1)	(916.3-1561.6)	(958.3-1611.7)

Discussion

The best estimate of the effect of the heat wave of August 2003 on the mortality of the Portuguese mainland population was 1316 deaths. For comparison periods further away from the start date of the heat wave, the estimates produced values of 1271 and 1227 deaths. These results were consistent among themselves, conveying additional confidence to the estimates, although for the reasons mentioned above, the value 1316 deaths, calculated based on the period 15-28 July, should be the most reliable.

Rural versus non-rural population

The exclusive use of civil registrars in district capitals only was chosen because of time and organisational restraints. This option

may have introduce some systematic bias, forexample, there may be under -representation of rural areas where :

1. The ability of the population to resist heat might be different from other areas – contributing to some inaccuracy in estimates;
2. Age distribution might be different – having more elderly citizens might translate in a greater effect on mortality.

In line with past experience which has found higher mortality in older age groups, this could represent an underestimation of mortality.

This rapid method is not meant to estimate rural and non-rural effects of heat waves. As long as the interest lies in identifying and assessing a heat wave effect, the use of mainly non-rural areas can be an additional factor of difficulty. The use of a balanced or proportional sample of civil registrar's offices in future estimates is advised to prevent this potential bias.

Preliminary nature and limitations of estimates

The urgency to find out the dimension of the heat wave's effects on mortality imposed the following limitations:

1. The period studied ended on 12 August. It is expected that the heat wave's influence continued beyond this date;
2. The use of a sample of national civil registrars of mainland Portugal made up of all district capitals instead of all concelhos.

The first limitation necessarily induces an underestimation of heat wave excess related deaths

The second limitation may produce either an under- or an overestimation, since the populations of the concelhos not represented in the sample may have experienced different effects of the heat wave.

The average number of deaths registered annually in the participating 31 national civil registrars corresponds to about 41.5% of the total deaths registered in mainland Portugal (data from 2001). Therefore, the likelihood that including deaths registered in the remaining national civil registrars would change the estimates profoundly is low.

Alternative explanations for the excess of deaths

The excess number of deaths could have originated, totally or partly, from simultaneous phenomena besides the heat wave:

1. The presence of a high number of tourists increases the population of the Portuguese mainland during the month of August. However, their presence is equally high during the month of July, especially in the last two weeks, which was the time period used as the main comparison period. Also, most tourists visiting Portugal during summer do not belong to the oldest age groups, and so are unlikely to have made much contribution to the heat wave related excess of deaths;
2. Visits by Portuguese who have emigrated abroad, and their descendents are more frequent in August than in July, and this could contribute to the increase of mortality, independently of the influence of the heat wave. However, such visitors tend to bein good health and belonging to younger age groups, and therefore more resistant to the harmful effects of heat waves than the elderly.
3. Road accidents are more frequent during the month of August, which could influence excess deaths. However, this should not influence the current estimates, since the number of fatal victims of road accidents in August is very similar to that of July (157 deaths were reported during July 2002 and 130 during August 2002 - data from Direcção Geral de Viação (Directorate-General for Transport) [9]).
4. A series of forest fires happened during the same time period as the heat wave. According to the general media, there were 18 fatalities. These deaths may only indirectly be attributed to the heat wave. While they influence the total number of deaths to 12 August 2003, only some of these deaths (and presumably a small proportion) will have been registered in the national civil registrars participating in this study.

The 2003 heat wave influenced the excess of mortality less than the 1981 heat wave

There may be several reasons for this:

1. Access to and quality of healthcare is better in 2003 than in 1981;
2. Contrary to the events of 1981 and 1991, there was an alert for the 2003 heat wave and intervention deployed by the Serviço Nacional de Bombeiros e Protecção Civil (National Service of Firemen and Civil Protection), in order to diminish the effect of the heat wave;
3. Athough there is no scientifically sustained confirmation yet, it seems natural that heat waves striking early in the year should have more influence on mortality than those which occur later. The adaptation of the individual to progressively rising temperatures should explain a higher resistance to heat.
4. The nature of the July/August 2003 heat wave was unusual, having three different temperature peaks. The daily maximum air temperatures dropped considerably for one day between the first and second peak (3-4 August) in the coastal districts of Portugal, where most of the Portuguese population lives. Therefore it can be argued that the majority of the Portuguese population was not exposed to a consecutive period of heat stress longer that that of 1981, and this could be a major explanation for the observed reduced heat wave impact.

Although all these reasons may be behind the reduction of the effects of the 2003 heat wave, it does not appear possible to determine the relative influence of each.

In conclusion, at the date of issue of the report, the heat wave of 2003 was estimated as having caused about 1316 deaths up to 12 August, mainly in the elderly.

Definitive 2003 heat wave effect

The work and methodology presented here gave sound evidence of severe impacts on the health and mortality of the population, and this stimulated the responsible institutions to exert unusual efforts to gather complete information and knowledge abut what really happened. The Portuguese Direcção-Geral da Saúde (General Directorate of Health) was able to obtainthe death certificates for summer 2003 earlier than usual to create a database. A joint report on the complete and final effects of the heat wave effects , prepared by the Direcção-Geral da Saúde and ONSA, was finished in April 2004, and replaced all previous plans for future studies [10].

This report showed that the heat wave's impact on mortality occurred between 30 July and 15 August. For the estimation of the expected number of deaths without the heat wave effects, mortality data by district, sex and age group for the years of 2000 and 2001 were used. A total excess mortality of 1953 deaths (1866-2039:95%CI) was estimated. These deaths were observed in the older age groups, mainly 75 years old and above. The number of excess deaths estimated for women were more than twice the number estimated for men. Mortality effects were observed in all Portuguese districts, and the non-coastal districts had higher relative increases in mortality (Guarda, Castelo Branco, Portalegre and Évora). Causes of deaths most strongly associated with the heat wave were 'heatstroke' (O/E=70.0) and 'Other disorders of fluid, electrolyte, and acid-base balance' (O/E = 8.65). Other important associated causes of death accounting for higher mortality were

'diseases of the circulatory system' (758 estimated excess deaths, of which about 370 were 'cerebrovascular disease', about 145 were 'ischaemic heart disease' and 118 were 'heart failure'), 'diseases of the respiratory system' (about 255 excess deaths) and 'all malignant neoplasms' (about 131 excess deaths).

These full effect estimations clearly show that the 2003 heat wave was different from the 1981 heat wave in several ways: most importantly, the mortality impact differed in age groups, with children being spared, and it was more intense for women.

Direct comparisons between final full heat wave effect and preliminary estimate is not possible, for two main reasons: the time periods in the two methodologies are different; and the underlying starting data are different.

While the final full effect estimate is based on the date of death, basic data of the preliminary estimation methodology is solely the number of deaths registered by the civil registrar's offices on each given working day, which does not account for locally displaced deaths, holidays and other similar phenomena.

This limitation could be overcome by having a wider period of civil registrar office notifications, allowing for all deaths during the intended period of study to be accounted for, but such a solution is against the intended nature of the methodology meant to give a timely estimate of possible effects of the heat wave. This is a valuable solution when definitive mortality data is not available quickly enough.

The sooner this rapid method is applied to estimate heat wave effects, either during or after the heat wave occurrence, the more likely it is that mortality impact estimates will be biased towards the lower limits, but when significant impact is shown, the method's objectives are met.

Further developments

In the summer of 2004, a system of daily mortality surveillance was established that will henceforth operate annually in tandem with the ÍCARO surveillance system. This new daily mortality surveillance system was created based on the experience and methodology described in this paper. This system consists mainly of collecting very simple data (the total number of registered deaths) on a daily basis from a sample of 67 civil registrar's offices distributed throughout the districts of mainland Portugal. Of these 67 offices, 31 are from district capitals and participated in the work presented here.

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References

1. Nogueira PJ, Nunes B, Dias CM, Falcão JM. Um sistema de vigilância e alerta de ondas de calor com efeitos na mortalidade: o índice Ícaro. Revista Portuguesa de Saúde Pública. Volume temático 1; 1999:79-84
2. Henschel A, Burton LL, Margolies L, Smith J E. An analysis of the heat deaths in St. Louis during July 1966. Am J Public Health. 1969; 59(12):2232-2242
3. Jones TS, Liang AP, Kilbourne EM, Griffin MR, Patriarca PA, Wassilak SG, Mullan RJ, Herrick RF, Donnell HD Jr, Choi K, Thacker SB. Morbidity and mortality associated with the July 1980 heat-wave in St Louis and Kansas City. JAMA; 1982; 247(24):3327-3331.
4. CDC Heat-related deaths--Philadelphia and United States, 1993-1994. MMWR Morb Mortal Wkly Rep. 1994; 43(25): 453-455.
5. Semenza JC, Rubin CH, Falter KH, Selanikio JD, Flanders WD, Howe HL, Wilhelm JL. Heat-related deaths during the July 1995 heat wave in Chicago. N Engl J Med. 1996;335(2):84-90.
6. Falcão JM, Castro MJ, Falcão MLM. Efeitos de uma onda de calor na mortalidade da população do distrito de Lisboa. Saúde em números. 1988;3(2):9-12
7. Garcia AC, Nogueira PJ, Falcão JM. Onda de calor de Junho de 1981 em Portugal: efeitos na mortalidade Revista Portuguesa de Saúde Pública. Volume temático 1. 1999; 1:67-77
8. Paixão EJ, Nogueira PJ. Efeitos de uma onda de calor na mortalidade. Vigilância epidemiológica. 2003; 21(1): 41-53.
9. Direcção Geral de Viação, Observatório de Segurança Rodoviária – Relatório de 2 000 Elementos Estatísticos, Continente. 2002
10. Nogueira PJ, Paixão EJ, Falcão JM, Botelho J, Catarino J, Carreira M, Calado R. Onda de calor de Agosto de 2003: os seus efeitos sobre a mortalidade da população portuguesa. Relatório científico. Observatório Nacional de Saúde e Direcção-Geral da Saúde 2004.
11. Silcocks P. Estimating confidence limits on a standardized mortality ratio when the expected number is no terror free. J Epidemiol Community Health. 1994;48:313-317.

Original Articles

Surveillance report

Summary of the mortality impact assessment of the 2003 heat wave in France

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France experienced a record-breaking heat wave between 2 and 15 August 2003. All the French regions were affected by this heat wave, which resulted in an excess of 14 800 deaths between 1 and 20 August. The increase in the number of excess deaths followed the same pattern as the increase in temperatures. No deviance from the normal death rate was observed in the month of August during the last third of the month, nor during the following three months. There was a clear discrepancy in the impact of the heat wave from city to city. If the effect of duration of consecutive days with high minimal temperatures and deviance with the seasonal normal temperature was patent, this could not explain all of the observed variability of the death incidence. The victims were mainly elderly women older than 75 years. In terms of relative risk and contribution to the

global toll, deaths linked to heat were the most important. Based on these results, the French government developed a Heat Health Watch Warning System and set up a preventive action plan for each region in 2004.

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Key words: Heat wave, France

Introduction

Europe experienced an unprecedented heat wave in the summer of 2003. In France, it was the warmest summer recorded for 53 years in terms of minimal, maximal and average temperature and in terms of duration. Between 2 and 15 August 2003, an intense heat wave affected the country. From the beginning of August, various signals received by the Ministry of Health aroused suspicion that a large scale epidemic might be occurring. Due to this exceptional situation, the Ministry of Health organised an accelerated process for the collection of death certificates from August and September. The Institut de Veille Sanitaire (InVS, National Institute of Public Health) and the Institut National de la Santé et de la Recherche Médicale (INSERM, National Institute of Health and Medical Research) were asked to assess the health impact of this heat wave. The aim of this article is to summarise and discuss the methods used for this assessment and its results.

Assessment of the total excess mortality in France

Methodology

In France, the physician fills in the death certificate and after folding the paper part containing the medical description of the cause of death to make it secret, sends it to the "mairie" (town council). The town council sends the census information (first name, last name age address] to the Institut National des Statistiques et Etudes Economiques (INSEE, national institute of statistics and economics) and the health information to the physician at the Departmental ('county') Health Office (Direction Départementale des Affaires Sanitaires et Sociales). The departmental health office checks the cause of death and sends it to INSERM to record national statistics. This process takes several months. During the heat wave, the town councils and the departmental health offices were asked to send their respective death certificates to INSERM and INSEE daily, and to give a daily count to InVS for August and September 2003. Regular cross-checking of the three sources meant that accurate information could be obtained [1].

InVS compared the observed number of deaths from 1 to 15 August 2003 with the average rate for the years 2000, 2001 and 2002, modified by population projections for 2003 (the last census was in 1999) [2]. The INSERM study compared the number of deaths by sex and age from 1 to 20 August 2003 with the mean daily number of deaths observed during July, August and September 2000, 2001 and 2002 [1]. More recently, INSERM produced additional results based on validated mortality data between 1 August and 31 December [3]. The reference used to assess the number of deaths in France for this period was the mortality rate by sex and age observed during the period 2000-2002, modified by an estimation of the evolution of death rates and population size for the period 2000-2003.

Meteo-France (the national meteorological service) produced minimal, maximal and average 24 hour temperatures on the basis of a sample of 180 stations representative of French cities [1].

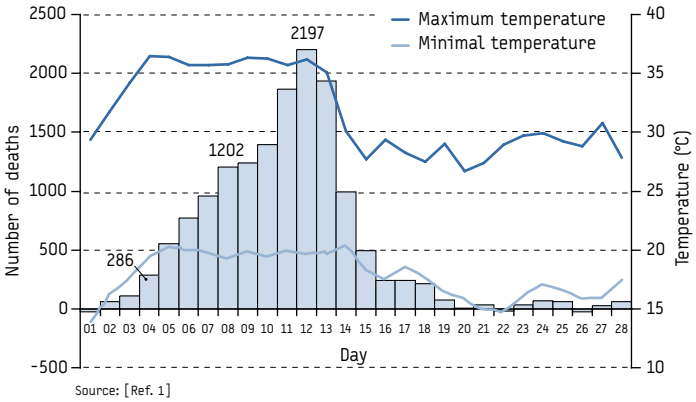
Results

The temperatures increased between 1 August (daily maximal temperature of 25°C) and 5 August (37°C) and maintained themselves at very high levels up to 13 August 2003. They fell abruptly to 28°C between 13 and 16 August (Figure 1). Moreover, the high temperatures and the stagnant atmospheric conditions significantly increased ozone levels, with observed concentrations ranging between 130 and 200 µg/m³ in almost every town between 3 and 13 August [1,2].

The increase in the number of excess deaths followed the same pattern as the increase in temperatures. Nationwide, the impact hit on 4 August, when there were 300 excess deaths. The daily excess rose progressively, reaching 1800 deaths on 8 August and about 2200 deaths on 12 August. It regressed quickly on 13 of August to return to normal levels on 19 August [1] [FIGURE].

FIGURE

Daily excess of deaths during August 2003 and minimal and maximal daily temperatures [1], France



Source: [Ref. 1]

The analysis of death certificates given by the departmental health offices allowed InVS to produce a first estimate on 28 August of 11 435 excess deaths (excess of 55%) between 1 and 15 August 2003 [2]. On 25 September, INSERM estimated the cumulative excess deaths between 1 and 20 August at 14 800 (excess of 60%) [1].The impact was greater for women (70% increase in excess total mortality) than for men (40% increase in excess mortality)(1). This was the case even for same age groups. Excess mortality reached 20% in the 45-74 year age group, 70% in the 75-94 year age group and 20% in people aged 94 years and over [1].

INSERM also showed that during the last third of the month of August and the month of September the mortality had reached the usual level [3]. October and November 2003 showed the usual death rates in every region.

Assessment of the total mortality in excess between cities

Methodology

For 13 cities, InVS received [TABLE] the death certificates for all deaths of local residents, except for fetal deaths, from the town councils [4] and meteorological data from representative stations in towns. The towns were representative of the different regions. For the Eastern third of the country,from South to North: Nice, Grenoble, Lyon, Dijon, and Strasbourg were chosen. For the middle third and from South to North Marseille and Paris were chosen. For the western third and from South to North Toulouse, Bordeaux, Poitiers, Le Mans, Rennes and Lille were chosen. The excess mortality rate was calculated as the division of the number of deaths 2003 minus the mean of 1999-2002 deaths by the mean of 1999-2002 deaths, for the period between 1 and 19 August.

TABLE

Excess deaths, number of maximal temperatures > 35°C, minimal temperatures > 22°C, average delta of mean temperatures between 1-19 August for thirteen cities, France, 2003

Cities	Number of deaths	Excess deaths (%)	Number of days with maximal temperature ⩾ 35°C	Number of days with minimal temperature ⩾ 22°C	Delta of daily mean temperature
Lille	200	4	3	0	4.0
Marseille	571	25	11	14	4.3
Grenoble	148	28	12	0	6.3
Rennes	156	36	6	2	5.6
Toulouse	315	36	12	6	6.6
Bordeaux	318	43	12	7	6.2
Strasbourg	253	51	10	0	5.9
Nice	341	53	1	18	4.3
Poitiers	184	79	11	1	7.3
Lyon	447	80	11	9	6.8
Le Mans	204	82	10	3	7.0
Dijon	168	93	11	4	7.4
Paris	1854	142	9	9	6.7

Results

Dijon, Paris, Poitiers, Le Mans and Lyon clearly showed the highest difference between the usual (1999-2002) and 2003 daily mean temperatures from 1 to 19 August 2003 (>6.7°C) [TABLE]. Toulouse and Bordeaux, presented similar meteorological characteristics but with a milder delta (respectively 6.6° and 6.2° C). Grenoble and Strasbourg, with deltas of 6.3°C and 5.9°C, did not experience very high minimal temperatures. Rennes was less affected by the heat wave, with lower numbers of days with high maxima or high minima and a mean delta of 5.6°C. Marseille and Nice had numerous days with very high minima, but their mean delta was relatively small (4.3°C). The number of excessively warm days in Lille was very low, as was the delta (4.0°C).

In the thirteen cities in the study, a lag of 1 to 3 days between the start of the heat wave and the increase in the number of deaths was observed [4]. An excess in mortality was found in every city, and the disparity of the impact of the heat wave depending on the city appeared clearly. In Dijon, Paris, Poitiers, Le Mans and Lyon, the excess in mortality was particularly marked (>78%) whereas in Lille, the excess of deaths was very low (+4%). Contrasts in the excesses of death could be noted between some towns with quite similar meteorological situations. The excess of deaths in Nice was of 53% whereas in Marseille it was 'only' 26%. Strasbourg suffered a 51% excess of deaths whereas Grenoble 'only' had an excess of 28%.

Assessment of the excess mortality by diseases

Methodology

The analysis of death causes was done by INSERM for the period between 1 and 20 August for the whole of France. This information was compared to the cause of deaths of 2000 and 2001 for the same period. Data for 2002 were not fully validated. The initial cause of death was taken into account with the classification in 65 categories and 17 CIM chapters from Eurostat. A chapter on death directly linked to heat was created by merging the categories of dehydration, hyperthermia and heatstroke [3].

Results

The analysis of deaths by causes of death between 1 and 20 of August from INSERM [3] did not show any significant impact of heat on deaths under ages of 5 years. For people aged under 45 years the observed excess were mild (19%), and only for deaths caused by undefined conditions, heatstroke, dehydration and hyperthermia, and only for men. Among the 2565 excess deaths observed in the 45-74 year age group, 439 were due to heat related illnesses, 418 to undefined causes, 365 to cardiovascular diseases, and 249 to cancer. The highest relative increase concerned heat related deaths (with 434 cases registered in 2003 compared to a mean of 9 cases for the same period in 2000-2001), mental illness (170%), undefined causes (110%), diseases of the nervous system (70%), genito-urinary diseases (70%), endocrine diseases (60%), infectious diseases (60%) and pulmonary diseases (50%). The relative increase was lower for cardiovascular diseases, cancers and accidental deaths (< 20%). Among the 11 891 excess deaths in people aged 75 years and over, 2852 were directly linked to heat, 2633 to cardiovascular diseases, 1265 to undefined causes, 1213 to respiratory diseases, and 781 to diseases of the nervous system. The relative progressions were most important for heat related diseases (1860%), infectious diseases (130%), accidental falls (130%) and undefined causes (110%). Relative excesses by causes of death were generally more pronounced in women than in men for the same age periods.

Discussion

France was very heavily by the 2003 heat wave. It suffered 14 800 excess deaths between 1 and 20 August (+60%). The calculation of this excess can be considered reliable. It is based on the cross-checking of different sources of information (InVS counts, INSEE data and INSERM data). This epidemic event was not immediately followed by any deficit in mortality. INSERM showed that the excess of death observed during the August heat wave had not yet been compensated for at the end of 2003.

No other country in Europe reached such a toll, but other countries differed from France in terms of geographic and temporal extent of the very intense heat wave. Throughout France, 2/3 of the meteorological stations recorded temperatures above 35°C [2].

It is also worth emphasising that elevated odds ratios have been observed in towns where the climatic phenomenon was similar in length and intensity. For example the relative excesses of deaths in Paris, Barcelona and Torino were important [2]. Results from a number of different studies all favour an important role for this exceptional heat stress in the toll registered. The INSERM study showed a strong correlation between the number (n=0-1; n=2-5; n=5-10) of consecutive very hot days (Tmax > 35°C and Tmin > 20°C) and the relative risk of excess deaths among administrative departments (RR=1.3 ; RR=1.5 ; RR=1.8) [1]. There is also a trend between the relative excess mortality among the thirteen cities and the delta between the usual temperatures and the observed ones for August 2003 as shown in table 1.

Other factors can explain the heterogeneity between towns and regions regarding the impact of extreme temperatures. A chronological study of deaths, temperature, and ozone in 9 cities showed that the proportion of observed deaths explained by these last two variables was very low for Lille, Strasbourg, Marseille, Toulouse, moderate for Bordeaux, Rouen and very important for Paris and Lyon [5]. This result is in favour of a geographical heterogeneity of vulnerability to heat wave. Sociodemographic factors can partly explain this difference. For example, the percentage of ages over 74 years is more elevated in Nice (12.7% in 1999) than in Marseille (9.2% in 1999). Other factors certainly intervene, such as the size of the cities, the urban heat island, cultural habits, or adaptation to very hot temperatures. For example, Marseille suffered a heat wave in 1983, and in 2003, an 'emergency plan' to help the public and the hospitals prevent extreme heat effects already existed. This meant that the population of Marseilles was more likely to cope better with a heat wave. The influences of those factors have been analysed by the InVS in specific studies focusing on pollution [5], and heat related risk factors [2].

Based on those results, the French government decided to develop a National Heat Health Watch Warning System (Système d'Alerte Canicule Santé (SACS)) adapted for each département. The objectives are to anticipate the health effects of heat waves and to alert the authorities in time to allow the setting up of preventive actions [6]. It has been developed on the basis of a retrospective analysis of mortality and minimal and maximal temperatures data in fourteen pilot cities. The cut-offs have been set in order to anticipate large scale events three days in advance, resulting in an excess mortality above 50% in Paris, Lyon, Marseille and Lille and above 100% in the smallest cities. The system was extended département-wide using the 98th centiles of minimal and maximal temperatures. The national action plan that integrates this watch warning system has four levels. They correspond to various degrees of activations of actors concerning public health surveillance, social supports, and medical preventive actions. It runs from 1 June to 31 September and results in a close cooperation between the meteorological services and the public health agencies. During 2004 no heat wave was observed but the climatologic predictions estimate that summers as hot as 2003 could be more frequent in the future [7].

The efficiency of the heat health watch warning systems has never been put to the test completely. However, some published results support the hypothesis of their effectiveness in the short term, as well as the possibility of adaptation of the population to hot temperatures in the long term [8-10].

References

1. Hémon D, Jougla E, Clavel J, Laurent F, Bellec S, Pavillon G. Surmortalité liée à la canicule d'août 2003 en France. *Bulletin Epidémiologique Hebdomadaire*. 2003;45-46:221-5.
2. InVS. Impact sanitaire de la vague de chaleur en France survenue en août 2003. Rapport d'étape, 28 août 2003. http://www.invs.sante.fr . 28-8-2003.
3. Hémon D, Jougla E. Surmortalité liée à la canicule d'août 2003. Suivi de la mortalité 21 Août- 31 Décembre 2003 – Causes médicales des décès 1–20 Août 2003. Rapport remis au Ministre de la Santé et de la Protection Sociale INSERM. 1-76. 26 Octobre 2004 Paris.
4. Vandentorren S, Suzan F, Medina S, Pascal M, Maulpoix A, Cohen JC, Ledrans M. Mortality in 13 French cities during August 2003 Heat Wave. Am J Public Health. 2004 Sep;94(9):1518-20.
5. Cassadou S, Chardon B, D'Helf M, Declercq C, Eilstein D, Fabre P, Filleul L, Jusot JF, Lefranc A, Le Tertre A, Medina S, Pascal L, Prouvost H. Vague de chaleur de l'été 2003 : relations entre température, pollution atmosphérique et mortalité dans neuf villes françaises. 2004 Rapport d'étude, InVS.
6. Laaidi K, Pascal M, Ledrans M, Le Tertre A, Medina S, Caserio C, Cohen JC, Manach J, Beaudeau P, Empereur-Bissonnet P. Le système français d'alerte canicule et santé 2004 (SACS 2004). Un dispositif intégré au Plan National Canicule. *Bulletin Epidémiologique Hebdomadaire*. 2004;30-31:134-136.
7. Menne B. The health impacts of 2003 summer heat-waves. Briefing note for the delegations of the fifty third session of the WHO regional Committee for Europe.WHO Europe, September 08 2003.
8. Donaldson GC, Keatinge WR, Nayha S. Changes in summer temperature and heat related mortality since 1971 in North Carolina, South Finland and South-East England. Environ Res. 2003;91(1):1-7
9. Kalkstein LS, Jamason PF, Greene JS, Libby J, Robinson L. The Philadelphia hot weather-health watch/warning system: development and application summer 1995. Bulletin of the American Meteorological Society 1996;77(7):1519-28.
10. Weisskopf MG, Anderson HA, Foldy S et al. Heat wave morbidity and mortality, Milwaukee, Wis, 1999 vs 1995: an improved response? Am J Public Health 2002 May; 92(5):830-3.

ORIGINAL ARTICLES

Surveillance report

MORTALITY IN SPAIN DURING THE HEAT WAVES OF SUMMER 2003

F Simón[1], G Lopez-Abente[1], E Ballester[1,2], F Martínez[1]

The effect of the elevated temperatures on mortality experienced in Europe during the summer of 2003 was observed in several countries. This study, carried out in Spain, describes mortality between 1 June and 31 August and evaluates the effect of the heat wave on mortality.

Observed deaths were obtained from official death registers from 50 provincial capitals. Observed deaths were compared with the expected number, estimated by applying a Poisson regression model to historical mortality series and adjusting for the upward trend and seasonality observed. Meteorological information was provided by the Instituto Nacional de Meteorología (National Institute of Meteorology).

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Spain experienced three heat waves in 2003. The total associated excess deaths were 8% (43 212 observed deaths compared with 40 046 expected deaths). Excess deaths were only observed in those aged 75 years and over (15% more deaths than expected for the age group 75 to 84 and 29% for those aged 85 or over). This phenomenon (heat-associated excess mortality) is an emerging public health problem because of its increasing attributable risk, the aging of the Spanish population and its forecasted increasing frequency due to global warming. The implementation of alert and response systems based on monitoring of climate-related risks, emergency room activity and mortality, and strengthening the response capacity of the social and health services should be considered.

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Key Words: Europe, Spain, epidemiology, heat, adverse effects, human, meteorological factors, mortality, seasons

Introduction

The association between elevated temperatures and mortality has been reported since the early 20th century [1,2]. The actual magnitude of heat-related mortality may be greater than reported, since heat-related deaths are not well defined and heat is usually not listed on death certificates as causing or contributing to death [3,4,5]. Heat waves, because of their magnitude and duration, offer unique opportunities to study this association.

Much of the excess mortality from heat waves is related to cardiovascular and other chronic diseases [6,7] and is concentrated in the elderly [1,2,8]. The impact of heat waves on mortality seems also to be higher in urban areas, due to the 'urban heat island effect' [9,10,11]. Some studies suggest that this effect could be due to interaction between temperatures and air pollution [12].

In 1991 and 1995 Spain experienced two heat waves, both associated with excess mortality [13-17]. However, heat-related mortality was not considered to be a public health priority in Spain, and specific warning and/or surveillance systems were not implemented [18].

During the summer of 2003 Europe experienced a heat wave that was remarkable both in the magnitude and the duration of the high temperatures recorded. Thousands of deaths were associated with this meteorological phenomenon, highlighting the current inabiligy to deal with this kind of health threat.

This paper presents a summary of the results of the study to describe mortality and detect any excess mortality experienced in summer 2003 in Spain that was carried out by the Instituto de Salud Carlos III.

The heat wave of 2003 in Spain

Summer temperatures in Spain are usually high. The mean daily temperature during the period 1971-2000 for June, July and August for 48 out of the 50 provincial capitals was 21.8°C. Mean maximum and minimum temperatures for the same period were 28°C and 15.7°C respectively (Instituto Nacional de Meteorología).

However, Spain experienced an increase in temperatures during the summer 2003. Mean daily temperatures for the period June-August, in the same group of cities, were 12.9% (2.7°C) higher than the observed mean of the period 1971-2000. Mean maximum and minimum temperatures for the same period were 11.2% (3°C) and 16.2% (2.3°C) higher respectively compared with the series 1971-2000.

Increased mean and mean minimum temperatures during this period were registered in all 48 provincial capitals (range: 3.7% to 33.1% for mean temperatures and range: 2.7% to 24.8% for minimum temperatures) and all but one registered increased mean maximum temperatures (range: -0.6% to 23.7%) during the period June-August 2003.

Mean daily temperatures of 33°C and over were recorded for at least half of the days (46/92 days) of the period in 15 out of 48 cities. In 8 of these 15 cities temperatures over 33°C were registered for more than 60 of the 92 days in the period.

Methods

In order to estimate any possible excess in mortality in Spain in summer 2003, we compared observed mortality during the period July-August 2003 with expected mortality in the provincial capitals of the 50 provinces of Spain.

Through a query made to the database at the Ministerio de Justicia (Ministry of Justice), observed mortality was obtained for 27 computerised death registers . The remaining 23 death registers were not computerised, and teams of two people travelled to the provincial offices to obtain the desired data, which was then inserted into the study database. We collected information on date of birth and death, place of death, and place of residence at death for every death certificate entered in the death register between 1 June and 20 August 2003.

To estimate the expected mortality, the Instituto Nacional de Estadística (National Statistics Institute, INE) provided time series of deaths from 1980 to 2002 (2002 data were provisional) for the 50 cities included in the study. For the prediction of deaths in 2003 we have fitted Poisson regression models for different time periods including the year of death as a continuous variable. Age in five year groups (with the oldest group being '85 years and over') and month of death were also included in the model to adjust predictions for variations in age structure of the population and seasonality. Models better fitting observed mortality in the first 5 months of 2003 were based on the 1996-2002 and 1990-2002 time periods. We used models using both time series for each one of the 50 cities included in the study and for each one of the following age groups: 64 years and under, 65 to 74 years, 75 to 84 years, 85 years and over.

Observed number of deaths were compared with expected and the percent variation was calculated for every city ([O-E/E]*100). An overall weighted mean percent variation, using expected number of deaths for each city as weighting variable, was also calculated.

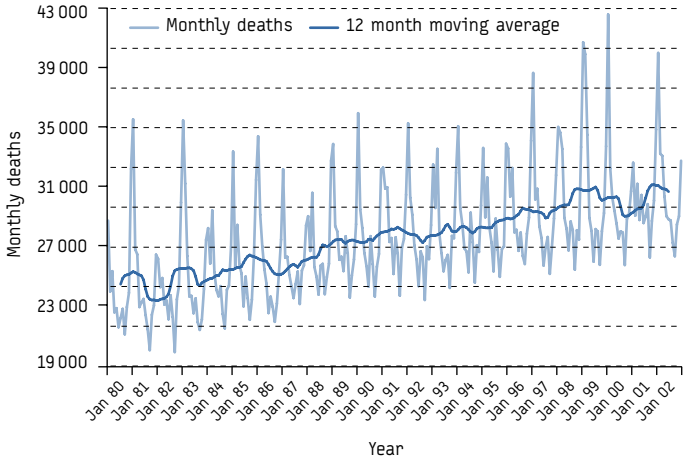
Results

The 50 cities included in the study represent 35% of the total population and all climate spectra in Spain. Median population per city is 152 690 inhabitants with a range between 31 506 and 3 016 788 inhabitants. Of all deaths registered in Spain in the period 1980-2002, 48.7% were registered in this group of cities. In the year 2002 this percentage was 48%.

There is great variability in the daily number of deaths registered in Spain. However, time series show a marked seasonality with peaks in winter months. Smaller peaks are observed in summer months. The increasing trend observed since 1980, probably due to the aging of the population, and to a lesser degree to population growth, seems to have stabilised in recent years [FIGURE 1]. The year of mortality trend stabilisation varies from one city to another.

FIGURE 1

Monthly deaths and 12 month moving average, Spain, 1980-2002

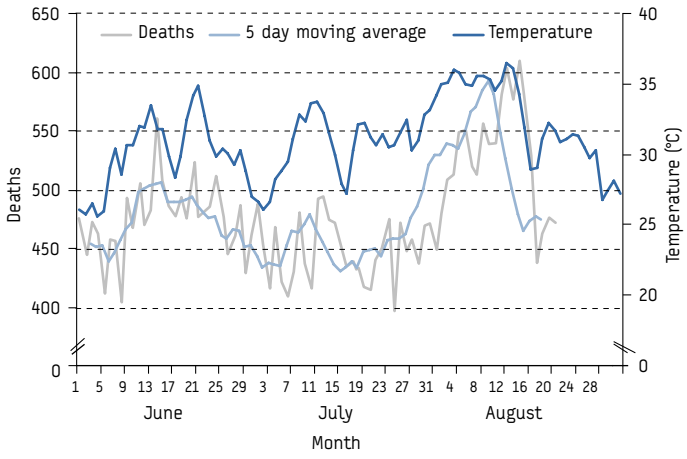


During June-August 2003 a total of 43 212 deaths were registered in the 50 provincial capitals under study. Of these, 14 236 (33%) occurred in June, 13 895 (32%) in July and 15 081 (35%) in August. For 141 deaths, the date of birth was not available. For the 43 071 deaths for which age could be calculated, 13 039 (30%) were of people aged 85 years or older, 13 831 (32%) were of people aged 75 to 84 years, 7888 (18%) were of people aged 65 to 74 years, and 8312 (19%) were of people aged 64 years and under.

Figure 2 shows daily deaths, a 5 day moving average of daily deaths, and mean daily temperatures in the 50 cities under study during summer 2003. In this figure we observe a peak in daily deaths during the second week of August. Two smaller peaks, in mid-June and during the second week of July are also observed. The three peaks observed in daily deaths coincide with the three waves of high temperatures suffered along the summer. Although there is an important variability in daily deaths and temperatures registered among the provincial capitals included in the study, the pattern observed in figure 2 is applicable to most of them.

FIGURE 2

Daily deaths, 5 day moving average and daily mean temperatures for 50 provincial capitals, Spain, June-August 2003



Tables 1 and 2 show the total expected and observed deaths and estimated excess mortality percent for the 50 provincial capitals and for the two time periods better predicting expected deaths (1996-2002 and 1990-2002). Excess deaths in summer 2003 compared with expected is 10.6% (4151 deaths) higher than expected using as predictor the model based on the1996-2002 time series and 7.9% (3166 deaths) using as a predictor the model based on the 1990-2002 time series.

TABLE 1

Expected (based on 1996-2002 time-series) and observed deaths; difference and percentage variation compared with expected deaths by provincial capital, Spain, June-August 2003

Capital city	Expected	Observed	Observed-Expected	Difference (%)
ALAVA	452	486	34	7.52
ALBACETE	407	485	78	19.16
ALICANTE	546	658	112	20.51
ALMERIA	418	494	76	18.18
AVILA	275	297	22	8
BADAJOZ	465	519	54	11.61
BALEARES	906	952	46	5.08
BARCELONA	3993	4674	681	17.05
BURGOS	486	576	90	18.52
CACERES	297	298	1	0.34
CADIZ	442	513	71	16.06
CASTELLON	433	496	63	14.55
CIUDAD REAL	279	267	-12	-4.3
CORDOBA	817	899	82	10.04
CORUNA (LA)	827	873	46	5.56
CUENCA	224	208	-16	-7.14
GERONA	404	469	65	16.09
GRANADA	873	873	0	0
GUADALAJARA	288	300	12	4.17
GUIPUZCOA	736	813	77	10.46
HUELVA	559	553	-6	-1.07
HUESCA	192	219	27	14.06
JAEN	449	466	17	3.79
LEON	454	479	25	5.51
LERIDA	450	526	76	16.89
LOGRONO	371	420	49	13.21
LUGO	413	410	-3	-0.73
MADRID	6209	6942	733	11.81
MALAGA	1266	1380	114	9
MURCIA	819	927	108	13.19
NAVARRA	666	725	59	8.86
ORENSE	440	446	6	1.36
OVIEDO	773	831	58	7.5
PALENCIA	316	361	45	14.24
PALMAS (LAS)	991	1060	69	6.96
PONTEVEDRA	362	360	-2	-0.55
SALAMANCA	529	568	39	7.37
SANTA CRUZ	607	623	16	2.64
SANTANDER	578	632	54	9.34
SEGOVIA	239	217	-22	-9.21
SEVILLA	2003	2314	311	15.53
SORIA	172	169	-3	-1.74
TARRAGONA	326	398	72	22.09
TERUEL	181	146	-35	-19.34
TOLEDO	411	420	9	2.19
VALENCIA	2172	2499	327	15.06
VALLADOLID	795	890	95	11.95
VIZCAYA	882	967	85	9.64
ZAMORA	263	304	41	15.59
ZARAGOZA	1605	1812	207	12.9
TOTAL	**39 061**	**43 212**	**4151**	**10.63**

TABLE 2

Expected (based on 1990-2002 time-series) and observed deaths; difference and percentage variation compared with expected deaths by provincial capital, Spain, June-August 2003

Capital city	Expected	Observed	Observed-Expected	Difference (%)
ALAVA	450	486	36	8
ALBACETE	427	485	58	13.58
ALICANTE	534	658	124	23.22
ALMERIA	475	494	19	4
AVILA	276	297	21	7.61
BADAJOZ	463	519	56	12.1
BALEARES	954	952	-2	-0.21
BARCELONA	4009	4674	665	16.59
BURGOS	513	576	63	12.28
CACERES	320	298	-22	-6.88
CADIZ	464	513	49	10.56
CASTELLON	491	496	5	1.02
CIUDAD REAL	301	267	-34	-11.3
CORDOBA	840	899	59	7.02
CORUNA (LA)	860	873	13	1.51
CUENCA	235	208	-27	-11.49
GERONA	402	469	67	16.67
GRANADA	909	873	-36	-3.96
GUADALAJARA	287	300	13	4.53
GUIPUZCOA	758	813	55	7.26
HUELVA	579	553	-26	-4.49
HUESCA	211	219	8	3.79
JAEN	466	466	0	0
LEON	489	479	-10	-2.04
LERIDA	487	526	39	8.01
LOGRONO	401	420	19	4.74
LUGO	413	410	-3	-0.73
MADRID	6186	6942	756	12.22
MALAGA	1295	1380	85	6.56
MURCIA	853	927	74	8.68
NAVARRA	681	725	44	6.46
ORENSE	456	446	-10	-2.19
OVIEDO	782	831	49	6.27
PALENCIA	332	361	29	8.73
PALMAS (LAS)	1004	1060	56	5.58
PONTEVEDRA	391	360	-31	-7.93
SALAMANCA	556	568	12	2.16
SANTA CRUZ	578	623	45	7.79
SANTANDER	613	632	19	3.1
SEGOVIA	240	217	-23	-9.58
SEVILLA	2058	2314	256	12.44
SORIA	183	169	-14	-7.65
TARRAGONA	335	398	63	18.81
TERUEL	184	146	-38	-20.65
TOLEDO	399	420	21	5.26
VALENCIA	2255	2499	244	10.82
VALLADOLID	818	890	72	8.8
VIZCAYA	908	967	59	6.5
ZAMORA	281	304	23	8.19
ZARAGOZA	1644	1812	168	10.22
TOTAL	**40 046**	**43 212**	**3166**	**7.91**

Assuming that 48% of deaths were registered in the provincial capitals (data for 2002) we can estimate between 6595 and 8648 excess deaths in Spain from 1 June to 20 August 2003, using the 1990-2002 or 1996-2002 time series respectively for our model.

Although results using both models, based on the 1990-2002 and 1996-2002 time series, do not differ very much, we consider that the later time series (1996-2002) better estimates expected deaths because of the stabilisation of the mortality trend in the last few years. The following results refer only to the comparison with the model based on the 996-2002 time series.

The excess deaths were higher in August (17% more than expected), but observed deaths were more than expected for the three months under study (9% in June and 5% in July) [TABLE 3]. Only the elderly were affected and important decreases in mortality were registered in people under 65 years throughout the entire period, while we observed 29% excess deaths among people 85 years and over [TABLE 3].

TABLE 3

Expected (based on 1996-2002 time-series) and observed deaths; difference and percentage variation compared with expected deaths by month and age group for 50 provincial capitals, Spain, June-August 2003

June	Observed	Expected	Observed-Expected	Difference (%)
0-64 years	2761	2858	-97	-3.39
65-74 years	2556	2765	-209	-7.56
75-84 years	4575	3999	576	14.40
> 84 years	4316	3374	942	27.92
TOTAL	**14 208**	**12 996**	**1212**	**9.33**
July	**Observed**	**Expected**	**Observed-Expected**	**Difference (%)**
0-64 years	2744	2914	-170	-5.83
65-74 years	2578	2812	-234	-8.32
75-84 years	4459	4063	396	9.75
> 84 years	4057	3423	634	18.52
TOTAL	**13 838**	**13 212**	**626**	**4.74**
August	**Observed**	**Expected**	**Observed-Expected**	**Difference (%)**
0-64 years	2807	2831	-24	-0.84
65-74 years	2754	2733	21	0.77
75-84 years	4797	3956	841	21.26
> 84 years	4666	3330	1336	40.13
TOTAL	**15 025**	**12 850**	**2175**	**16.92**
June - August	**Observed**	**Expected**	**Observed-Expected**	**Difference (%)**
0-64 years	8312	8603	-291	-3.38
65-74 years	7888	8310	-422	-5.08
75-84 years	13 831	12 018	1813	15.08
84 years	13 039	10 127	2912	28.76
TOTAL	**43 071**	**39 058**	**4013**	**10.27**

Table 4 shows expected and observed deaths and estimated mortality difference percent for the period January- August 2003. Deaths registered in January and February, and to a lesser extent in March, were fewer than expected. However, the excess detected in the summer period overcompensated for this difference and for the first 8 months of 2003 we detected 1964 (1.7%) more deaths than expected.

TABLE 4

Expected (based on 1996-2002 time-series) and observed deaths; difference and percentage variation compared with expected deaths by month for 50 provincial capitals, Spain, January-August 2003

	January	February	March	April	May	June	July	August	Total
Observed	16 777	14 418	15 208	14 042	14 051	14 236	13 895	15 081	117 708
Expected	17 851	15 671	15 455	13 906	13 800	12 994	13 213	12 854	115 744
Observed - Expected	-1074	-1253	-247	136	251	1242	682	2227	1964
Difference (%)	-6.02	-8	-1.6	0.98	1.82	9.56	5.16	17.33	1.7

Discussion

Observed deaths in June, July and August 2003 in Spain were between 7.9% and 10.6% higher than expected. Although excess mortality was more important in August, excess deaths were observed from June. Significant excess mortality was observed only in the elderly (75 years and older), while among those 64 years and younger, mortality decreased during this period. Access to air conditioning at work and use of swimming pools and other practices that lower body temperature among younger people could account for part of this reduction. Further studies of mortality in people aged 74 years and under are needed to explain these findings.

The objective of this study was to estimate any excess mortality experienced in Spain during summer 2003. An association between mortality and temperatures or other variables such as ozone and other pollutants has not been tested. However, the known association between high temperatures and mortality, the fact that the three heat waves experienced in Spain in the summer of 2003 occurred near in time to the three periods of high mortality registered and the distribution of this high mortality throughout the country reinforce the hypothesis of this association.

Based on these results, estimated excess deaths in Spain could be between 6595 and 8648. However, this study included data from provincial capitals and therefore, although they cover a wide range of city sizes, the urban heat island effect [9,10,11] described in the literature could account for part of this excess mortality, and results would not be representative of mortality in Spain, because it may differ in rural areas.

A second study of mortality carried out by the Instituto de Salud Carlos III in a random sample of 107 out of 7458 rural villages with fewer than 10 000 inhabitants, representing a total of 140 807 people, estimated a 40% increased mortality compared with the mean mortality observed in the three previous years (2000-2002) [18]. This study strengthens the magnitude of the results presented in this article.

Mortality experienced in Spain during the winter of 2002-2003 was marginally less than mortality observed during the previous winter. It could be argued that people who unexpectedly did not die during the preceding winter were the people who died during the summer. Data from a newly established mortality surveillance system (not presented in this article) show an excess mortality in the months following the summer, probably associated to an early appearance of the 2003-2004 influenza season. These results would not support the 'harvesting' theory.

Population groups at high risk, such as people 85 years and older, as identified in this study and possibly because of the mechanisms explained by Kenney et al [19] and Foster et al [20], can be identified and specific preventive measures aiming exposure reduction can be implemented if good coordination between surveillance and alert systems and social and health services is achieved.

Results of several studies showing the association between high temperatures and mortality during heat waves in several cities in Spain were published during the 1990s. However, the magnitude and media coverage, and therefore the social impact of the heat wave experience in summer 2003 transferred the debate from academia to the community and political arena.

This debate has altered decision makers' perception of heat-related health problems and the control of heat-related mortality has become a priority. For summer 2004 the Spanish government launched the *Plan de acciones preventivas contra los efectos del exceso de temperaturas sobre la salud* (Prevention plan against adverse effects on health of high temperatures) [21], improved for the summer 2005 and created an interministerial steering commission for this initiative. This plan included:

- A temperature-based alert system using as alert threshold the 95th centile of observed daily maximum temperatures during the last 25 years.
- Awareness campaigns addressed to high risk groups, the general population and healthcare and social services professionals.
- A voluntary register of people at high risk who could benefit from support activities delivered by the Red Cross and other social organisations.
- Development of conduct protocols during heat waves for healthcare and social services professionals.
- A daily mortality surveillance system.

References

1. Mackenbach JP, Borst V, Schols JM. Heat-related mortality among nursing-home patients. Lancet. 1997;349:1297-8.
2. Faunt JD, Wilkingson TJ, Aplin P, et al. The effect in the heat: heat-related hospital presentations during a ten days heat wave. Aust N Z J Med 1995;25: 117-21
3. Heat-related mortality – Chicago, July 1995. MMWR Morb Mortal Wkly Rep. 1995; 44:577-9
4. Donoghue ER, Graham MA, Jentzen JM, et al. Criteria for the diagnosis of heat-related deaths: National Association of Medical Examiners. Position paper. National Association of Medical Examiners Ad Hoc Committee on the Definition of Heat-Related Fatalities. Am J Forensic Med Pathol. 1997; 18:11-14
5. Wolfe MI, Kaiser R, Naughton MP, et al. Heat-related mortality in selected United States cities, summer 1999. Am J Forensic Med Pathol. 2001; 22:352-7
6. Bonner RM, Harrison MH, Hall CJ, Edwards RJ. Effect of heat acclimatization on intravascular responses to acute heat stress in man. J Appl Physiol . 1976;41(5):708-13.
7. Kilbourne EM, Keewahn C, Jones S, Thacker SB. Risk factors for heat stroke. JAMA. 1982;247(24):3332-4.
8. Heat-Related deaths-four states, July-August 2001, and United States, 1979-1999. MMWR Morb Mort Wkly Rep. 2002;51:567-70
9. Lee DH. Seventy-five years of searching for a heat index. Environ Res. 1980;22:331-56
10. Lansberg HE,. The urban climate. New York, NY: Academic Press, Inc, 1981.
11. Buechley RW, Van Bruggen J, Truppi LE. Heat Islands equals death islands? Environ Res. 1972;5:85-92
12. Katsouyanni K, Pantazopoulou A, Touloumi G, Tselepidaki I, Moustris K, Asimakopoulos D, Poulopoulou G, Trichopoulos D. Evidence for interaction between air pollution and high temperature in the causation of excess mortality. Arch Environ Health. 1993 Jul-Aug;48(4):235-42.
13. Saez M, Sunyer J, Castellsague J, Murillo C, Anto JM. Relationship between weather temperature and mortality: a time series analysis approach in Barcelona. Int J of Epidemiol. 1995;24(3):576-82.
14. Ballester F, Corella D, Pérez-Hoyos S, et al. Mortality as a function of temperature: a study in Valencia, Spain, 1991-1993. Int J Epidemiol. 1997;26:551-61.
15. Díaz J, García R, Ribera P, Alberdi JC, Hernández E, Pajares MS, López R, Otero A. Modeling of air pollution and its relationship with mortality and morbidity in Madrid (Spain). Int Arch Occup Environ Health. 1999;72:366–376.
16. Alberdi JC, Díaz J, Montero JC, Mirón n IJ. Daily mortality in Madrid community (Spain) 1986–1991: relationship with atmospheric variables. Eur J Epidemiol. 1998; 14:571–578.
17. Montero JC, Mirón IJ, Díaz J, Alberdi JC. Influencia de variables atmosféricas sobre la mortalidad por enfermedades respiratorias y cardiovasculares en los mayores de 65 años en la Comunidad de Madrid. Gaceta Sanitaria 1997;11:164–170.
18. Martinez Navarro F, Simon-Soria F, López-Abente G, 2004. Valoración del Impacto de la Ola de Calor del Verano de 2003 sobre la Mortalidad, Gac Sanit 2004; 18(Suppl 1):250:8
19. Kenney WL, Hodgson JL. Heat tolerance, thermoregulation for aging. Sports Med. 1987;4:446-56
20. Foster KG, Ellis FP, Dore C, et al. Sweat responses in the aged. Age Aging 1976;5:91-101.
21. Plan de acciones preventivas contra los efectos del exceso de temperaturas sobre la salud, Ministerio de Sanidad y Consumo, Spain (http://www.msc.es)

ORIGINAL ARTICLES

Surveillance report

THE IMPACT OF THE SUMMER 2003 HEAT WAVES ON MORTALITY IN FOUR ITALIAN CITIES

P Michelozzi[1], F de'Donato[1], L Bisanti[2], A Russo[2], E Cadum[3], M DeMaria[3], M D'Ovidio[1], G Costa[4], CA Perucci[1]

This study evaluates the impact of the 2003 heat wave on cause-specific mortality and the role of demographic characteristics and socioeconomic conditions that may have increased the risk of mortality in four Italian cities: Bologna, Milan, Rome and Turin.

Daily mortality counts, for the resident population by age, sex and cause of death were considered. Daily excess mortality was calculated as the difference between the number of deaths observed and the smoothed average. The impact of heat on health is measured in terms of maximum apparent temperature.

The greatest excess in mortality was observed in the north west of Italy (Turin, +23% and Milan, +23%). The old (75-84 years) and the very old (85+ years) were the age groups most affected, and when stratifying by sex, the increase in mortality seemed to be greater among females. The greatest excess in mortality was registered in those with low socioeconomic status in Rome (+17.8%) and in those with lower education levels in Turin (+43%).

The analysis of cause-specific mortality not only confirms results from previous studies of an increase in heat-related mortality by respiratory and cardiovascular diseases, but also shows a significant excess in mortality for diseases of the central nervous system and for metabolic/endocrine disorders.

Results from 2003 highlight the necessity of targeting future prevention programmes at the susceptible sub-groups identified. The introduction of warning systems alongside efficient preventive plans and the monitoring of mortality during heat waves may represent a valid tool for the reduction of heat-related deaths.

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Keywords: heat wave, mortality, heat-related deaths, Italy

Introduction

Record high temperatures were observed across Europe during the summer of 2003. In Italy, the highest monthly mean was registered in many cities in August, with record maximum temperatures above 35°C for several consecutive days. There is debate among experts as to whether extreme temperatures, as observed in summer 2003, are a normal fluctuation in the climate or a sign of global warming attributable to human influences on the climate system [1].

The full impact of climate change on health still remains unclear, and an accurate analysis and quantification of the possible effects, both in the short and long term, has still to be defined [2,3]. The effect of extreme temperatures (often referred to as heat waves) on health is well documented throughout the literature and is known to enhance mortality from cardiovascular, cerebrovascular, and respiratory conditions [4-6].

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One of the first documented episodes of Italian urban populations affected by heat was the heat wave of summer 1983 in Rome, which was associated with a 35% increase in mortality [4]. An evaluation of heat-related mortality in 21 Italian provinces was carried out by the Istituto Superiore di Sanità (Italian National Institute of Health) and over 4000 excess deaths (14% increase) were estimated among the elderly [7]. The study also reported a large heterogeneity of the effect among the Italian cities, with the highest increase in mortality observed in the provinces of the north west, followed by the cities of the south, and with the lowest effect observed in the central provinces and the north east [7]. These differences are mainly due to the different exposure levels during summer 2003, but may also be attributable to a different vulnerability of the populations related to individual, social and environmental factors.

This article presents a more detailed evaluation of the impact of heat waves on mortality during the summer of 2003 (1 June – 31 August) in four major Italian cities: Bologna, Milan, Rome and Turin. The aim is to analyse the impact of heat waves on cause-specific mortality and to analyse the role of demographic characteristics and socioeconomic conditions that may increase the risk of mortality.

Data and methods

Daily mortality counts, for the resident population by age, sex and cause of death were obtained from the local mortality information systems in each city. The impact of heat on health is measured in terms of maximum apparent temperature (Tappmax)[1] which is an index of human discomfort based on air temperature and dew point temperature [8]. The latter combines two meteorological variables (temperature and humidity) that have been shown to have an impact on human health.

Expected daily mortality was computed as the mean daily value from a selected reference period (1995-2002 for Rome, Milan and Bologna and 1998-2002 for Turin). The daily mean expected value was smoothed using a smoothing spline. Daily excess mortality was calculated as the difference between the number of deaths observed on a given day and the smoothed daily average. Confidence limits were determined assuming a Poisson distribution.

In Rome, excess mortality by socioeconomic level was evaluated for the census tract of residence using a deprivation index based on a series of components, namely education, occupation, unemployment, number of household members, overcrowding and household ownership data [9]. The indicator includes four classes: high, medium-high, medium-low and low. In Turin, a socioeconomic indicator for the over-65 years age group was developed based on the level of education subdivided into three classes (high, medium, low).

Results

During the summer of 2003, Tappmax was higher than the mean for the reference period in all cities; the greatest increase was observed in Milan (+4.4°C), followed by Rome (+4.1°C), Turin (+3.4°C) and Bologna (1.6°C) [TABLE 1].

A city-specific definition of heat wave was developed in order to better reflect local conditions. Heat waves have been identified as days with Tappmax above the 90th annual centile and for the first day, an increase of 2°C compared with the previous day. This definition was made on the basis of the literature reviewed and on the relationship observed between temperature and mortality. Three major heat wave periods occurred in Rome, and two major heat waves occurred in the north of Italy: a minor one at the beginning of the summer (mid-June) and a major one in August [FIGURE].

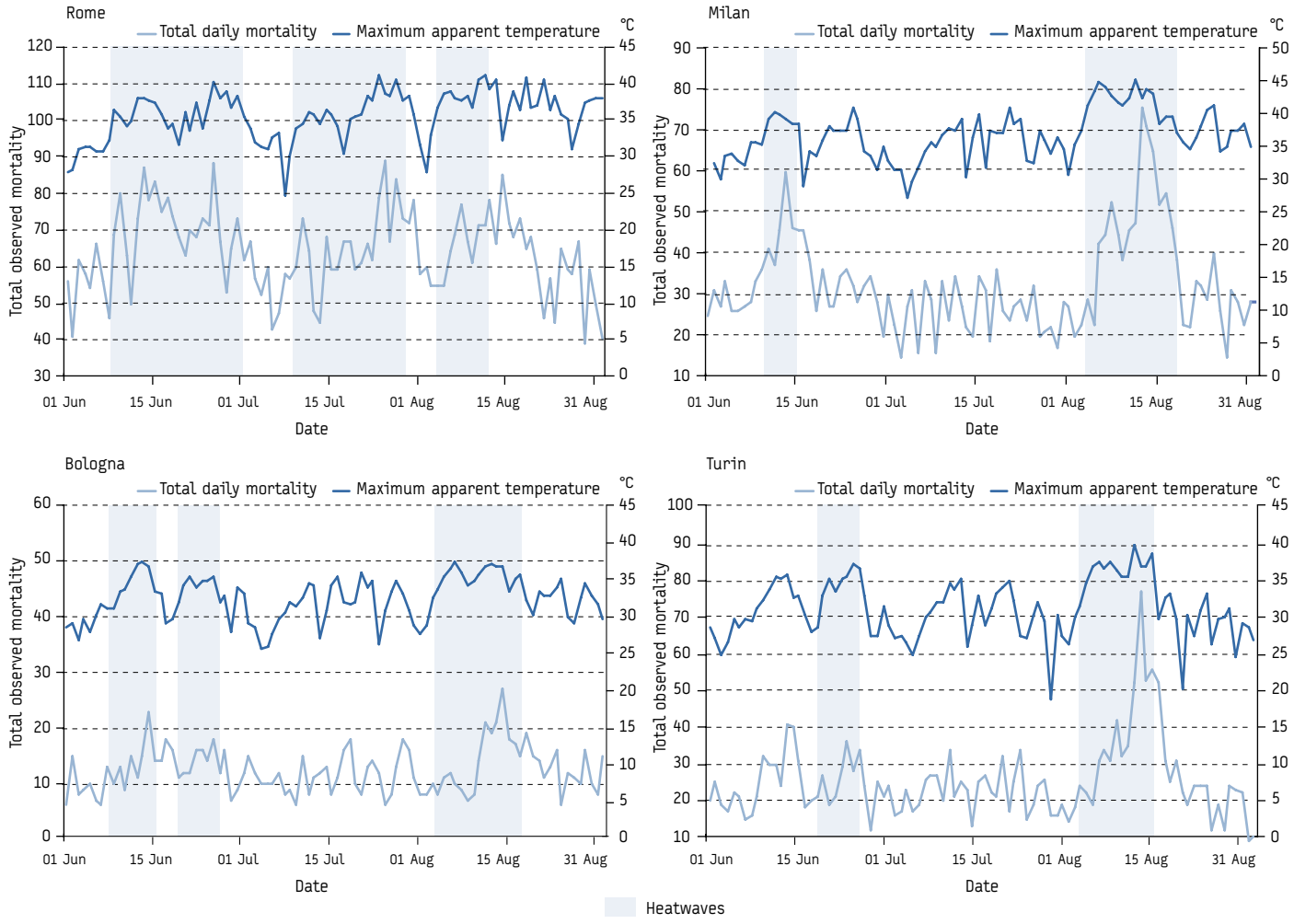
TABLE 1

Maximum apparent temperature and percentage of variation in mortality for Rome, Milan, Turin, and Bologna during summer 2003 (June-August), Italy

	City (Reference period)			
Mortality	**Rome (1995-2002)**	**Milan (1995-2002)**	**Turin (1998-2002)**	**Bologna (1996-2002)**
2003	6009	2968	2332	1432
Reference period	5065	2409	1755	1257
% variation	19	23	33	14
Maximum apparent temperature (°C)	**Rome (1995-2002)**	**Milan (1995-2002)**	**Turin (1998-2002)**	**Bologna (1996-2002)**
2003	35.2	32.7	31.7	32.0
Reference period	31.1	28.3	28.6	30.4
Temperature increase (°C)	4.1	4.4	3.4	1.6

FIGURE

Total daily mortality and maximum apparent temperature, Italy, 1 June-31 August 2003



The results of the analyses indicate a strong association between daily mortality and temperature; with peaks in mortality corresponding to peaks in temperature or with a lag of 1-2 days [FIGURE].

The heat waves recorded between June and August 2003 are associated with significant health effects; a total of 944 excess deaths were observed in Rome (+19%), 577 (+33%) in Turin, 559 (+23%) in Milan and 175 (+14%) in Bologna.

In Rome, excess mortality was observed throughout the summer, but predominantly during the three heat waves observed [8]. The first heat wave (9 June–2 July) was associated with an increase in mortality of 352 deaths; a total of 319 excess deaths occurred during the second heat wave period (10–30 July) and 180 excess deaths during the third (3–13 August) [FIGURE]. In the northern cities, although temperatures above the reference mean were observed throughout the summer, excess mortality was mainly concentrated in the first part of August, when weather conditions became more extreme [FIGURE]. In Milan, 380 excess deaths were recorded during the August heat wave (5-18 August), while in Turin, 257 excess deaths were recorded during the heat wave from 3-14 August [FIGURE]. In Bologna, temperatures were less extreme throughout the summer and heat wave periods were shorter, with less impact on mortality, and 62 excess deaths during the August heat wave (3-17 August).

When subdividing by age group, excess mortality increased dramatically with age; the greatest impact observed in the old (75-84 years) and the very old (85+ years) age groups. In the latter group, mortality increased by 50% in Turin, 40% in Milan, 38% in Rome, and 33% in Bologna [TABLE 2]. When stratifying by age group, there is probably some residual confounding related to sex, in that there is a larger proportion of females in the older age groups. In fact, when stratifying by sex, the increase in mortality seems to be greater among females, [TABLE 2] suggesting a possible higher susceptibility.

The analyses of cause-specific mortality illustrated how the greatest excess in mortality was observed for central nervous system, circulatory, and respiratory diseases and metabolic/endocrine and psychological illnesses [TABLE 3].

TABLE 2

Total and excess mortality by age group and sex in Bologna, Milan, Rome, and Turin during the summer period (June-August) 2003 compared to the reference period, Italy

Mortality	Rome				Milan			
	Observed	Excess	%	95% CI	Observed	Excess	%	95% CI
All ages	6009	944	**19**	15.6-21.6	2968	559	**23**	18.8-27.6
0-64	915	-58	**-6**	-12.1-0.1	372	-35	**-9**	-17.9-0.7
65-74	1163	51	**5**	-1.4-10.6	480	-23	**-5**	-13.1-4.0
75-84	1938	397	**26**	20.2-31.4	1020	305	**43**	33.9-51.4
85	1993	554	**38**	32.4-44.6	1096	312	**40**	31.5-48.1
Sex								
Male	2768	246	**10**	5.7-13.8	1299	141	**12**	6.1-18.3
Female	3241	698	**27**	23.1-31.8	1669	418	**33**	27.0-39.8

Mortality	Turin				Bologna			
	Observed	Excess	%	95% CI	Observed	Excess	%	95% CI
All ages	2332	577	**33**	27.5-38.3	1432	175	**14**	8.0-19.8
0-64	307	21	**7**	-4.7-19.4	154	-10	**-6**	-20.9-8.7
65-74	416	58	**16**	5.0-27.4	202	-41	**-17**	-28.3-5.4
75-84	752	213	**40**	29.5-49.5	514	92	**22**	11.3-32.3
85	857	285	**50**	39.8-59.9	562	139	**33**	21.9-43.8
Sex								
Male	1074	215	**25**	17.6-32.5	686	84	**14**	5.4-22.5
Female	1258	362	**40**	32.6-48.2	752	93	**14**	6.0-22.3

TABLE 3

Total and excess mortality by cause of death in Rome, Milan, and Turin during the summer period (June-August) 2003 compared to the reference period, Italy

Causes of death	Rome				Milan				Turin			
	Observed	Excess	%	95% CI	Observed	Excess	%	95% CI	Observed	Excess	%	95% CI
Tumours	1921	142	**8**	3.2-12.8	926	-9	**-1**	-7.3-5.4	656	17	**3**	-5.2-10.5
Circulatory	2328	452	**24**	19.1-29.2	1044	212	**25**	17.9-33.1	892	261	**41**	32.1-50.6
Respiratory	327	91	**38**	23.4-53.4	282	127	**82**	60.7-103.2	201	73	**57**	35.3-78.7
Digestive system	227	-26	**-10**	-22.0-1.4	121	18	**17**	-3.5-38.4	97	12	**14**	-8.6-36.8
Genitourinary	81	18	**29**	1.0-57.3	57	16	**39**	2.9-75.1	40	13	**48**	2.2-94.1
Metabolic/endocrine gland disorders	307	60	**24**	10.2-38.0	111	45	**68**	36.9-99.5	103	61	**145**	97.9-192.6
Psychological illnesses	96	39	**70**	35.8-103.8	38	4	**12**	-23.8-47.3	70	28	**67**	27.6-105.7
Central nervous system	254	117	**86**	63.2-108.9	133	72	**118**	81.0-155.1	85	47	**124**	76.1-171.2
All causes	6009	944	**19**	15.6-21.6	2968	559	**23**	18.8-27.6	2332	577	**33**	27.5-38.3

In Rome, the most significant excess was registered for diseases of the central nervous system (+86%) and respiratory diseases (+38%). When subdividing by age group, the excess, for both causes, was greatest in the old (+123%, +52%) and the very old (+100% and +45%) age groups. In Turin, a statistically significant increase in mortality was observed for metabolic/endocrine disorders (+145%), diseases of the central nervous system 124%) and respiratory diseases (+57%). Cardiovascular disease registered the greatest excess in Turin (+41%) [TABLE 3]. In Milan, the most significant excess in mortality was associated with metabolic/endocrine disorders (+68%), respiratory diseases (+82%) and disorders of the central nervous system (+118%). Analysis by socioeconomic level illustrates the greatest excess among the lower levels in both Turin (+43% increase in deaths of those with a low level of education) and Rome (+17.8% increase in deaths of those with low socioeconomic level), suggesting that this could be an important risk factor.

Discussion

The unusual heat waves of summer 2003 had a strong impact on the population in terms of mortality, especially in the north west, where peak temperatures reached record values. Daily mortality trends and peaks in mortality showed a temporal variation associated with temperature trends [9,11]. Furthermore, prolonged periods of high temperatures may have a stronger effect on health compared with periods with extreme peak values but a lower mean. During summer 2003, the persistent high temperatures were a strong determinant of the increase in observed mortality.

This study gives a valid insight into the effects of heat waves on health in medical terms, confirming previous results of increases in heat-related mortality by respiratory and cardiovascular diseases [5,13,14] and showing that extreme heat can worsen the conditions of people suffering from chronic disease. The most interesting result that arises form this study is the increase in deaths caused by diseases of the central nervous system in all cities which include different illnesses associated with the elderly (e.g., Parkinson's disease, Alzheimer's disease) [13] and other illnesses which require constant medication which may enhance the susceptibility of these subjects [15].

These results may be an important tool for identifying susceptible populations, and developing effective warning systems and prevention programmes. In Italy, as in other countries, the possible effects of global warming could make susceptible subgroups more vulnerable [2,3] and together with the increasing proportion of elderly people, may enhance heat-related mortality. It is important to recall the heterogeneous nature of the health impact of heat waves in terms of characteristics, such as the intensity and temporal variation in relation to the meteorological conditions between the different cities. Demographic and social factors, as well as the level of urbanisation, air pollution and the efficiency of social services and healthcare units, represent important local modifiers of the impact of heat waves on health. Results from 2003 highlight the necessity of implementing further preventive actions targeting the groups of susceptible people involved (over 75+, especially females) as well as deprived urban areas and low income populations.

Concerning the latency between the peak in temperature and the increase in the mortality, the data showed that peaks in mortality were observed 1-2 days following the heat wave. These results are consistent with results of previous time series studies that reported temperature lags at 0-3 days as having the maximum effect on mortality, and demonstrate that heat related-mortality is a very acute event requiring timely intervention.

Some methodological aspects need to be discussed. Firstly, a limited time window of three months was used as a more complete time series was not available. The choice of reference period is a controversial topic throughout the literature, as by using different reference periods, different estimates of excess mortality are produced. Summer 2003 mortality was compared with that of a reference period which was selected to be long enough to account for the variability of the exposure variable and of the observed effect, and, on the other hand, not too long, in order to account for long-term variation of mortality due to variations in the denominator and of mortality rates. However, the limited time window analysis did not permit an evaluation of a possible harvesting effect (displacement of mortality), but lower excess mortality during the third heat wave period in Rome, for example, could be attributed to a reduction in the susceptible population, as observed in other cities [10].

During the summer months, many Italian cities are affected by seasonal migration, and populations in urban areas are reduced (e.g., Milan, Rome) [12]. It is important to note that the migratory pattern differs from year to year, depending on when heat waves occur, and may be unequally distributed among the population. Susceptible groups, such as the elderly and ill people with lower socioeconomic status, often remain in the city, creating a bias in predicted excess death. The high number of excess deaths in these subgroups might reflect the higher proportion of elderly people of low socioeconomic status who remain in the city during the summer. Several socioeconomic factors might have an impact on health, including poor housing quality, lack of air conditioning, lack of access to health and social services, and individual behaviours (e.g., alcohol consumption and taking medication).

The evaluation of the heat waves of 2003 emphasise the importance of introducing further preventive measures, both for the general population and for susceptible groups, to reduce heat-related deaths during summer. Heat stress conditions may be predictable, and appropriate prevention measures may reduce heat-related mortality. This is achievable if efficient and effective warning systems are introduced to alert residents in urban areas to the oppressive weather conditions. In 2004, the Italian Department for Civil Protection implemented a national programme for the evaluation and prevention of the health effects of heat waves during summer. A Heat/Health Watch/Warning System (HHWWS) [6,16,17] and city-specific prevention programmes were activated during summer 2004 in Bologna, Milan, Rome and Turin, while in four other cities (Brescia, Genoa, Palermo and Florence) warning systems were run experimentally for the first time. Warning systems and prevention programmes will be extended to other cities in summer 2005 as part of the national plan.

The implementation of warning systems and prevention programmes at both the national and local level and the monitoring and surveillance of mortality during heat waves may represent a valid tool for the reduction of heat-related deaths. Furthermore, the national plan includes the identification of susceptible subgroups, such as the elderly aged 75+ and people with specific illnesses who are at higher risk during heat waves. Health guidelines developed by the Ministry of Health have been put in place for the implementation of appropriate prevention programmes. On the basis of the data collected during summer 2004, it will be possible to assess and compare the performance of intervention programmes implemented in each city and to evaluate the reduction of heat-related deaths.

References

1. Schär C and Jendrinsky G. Hot news from summer 2003. Nature. 2004 Dec 2;432(7017):559-60.
2. Yoganathan D, Rom WN. Medical aspects of global warming. Am J Ind Med. 2001 Aug;40(2):199-210.
3. Patz JA, McGeehin MA, Bernard SM, et al.. The potential health impacts of climate variability and change for the United States: executive summary of the report of the health sector of the US National Assessment. Environ Health Perspect. 2000 Apr;108(4):367-76. Albertoni F, Arcà M, Borgia P, Perucci CA, Tasco C. Heat-related mortality Latium Region summer 1983. MMWR Morb Mortal Wkly Rep. 1984 Sep 21;33(37):518-21.
4. Semenza J, et al. 1996. Heat-Related Deaths during the July 1995 Heat Wave in Chicago. N Engl J Med. 1996 Jul 11;335(2):84-90.
5. Michelozzi P, de' Donato F, Accetta G, Forastiere F, D'Ovidio M, Perucci CA, Kalkstein L, Impact of heat waves on mortality – Rome, Italy, June-August 2003. MMWR Morb Mortal Wkly Rep. 2004 May 7;53(17):369-71.
6. Conti S. et al. Epidemiological study of mortality during the summer 2003 heat wave in Italy. Environ Res. 2005;98(3):390-9
7. O'Neill MS, Zanobetti A. and Schwartz J. Modifiers of the Temperature and Mortality Association in seven US cities. Am J Epidemiol. 2003 Jun 15;157(12):1074-82.
8. Michelozzi P, Perucci CA, Forastiere F, Fusco D, Ancona C, Dell'Orco V. Inequality in health: socio-economic differentials in mortality in Rome, 1990-95, J Epidemiol Community Health. 1999 Nov;53(11):687-93.
9. Braga AL, Zanobetti A, Schwartz J, The time course of weather-related deaths. Epidemiology. 2001;12:662–7.
10. Hajat S, Kovats R, Atkinson R, Haines A. 2002. Impact of hot temperatures on death in London: a time series approach. J Epidemiol Community Health. 2002 May;56(5):367-72.
11. Michelozzi P, Fano V, Forastiere F, Barca A, Kalkstein LS, Perucci CA. Weather conditions and elderly mortality in Rome during summer. Bull World Met Org. 2000; 49(4):348-355.
12. Semenza, J.C. et al. 1999 Excess hospital admissions during the July 1995 heat wave in Chicago, Am J of Prev Med. 16: 269-277.
13. Weisskopf M, et al. 2002. Heat Wave Morbidity and Mortality, Milwaukee, Wisconsin, 1999 vs 1995: An Improved Response?, Am J of Public Health, 92(5):830-833.
14. Barrow MW. And Clark D.O. Heat-related Illnesses. Am Fam Physician. 1998;58(3):749-56, 759
15. Kalkstein LS, Nichols MC, Barthel CD, Greene JS. A New Spatial Synoptic Classification: Application to Air Mass Analysis. Int. J of Climatology 1996;16:983–1004.
16. Sheridan SC. The Re-development of a Weather Type Classification Scheme for North America. Int. J of Climatology. 2002;22:51–68.

ORIGINAL ARTICLES

Surveillance report

THE EFFECT OF THE SUMMER 2003 HEAT WAVE ON MORTALITY IN THE NETHERLANDS

J Garssen[1] , C Harmsen[1] , J de Beer[2]

In the Netherlands, between 1400 and 2200 deaths in the summer of 2003 may have been heat-related. The fact that the maximum temperatures were lower than in some other European countries, and occurred in less heavily populated areas, may have led to mortality figures that were relatively less dramatic. The temporarily increased death rates are only partly due to a forward shift of mortality. Heat-related mortality was most pronounced among the elderly in nursing homes.

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Key words: dehydration, heat-related mortality, heat wave, institutionalised population, mortality, temperature, The Netherlands

Introduction

Since the beginning of the 19th century, 33 spells of exceptionally warm weather in the Netherlands have been officially labelled heat waves by the Koninklijk Nederlands Meteorologisch Instituut (Royal Dutch Meteorological Institute). For this purpose, Dutch meteorologists use a definition that is, in view of the generally mild, maritime climate of the Netherlands, less demanding than those of countries at lower latitudes. A warm spell qualifies as heat wave if it consists of at least five days with a maximum temperature of 25°C or above, including at least three 'tropical' days with a maximum temperature of 30°C.

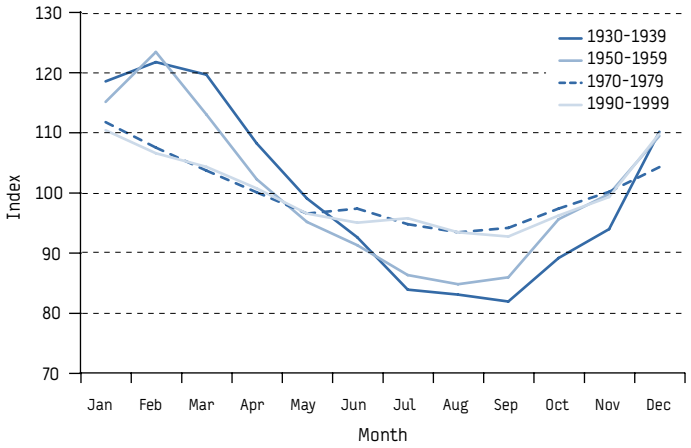
The summer 2003 heat wave amply satisfied these criteria: it lasted from 31 July to 13 August, a total of fourteen days, including seven tropical days, and it was preceded by four tropical days in mid-July. This earlier warm spell failed the heat wave requirements, as the tropical days were interrupted by a single cool day.

The recent heat wave is neither the longest, nor the hottest on record. Of the 33 heat waves on record, one lasted eighteen days (1975) and two seventeen days (1947 and 1976, the latter including ten tropical days). Nor did it break the record for the highest maximum temperature: the 7 August 2003 maximum of 35.0°C has twice been surpassed in the past century, with an all time high of 36.8°C in 1947.

The relationship between climate and excess mortality is a complex one. It can be represented in a V-shape, with the lowest all cause mortality rate in the Netherlands at an average daily temperature of 16.5°C [1]. As the average summer temperatures are much closer to this optimum than average winter temperatures, the mortality risk is normally below average in summer, and well above average in winter. As shown in Figure 1, the effect of climate on mortality has strongly decreased between the 1950s and 1970s, but does not seem to have changed significantly since then. This trend has only been influenced by climate change over the past century to a very minor extent. The indices in Figure 1 show the degree to which the monthly number of deaths in the relevant decade is higher or lower than the number that would be expected if deaths were spread evenly over the year (a value of 110 representing a 10% higher mortality). The lower summer indices in earlier periods are largely caused by the detrimental effect of cold weather, inflating the average mortality risk. In the Netherlands, as in all other countries with mild climates, annual cold-related mortality is higher than heat-related mortality [2].

FIGURE 1

Mortality risk (all ages and causes combined) by month, various periods (monthly average = 100)



Data, method of estimation and results

The Centraal Bureau voor de Statistiek (Statistics Netherlands) collects information on the cause of death for all persons who are considered official residents of the Netherlands. By linking this information to more detailed demographic data provided by the municipal population registers, it is possible to determine the various relationships between personal characteristics and cause of death. Unfortunately, this procedure is inappropriate for the study of heat-related mortality, both in the Netherlands and elsewhere. Even in unusually hot summers, very few deaths are directly or indirectly attributed to these external causes. In 2003, only four deaths were attributed to exposure to excessive natural heat (ICD-10 code X30,

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2. Nederlands Interdisciplinair Demografisch Instituut (Netherlands Interdisciplinary Demographic Institute), Den Haag, The Netherlands

including hyperthermia, heatstroke and heat exhaustion) or to the effects of heat and light (T67) as a primary or secondary cause of death.

A common method for estimating the extent of excess mortality during a certain period involves the comparison with mortality rates in one or more earlier years. A drawback of this method is the fact that unusually low or high temperatures during these earlier periods affect the estimate and are difficult to adjust for. We therefore followed a different indirect estimation procedure that is independent of both mortality rates in earlier years and the official Dutch definition of heat wave.

We first calculated the average maximum daily temperature per month in the period June-September for the most recent 30-year period (June 19.8°C, July 22.1°C, August 22.3°C and September 18.7°C). The temperatures were those recorded by the Royal Dutch Meteorological Institute at De Bilt, which is located in the centre of the Netherlands.

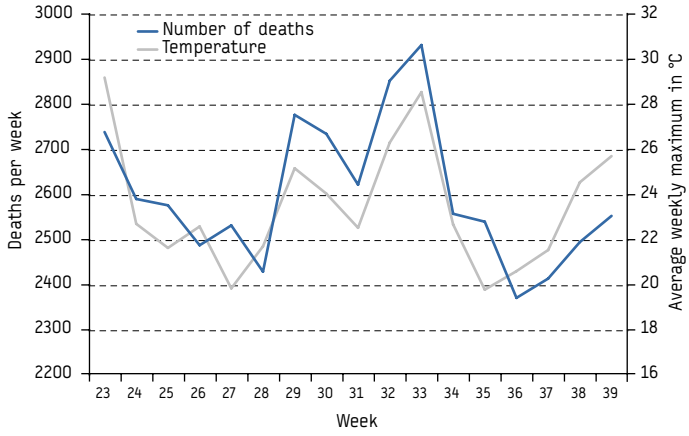
We then calculated the weekly averages of the daily maximum temperatures and carried out a linear regression analysis between the weekly temperature curve (independent variable) and the weekly mortality curve (dependent variable). A linear regression was considered appropriate because the period of observation is relatively short, and all temperatures were higher than the optimum temperature of 16.5°C. For the purpose of this analysis, weekly values were selected as the optimal trade-off between daily values (with high random fluctuations) and monthly values (in which variations in temperature tend to obscure the effect of hot spells). As temperature does not usually have an immediate effect on mortality, we estimated the average time lag between both variables by determining the best fit between the mortality and temperature curves.

Allowing for the resulting time lag of three days, we obtained an estimate of the regression coefficient of 33.5 deaths per week per degree Celsius [Figure 2] ($r^2 = 0.57$). The standard error (7.5 deaths per week per degree Celsius) was used to obtain a low estimate of the absolute number of heat-related deaths per degree Celsius (26.0) and a high estimate (40.9), with a two thirds probability. The total excess mortality in the period June-September 2003 was finally estimated at between 1400 and 2200 deaths, implying an increase of approximately 3% to 5% above the number normally recorded during this period. The number of excess deaths during the heat wave of 31 July – 13 August may have been around 500.

The effect of heat on mortality shows a strong increase with age (0-64 years $r^2 = 0.16$; 65-79 years $r^2 = 0.43$; 80+ years $r^2 = 0.65$).

Figure 2

Mortality and average maximum temperature per week, The Netherlands, June-September 2003



A numerical example illustrates the estimation procedure. Week 33 (11-17 August) had an average daily maximum temperature of 30.6°C, 8.3°C higher than the 30-year average for August (22.3°C). The estimated number of excess deaths is therefore 8.3 times 33.5 (the estimated regression coefficient), hence 278 deaths. The actual number of deaths during this week was 2826. This would imply that almost 10% of all deaths during this hot spell were heat-related.

Discussion

The effect of extreme temperatures on mortality has been demonstrated in numerous studies. Although the media regularly inform the public of this fact during episodes of exceptionally warm weather, public calls for action to prevent heat-related deaths have been rare in the Netherlands. Interest in the possible excess mortality in the Netherlands was largely fuelled by reports from France, where much higher temperatures resulted in about 15 000 heat-related deaths in August 2003 [3]. Considering the difference in population size between the two countries, heat-related mortality in France may therefore have been about three times higher than in the Netherlands.

As far as we are aware, the publication of this estimate prompted only a little activity to investigate the specific conditions that led to the excess mortality, and no large-scale public actions to prevent heat-related deaths in the future. The general feeling that the only victims of the extreme summer temperatures were very elderly and frail people who would anyway have died within a few weeks (this is sometimes referred to as 'harvesting') may partly account for this equanimity.

The Netherlands should not be complacent about taking actions to protect those at increased risk of heat-related mortality simply because excess mortality among the elderly was much lower than in a number of other countries, particularly France. Even if very high temperatures, unlike very low temperatures, result in 'harvesting', this cannot account for all the excess deaths. Some researchers have demonstrated a temporary fall in the number of deaths following a heat wave [4-7], but the findings of recent research on heat-related excess mortality in the Netherlands are less conclusive: a forward shift of mortality was found in some heat waves, but not in others [2]. The French heat wave mortality peak of 2003 was not counterbalanced by a trough in the remaining months of the year [3]. Figure 3, representing average and observed mortality among persons aged 80 years or above in the period May-November 2003, suggests that some forward shift may have taken place in the Netherlands, but this shift does not fully compensate the heat-related excess mortality.

FIGURE 3

Observed and expected number of deaths in patients aged 80 years or more, The Netherlands, May-November 2003

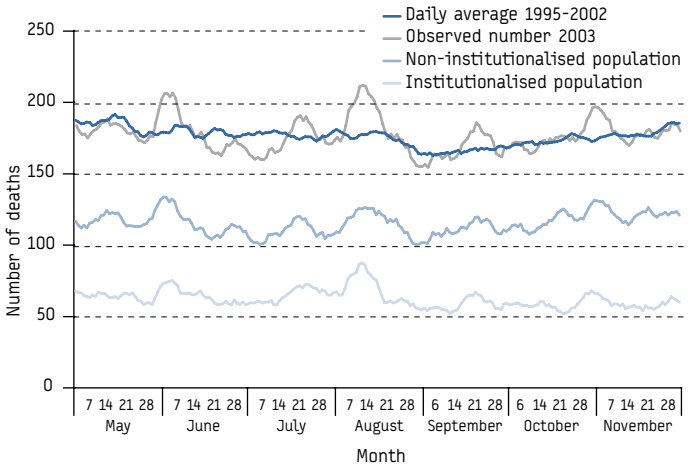
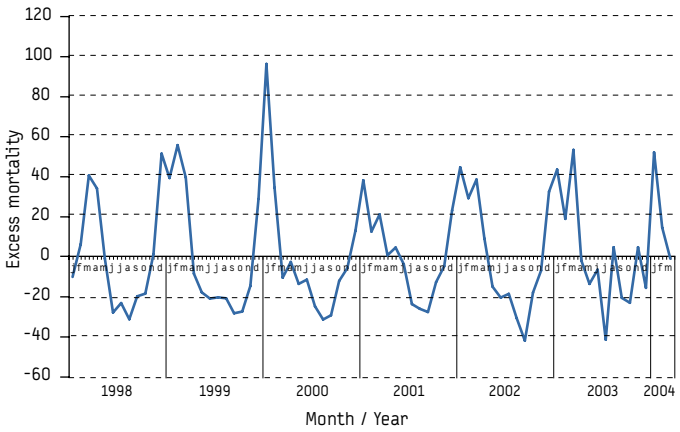


FIGURE 4

Difference between observed and expected daily number of deaths, per month, The Netherlands, 1998-2004



Also, above-average mortality during hot weather is most pronounced among the elderly, but not restricted to them. The observed number of deaths in August 2003 among persons aged 40-59 years was 11% higher than the expected number calculated on basis of data for the period 1995-2002. Mortality did not increase in the younger age groups.

The mortality figures of the Netherlands were less dramatic than those of France, but this may be because a smaller proportion of the population were exposed to extreme temperatures, and not because the Netherlands provides superior care for people at high risk. While the heat wave in France strongly affected the metropolitan areas (Centre and Ile-de-France), the maximum temperatures in the Netherlands were far lower than in France, and occurred in the relatively less densely populated regions. The absolute maximum temperature in the Netherlands was registered at the weather station of Maastricht, in the far southeast (36.2°C, as opposed to 42.6°C in Orange, France). In the far northwest, the highest value only once surpassed the 30-degree barrier (30.2°C in Den Helder). As the western coastal provinces are more densely populated than the eastern landlocked provinces, the lower temperatures in these provinces may have had a substantial downward effect on the overall mortality rates for the Netherlands. Compared to the average number of deaths in August for the period 1995-2002, the number of deaths in August 2003 was indeed 13% higher in all eastern provinces taken together (Groningen, Drenthe, Overijssel, Gelderland and Limburg). In the western coastal provinces (Noord-Holland, Zuid-Holland and Zeeland) the August 2003 mortality rate was 2% lower.

Therefore, even in a small country like the Netherlands, regional differences in climate contribute to evening out the harmful effect, measured at the national level, of hot weather on health. This effect, in absolute terms, is furthermore less noticeable, as the upward influence of heat waves takes place when the general mortality risk is lower than the yearly average. Therefore, even during the heat wave of 2003, the number of deaths in August was hardly above the number that would be expected if deaths were spread evenly over the year [FIGURE 4].

This does not mean that there is no need for policy actions, however, or for keeping a more watchful eye on particular risk groups. Among these risk groups are people suffering from dementia, who need to be prompted by others to take preventive measures in order to avoid dehydration and hyperthermia [8]. The lowest curve in Figure 3 shows that the effect of the August 2003 heat wave was more marked in the elderly in nursing homes than in the non-institutionalised elderly population. This institutionalised population has a much higher share of frail and demented persons than the non-institutionalised population.

References

1. Huynen MMTE, P Martens, D Schram, MP Weijenberg and AE Kunst. The impact of heat waves and cold spells on mortality rates in the Dutch population. Environ Health Perspect. 2001 May;109(5):463-70.
2. Keatinge WR, GC Donaldson, E Cordioloi, M Martinelli, AE Kunst, JP Mackenbach et al. Heat-related mortality in warm and cold regions of Europe, observational study. BMJ. 2000 Sep 16;321(7262):670-3..
3. Pison G. 60 million people in metropolitan France. Population & Societies 2004; 399:1-4.
4. Kunst AE, WNC Looman and JP Mackenbach. Outdoor temperature and mortality in the Netherlands: a time-series analysis. Am J Epidemiol. 1993 Feb 1;137(3):331-41
5. Eng H and JB Mercer. Seasonal variations in mortality caused by cardiovascular diseases in Norway and Ireland. J Cardiovasc Risk. 1998 Apr;5(2):89-95.
6. Rooney C, AJ McMichael, RS Kovats and MP Coleman. 1998. Excess mortality in England and Wales, and in greater London, during the 1995 heatwave. J Epidemiol Community Health.1998; 52:482-486.
7. Braga ALF, A Zanobetti and J Schwartz. The effect of weather on respiratory and cardiovascular deaths in 12 US cities. Environ Health Perspect. 2002; 110:859-863.
8. Mackenbach JP, V Borst and JM Schols, Heat-related mortality among nursing-home patients. Lancet 1997; 349:1297-1298.

THE IMPACT OF THE 2003 HEAT WAVE ON DAILY MORTALITY IN ENGLAND AND WALES AND THE USE OF RAPID WEEKLY MORTALITY ESTIMATES

H Johnson[1], RS Kovats[2], G McGregor[3], J Stedman[4], M Gibbs[5], H Walton[6]

This paper describes a retrospective analysis of the impact of the 2003 heat wave on mortality in England and Wales, and compares this with rapid estimates based on the Office for National Statistics routine weekly deaths reporting system. Daily mortality data for 4 to 13 August 2003, when temperatures were much hotter than normally seen in England, were compared with averages for the same period in years 1998 to 2002. The August 2003 heat wave was associated with a large short-term increase in mortality, particularly in London. Ozone and particulate matter concentrations were also elevated during the heat wave. Overall, there were 2139 (16%) excess deaths in England and Wales. Worst affected were people over the age of 75 years. The impact was greatest in the London region where deaths in those over the age of 75 increased by 59%. Estimated excess mortality was greater than for other recent heat waves in the United Kingdom.

The estimated number of deaths registered each week is reported by the Office for National Statistics. The first clear indication of a substantial increase in deaths was published on 21 August 2003. This provided a quick first estimate of the number of deaths attributable to the heat wave and reflected the pattern of daily deaths in relation to the hottest days, but underestimated the excess when compared with the later analysis.

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Key words: heat wave 2003, mortality, England and Wales

Introduction

Like other countries in Europe, the United Kingdom experienced a heat wave in early August 2003. Temperature records were broken. On 10 August, Brogdale in Kent registered the United Kingdom's highest temperature ever recorded, of 38.5°C (101.3°F). In the south east of England, maximum temperatures exceeded 32°C (89.6°F) on three consecutive days between 4 and 6 August and then on five consecutive days between 8 and 12 August. Average August daily maximum temperature in the south of England is around 21.2°C (70.2°F).

The Office for National Statistics (ONS) and its predecessors have produced weekly national mortality data since the 1850s. The purpose of our weekly deaths system is to provide a quick estimate of any increase in deaths related to events such as an influenza outbreak, or period of exceptional weather.

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This paper will examine the impact of the 2003 heat wave on mortality in England and Wales by age group and region. Air pollution and temperature data will also be presented. The impact on mortality will be compared with the rapid estimates produced by the weekly deaths reporting system, which produced the first estimates of excess mortality in England and Wales in August 2003.

Method

The specific heat wave episode in August was defined as starting when maximum daily Central England Temperature (CET) first exceeded average values (1971 to 2000) by 8°C and ending when temperatures returned to average levels. Excess mortality by age group and region was calculated for the 10 day heat wave period (4 to 13 August 2003). In addition, a value for excess mortality over the whole of July and August was also calculated; no further calculations were made for this time period.

The mortality data, based on date of death, were adjusted on a regional basis for the small proportion of deaths still unregistered at the time of the analysis (approximately 1%). Deaths were assigned to Government Office Regions (GORs) of residence.

Excess mortality was calculated as observed deaths minus the expected mortality (average of deaths in the same years 1998 to 2002). The number of observed deaths was treated as a Poisson variable. The 95% confidence limits for this value were then subtracted from expected mortality to give confidence limits for excess mortality. These limits were then calculated as a percentage of expected mortality to give percentage confidence limits for excess mortality.

The Met Office (the government agency that supplies meteorological data on the weather and climate) supplied temperatures for each GOR during the episode. Within each GOR, the maximum and minimum of the daily maxima were then identified. Daily values were generated for a national 5 km grid by interpolation of data from approximately 560 stations. Daily data for the London Weather Centre weather station, and Central England Temperature (CET) were downloaded from the British Atmospheric Data Centre. CET is representative of a roughly triangular area in central England enclosed by the cities of Preston, London and Bristol.

Measurements of the ambient air concentrations of ground level ozone (daily maximum of a running 8 hour mean) and PM10 (particulate matter of diameter less than 10 µm) (24 hour mean) were obtained from the UK National Air Quality Archive. Air pollution data was collected to allow a description only of a potential confounder of the association with temperature.

Excess pollutant exposure was calculated as the difference between the daily regional concentrations averaged over the episode and the equivalent values observed during same period in 2002, when mean concentrations were considered to be typical mean values for August.

Our current rapid weekly response system takes deaths which have been registered in England and Wales in the previous week and uses this to make an estimate of what the final registered numbers will be [1]. Estimates of excess were made by comparing the registered deaths for each heat wave week in 2003 with the average number of deaths registered for the same week in the previous five years.

Subsequent analysis based on the day when deaths occurred will include deaths which were registered immediately as well as deaths which were registered in the weeks or months following the death.

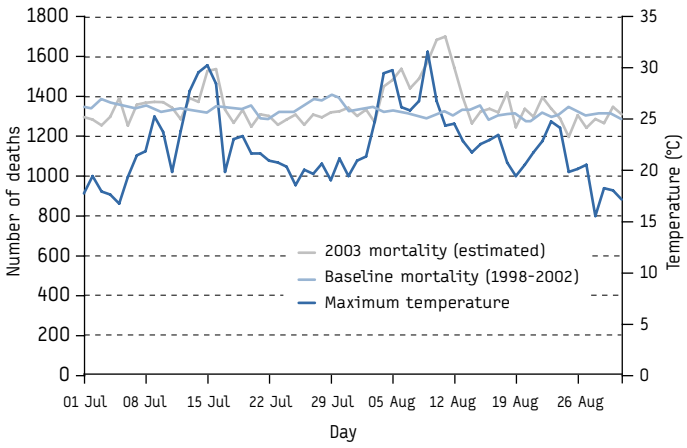
Results: England and Wales

In England and Wales, there were 2139 excess deaths (16% increase, CI: 14% to 18%) during the August heat wave. The Central England Temperature (CET) peaked at 31.5°C (88.7°F) on 9 August [FIGURE 1]. This coincided with the peaks in the concentrations of ozone and PM10 in England. The peak in daily deaths in England and Wales occurred two days later on 11 August. In England and Wales, mortality in people over the age of 75 increased by 22% (CI: 20% to 25%), more than the increase seen for other age groups: (11% (CI: 6% to 15%) for the 0-64 age group and 3% (CI: -1% to 6%) for the 65-74 age group).

Overall in July there were fewer deaths than expected (-1%), despite a slight increase in temperatures and mortality during mid-July (FIGURE 1). Overall in August there was an excess of 5%. The increase in mortality over the heat wave episode (4-13 August) was followed by a decrease in deaths (-4%) in the period 24 to 29 August 2003.

FIGURE 1

Maximum central England temperature and daily mortality, England and Wales, July and August 2003



Results: Regions

The impact was greatest in the southern half of England, particularly in London, where deaths for all ages increased by 42% (CI: 36% to 48%) [TABLE 1].

TABLE 1

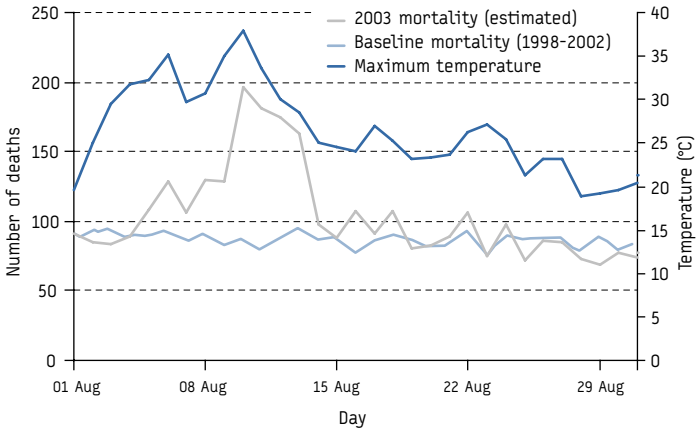
Proportion of excess deaths by Government Office Region, England and Wales, 4-13 August 2003

Government Office Region	Age group			
	0-64	65-74	75+	All ages
London	13	18	59	42
South East	13	17	26	22
South West	17	11	25	22
Eastern	28	-10	27	20
East Midlands	23	-2	21	17
West Midlands	2	4	14	10
Yorkshire and the Humber	-3	-6	15	8
North West	-4	-2	8	4
North East	6	-6	3	1
Wales	5	-10	10	5
ENGLAND AND WALES	**11**	**3**	**22**	**16**

All regions had an excess for people over the age of 75 years. However the greatest excess in the over 75 age group was in the London region with a 59% (CI: 51% to 67%) increase. London experienced night time temperatures of 26-27°C (79 to 81°C) during the heat wave, and a maximum of 37.9°C (100.2°F) was recorded in London on 10 August ([FIGURE 2].

FIGURE 2

Daily mortality, 75+ years, London Government Office Region, England and Wales, August 2003



Concentrations of ozone and PM10 peaked in London on 6 and 8 August respectively [FIGURE 3]. Excess concentrations of PM10 and ozone were highest in London and South East regions respectively [TABLE 2].

FIGURE 3

Concentrations of ozone (daily maximum of running 8 hour mean) and PM_{10} daily mean, London, England, August 2003

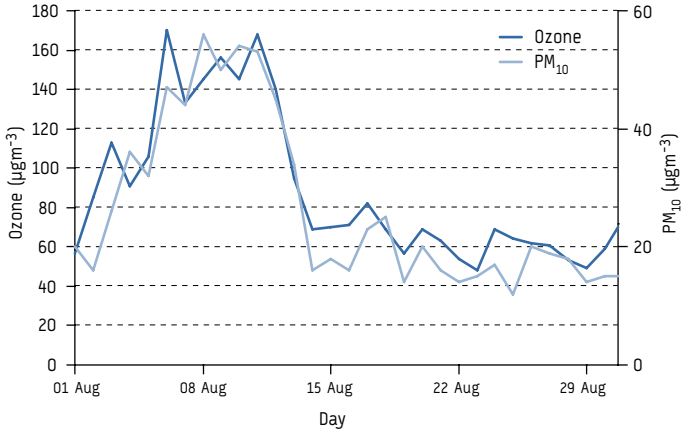


TABLE 2

Temperature (°C) and average excess exposure to ozone and particulate matter (µgm^{-3}) by Government Office Region, England and Wales, 4-13 August 2003

Government Office Region	Temperature (°C)		Ozone (µgm^{-3})	PM_{10} (µgm^{-3})
	Minimum maximum temperature	Maximum temperature	Excess	Excess
London	34.7	38.1	86	26
South East	27.5	38.5	90	20
South West	22.2	33.9	68	24
Eastern	26.6	38.1	65	20
East Midlands	23.1	35.5	61	22
West Midlands	29.0	35.0	48	17
Yorkshire & the Humber	23.7	32.9	37	21
North West	23.3	32.9	48	14
North East	24.2	30.9	31	12

Results: Comparison with initial estimates from the weekly deaths reporting system

Data presented above [FIGURE 1] of the number of deaths occurring each day show that deaths started to increase on 4 August 2003. This was included in the week of 2 to 8 August (registration week 32). An estimate was made of deaths registered in this week on Thursday 14 August. Our estimation method takes into account short delays in data being sent to ONS [1].

The first clear indication of the upturn in deaths registered following the hot temperatures was given by ONS on 21 August, when an estimate of 907 excess deaths was made for registration week 33, 8 to 15 August 2003. This estimate was of a similar order of magnitude to the final excess mortality for that week.

However, this method did not indicate well the mortality excess in the week following the heat wave. The initial estimate of excess mortality was -75, but the final excess was 309 deaths for that week. The excess in registrations in this week are likely to be deaths that occurred in the previous two weeks but that were not registered until week 34.

Table 3 shows initial and final information on death registrations in England and Wales for the period 2 to 22 August 2003. Registrations for the weeks before and after this period were around average levels. Final number of deaths registered in weeks 32 to 34 (2 to 22 August) were a total of 1828 deaths above average (average of the same week over the previous five years). This final estimate of death registrations is much higher than the initial estimated excess over the same period of 910 deaths.

Subsequent work was based on the days when deaths actually occurred. As already described, there were 2139 excess deaths over the episode of 4 to 13 August, when temperatures were at their highest. As expected, this was more than the final excess of 1828 deaths registered over the three weeks, as deaths registered much later than week 34 are included in the number of deaths by date of occurrence.

Discussion

The heat wave had a major effect on mortality in England and Wales, but not to the extent of that observed in France where hot temperatures were maintained for much longer [2].

Excess mortality was much greater than that observed with previous heat waves in the UK. In Greater London it was estimated that the 2003 heat wave was associated with a 40% increase in mortality (all ages) compared with an excess of 16% in 1995 and 15% in 1976 [3,4]. Excess mortality in England and Wales was 10% in 1976, compared with 16% in 2003. Temperatures during the 1976 event were of a comparable magnitude, but the increasing ageing population in England and Wales [5] may have contributed to the increased 2003 excess.

The 2003 heat wave in the United Kingdom occurred relatively late in the summer. Deaths in July overall were slightly below expected levels. Temperatures and mortality did increase in mid-July, and mortality was above what would normally be expected for the time of year. However, high temperatures were not sustained, and did not reach the levels seen in August. There was a small dip in mortality following the heat wave in August, indicating possible displacement of a proportion of deaths by the heat wave.

High ozone concentrations are an important co-exposure during heat waves in England. High ozone concentrations were reported during the 1976 heat wave [6]. Excess exposure to ozone and PM10 were recorded for all regions in England, most notably in London and the South East. Between 21% and 38% of the excess deaths (where excess deaths were predictions based on previous time series studies of air pollution and mortality) in the 2003 heat wave were

TABLE 3

Initial and final numbers of total death registrations and excess registrations, registration weeks 32 to 34, England and Wales, 2003

Registration week	Death registrations after one week	Initial estimated registrations	Final number of death registrations	Initial estimated excess	Final excess
32 (2-8 August 2003)	8716	9246	9575	78	407
33 (9-15 August 2003)	9201	10 132	10 337	907	1112
34 (16-22 August 2003)	8520	9276	9660	-75	309

estimated to be attributable to ozone and PM10, although that study assumed no interaction between high temperatures and high pollutant exposures [7]. This study has not attempted to separate out the effects of pollutants and temperature.

Cities are usually more affected by increasing temperatures than surrounding areas where building density is lower [8]. The nocturnal urban heat island in London is greatest in the summer months, and has increased since the 1960s [9].

The elderly (over 75 years) are most vulnerable to heat related mortality, as has been shown in other heat wave studies in the UK [3] and in other countries [10]. When older people live alone, they may not receive the care they need during a heat wave (for example, adequate hydration) and they are also unlikely to call for medical attention, and therefore may die at home without being admitted to hospital [11].

Smaller increases were seen in many regions in the 0-64 year age group, which may reflect an increase in mortality in children and infants who are also at risk from heat-related deaths [8], or an increase in mortality in sick adults (e.g., those with chronic cardiorespiratory disease).

The 2003 data used for mortality is provisional. There is some uncertainty about the number of deaths that have still not been registered, but a reliable estimate of final values can be made. The weekly deaths reporting system provided a useful indication of the impact of the hot weather in England and Wales, although initial figures were an underestimate. The peak in the number of deaths occurring in England and Wales was on 11 August 2003; the registration week which included this date showed a clear excess (the system picked up the biggest impact week). Any heat warning system would also need to make use of additional information such as temperature data.

When deaths are registered the information is passed to ONS. When a death is registered in a particular week it does not mean that the death necessarily occurred in that week; some deaths are registered in the weeks following the death. Data by date of occurrences is not therefore available as rapidly as deaths by date of registration. Estimates based on the numbers of deaths registered for the week therefore provide a more timely indicator. Initial figures by date of death were published in October 2003 [12].

As climate change continues, heat waves are very likely to increase in frequency and intensity [13] and are likely to exacerbate London's urban heat island [9]. The weekly deaths reporting system can play a useful role as a quick indication of the impact on mortality of an event such as a heat wave. The prevention of deaths has been addressed in a heat wave plan that has recently been published by the Department **of** Health [14].

References

1. Kelly S, Lawes H. Weekly deaths in England and Wales. Health Statistics Quarterly. 1999; 1: 40-43
2. Kovats RS, Wolf T, Menne B. Heatwave of August 2003 in Europe: provisional estimates of the impact on mortality. Eurosurveillance Weekly; Volume 8/ Issue 11 [11 March 2004] http://www.eurosurveillance.org/ew/2004/040311.asp#7
3. Rooney C, McMichael AJ, Kovats RS, Coleman M. Excess mortality in England and Wales, and in Greater London, during the 1995 heatwave: J Epidemiol Community Health. 1988;52: 482-486.
4. McMichael AJ, Kovats RS. Assessment of the Impact on Mortality in England and Wales of the Heatwave and Associated Air Pollution Episode of 1976. 1998. Report to Dept of Health. London, Dept of Epidemiology and Population Health, LSHTM.
5. Office for National Statistics. Focus on: Older people 'Population' [7 May 2004] http://www.statistics.gov.uk/cci/nugget.asp?id=874
6. MacFarlane A, Haines A, Goubert S, Anderson R, Ponce de Leon A, Limb E. 'Air pollution, climate and health: short-term effects and long-term prospects'. The Health of Adult Britain 1841-1994, 1997, Charlton J, Murphy M (Eds) The Stationary Office/ Office for National Statistics, London.
7. Stedman JR. The predicted number of air pollution related deaths in the UK during the August 2003 heatwave. Atmos Environ. 2004; 38:1087-1090.
8. WHO. Heat-waves: risks and responses. Health and Global Environmental Change Series No.2, Copenhagen, 2004.
9. Wilby RL. Past and projected trends in London's urban heat island. Weather 2003; 58: 251-260.
10. Institut de Veille Sanitaire. Impact sanitaire de la vague de chaleur en France survenue en août 2003. Paris, Département des maladies chroniques et traumatismes, Départment santé environment. Impact sanitaire de la vague de chaleur en France survenue en août 2003. Rapport d'étape. 29 août 2003. http://www.invs.sante.fr/publications/2003/chaleur_aout_2003/rap_chaleur_290803
11. Semenza JC, McCullough JE, Flanders WD, McGeehin MA, Lumpkin JR. Excess hospital admissions during July 1995 heat wave in Chicago: Am.J.Prev.Med 1999; 16: 269-277.
12. Office for National Statistics. Summer mortality: Deaths up in August heatwave [3 October 2003] http://www.statistics.gov.uk/cci/nugget.asp?id=480
13. WHO. Climate Change and Human Health – Risks and Responses. Summary, 2003: http://www.who.int/globalchange/climate/en/ccSCREEN.pdf
14. Department of Health. 'NHS Heatwave Plan for England, Protecting Health and Reducing Harm from Extreme Heat and Heatwaves' [30 July 2004] www.dh.gov.uk/publications

WOUND BOTULISM IN INJECTORS OF DRUGS: UPSURGE IN CASES IN ENGLAND DURING 2004

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Wound infections due to *Clostridium botulinum* were not recognised in the UK and Republic of Ireland before 2000. *C. botulinum* produces a potent neurotoxin which can cause paralysis and death. In 2000 and 2001, ten cases were clinically recognised, with a further 23 in 2002, 15 in 2003 and 40 cases in 2004. All cases occurred in heroin injectors. Seventy cases occurred in England; the remainder occurred in Scotland (12 cases), Wales (2 cases) and the Republic of Ireland (4 cases). Overall, 40 (45%) of the 88 cases were laboratory confirmed by the detection of botulinum neurotoxin in serum, or by the isolation of *C. botulinum* from wounds. Of the 40 cases in 2004, 36 occurred in England, and of the 12 that were laboratory confirmed, 10 were due to type A. There was some geographical clustering of the cases during 2004, with most cases occurring in London and in the Yorkshire and Humberside region of northeast England.

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Key words: botulism, *Clostridium botulinum*, IDUs, wound infections

Introduction

Heroin, cocaine and amphetamines are among the most widely injected drugs, and complications in injecting drug users (IDUs) resulting in infections are the most frequent reason for admission to hospital in this group of patients [1]. Soft tissue infections caused by spore-forming bacteria in IDUs emerged as a serious problem in the UK in 2000. Cases of infections due to *Clostridium novyi* [2], *Clostridium botulinum* [3,4], *Clostridium tetani* [5], *Clostridium histolyticum* [6], and *Bacillus cereus* [7] were subsequently reported in this patient group. The major risk factors for all these infections was thought to be the availability of higher purity heroin, and 'skin-popping' (subcutaneous injection) or 'muscle-popping' (intramuscular injection) which is sometimes practised by IDUs when access to veins is lost [2,3,5]. A larger amount of an acidulant, such as citric acid, may be needed to make higher purity heroin soluble for injection; this is likely to increase the resulting tissue damage when subcutaneously or intramuscularly injected, and is thus important for the initiation of a wound infection.

Wound botulism occurs when spores of *C. botulinum* contaminate a wound, germinate and produce botulinum neurotoxin in vivo. The symptoms of botulism are caused by the neurotoxin which blocks the release of acetylcholine at the neuromuscular junction, resulting in a descending flaccid paralysis. Patients with botulism typically present with blurred vision, drooping eyelids, slurred speech, difficulty in swallowing, dry mouth, and muscle weakness. Patients usually have no fever or loss of sensation and awareness. If untreated, paralysis may progress to the arms, legs, trunk and respiratory muscles. If onset is very rapid there may be no symptoms before sudden respiratory paralysis [8].

Methods

Cases of wound botulism were defined, as outlined elsewhere [9], as illness resulting from toxin produced by *C. botulinum* that has infected a wound producing symptoms including diplopia, blurred vision, bulbar weakness and symmetric paralysis. Laboratory confirmation was obtained by the detection of botulinum neurotoxin in serum or wound tissue and/or the isolation of *C. botulinum* from a wound [9].

In the United Kingdom (UK), cases of botulism are reported through national voluntary reporting to the Health Protection Agency (HPA) Centre for Infections (CfI) and by submission of samples for laboratory confirmation to CfI, which also receives referred samples from the Republic of Ireland. Laboratory confirmation is achieved as described elsewhere [10,11,12]. Further clinical details from affected patients are obtained by administration of a standard questionnaire to patients by clinicians and microbiologists.

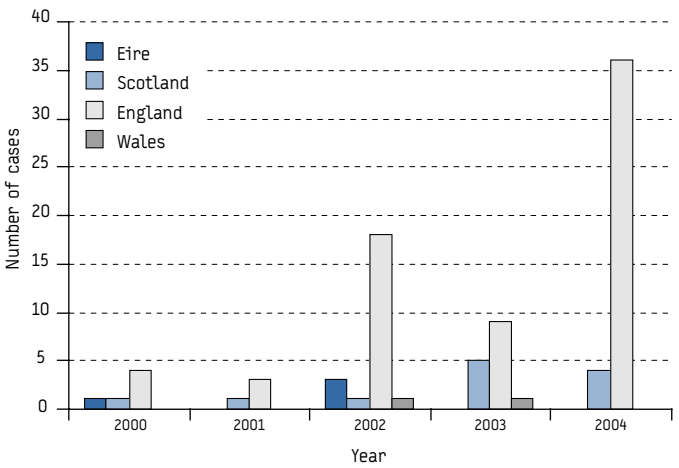
Results

Yearly totals of reports of wound botulism by country in the UK and Republic of Ireland are shown in Figure 1. No cases were recognised before 2000 and a total of 88 cases were reported between 2000 and 2004. Seventy cases were in England, 12 in Scotland, 2 in Wales and the remaining 4 in the Republic of Ireland. No cases were reported from Northern Ireland. All cases occurred in IDUs. The ages were known for 75 of the 88 cases, and the mean age was 34 years (range 22 to 48). Sixty one of the cases were in men and 27 in women: in 2004, where information on gender was provided, 27 were in men and 13 were in women. Details of clinical presentation, outcomes and drug use will be presented elsewhere as data collection is ongoing.

Overall, 40 (45%) of the 88 cases were laboratory confirmed by the detection of botulinum neurotoxin in serum (33 cases), or by the isolation of *C. botulinum* from wounds (25 cases). Neurotoxin was detected in serum together with the isolation of *C. botulinum* from wounds in 18 of the cases. Neurotoxin only was detected in the serum of 15 of the cases, and *C. botulinum* only was isolated from wounds in the remaining seven cases. Based on the neurotoxin detected and/or the *C. botulinum* isolated from the 40 laboratory confirmed cases, 35 were due to type A, three to type B and two to types A and B.

FIGURE 1

Cases of wound botulism in injecting drug users in the UK and Republic of Ireland, 2000-2004



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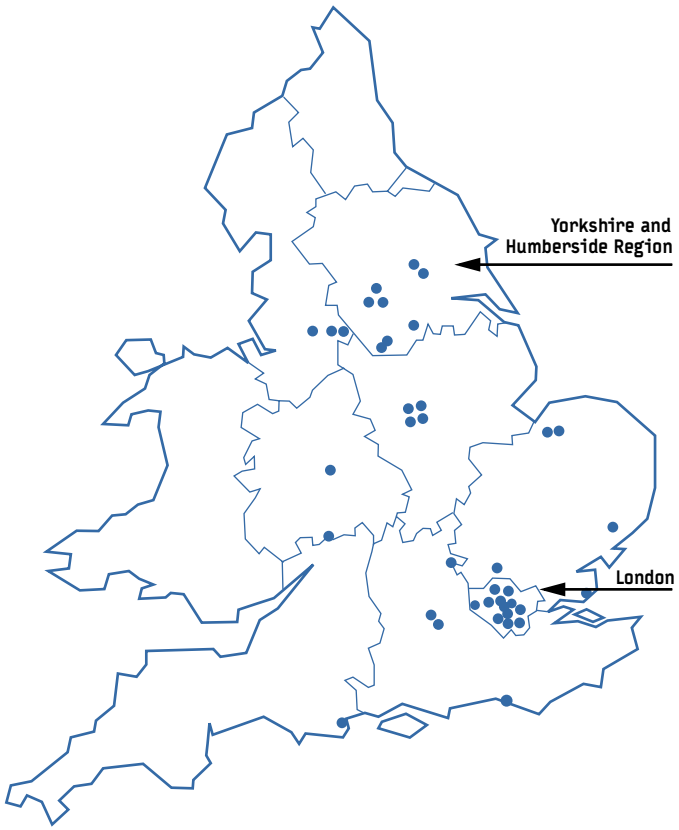
During 2004, 36 of the 40 cases reported were in England. Twelve of the patients in England were laboratory confirmed, and 10 of these cases were due to type A, one to types A and B, and one to type B. There was some geographical clustering. with cases concentrated in two regions: Yorkshire and Humberside, and London [Figure 2].

Figure 2

Distribution of wound botulism cases in 2004 by region in England



Discussion

The recognition of wound botulism in injectors of heroin in the UK coincided with increased recognition of soft tissue infections due to other species of endospore forming bacteria [2,5,6,7]. It is not clear if the emergence of these diseases represents the presentation of new diseases in the UK, or is due to ascertainment bias because of diagnosis of diseases not previously recognised. However, the recognition of cases of food and infant botulism together with surveillance systems to capture reports of cases clearly existed in the UK before the detection of the first cases in IDUs in 2000. This suggests that, at least for botulism, these soft tissue infections represent an emerging hazard for this patient group. There was increased recognition of wound botulism in IDUs in California in the mid-1990s [13]. The emergence of wound botulism in IDUs in the United States and the UK may have resulted in part from better recognition of cases and increased medical surveillance of this group, bit this is unlikely to be the only explanation for the increase in reported cases. The outbreaks may also have been due to contamination events of specific batches of heroin, or they may reflect changes in drug composition or purity. The availability of 'black tar' heroin in the United States (which differs to that generally used in the UK) was identified as a contributing factor for the Californian outbreak [13]. No explanation could be found for the clustering of the wound botulism cases in 2004. However, this clustering together with an absence of cases in other areas believed to have high prevalence of IDUs (such as Glasgow and the north west of England) supports the hypothesis that there was a causal relationship between the patients. Clustering of cases had not previously occurred in the north east of England.

A small number of wound botulism cases in IDUs has been reported in several other European countries. The first cases were reported in Norway in 1997 [14], followed by at least three further cases [15,16]. Between September 1998 and February 1999, nine cases of wound botulism in IDUs were identified in Switzerland [17-22], and one in Holland [23]. The authors have been unable to locate additional case reports amongst IDUs from other European countries.

Since a major risk factor for all of these soft tissue wound infections is 'skin-' or 'muscle-popping' [2,3,5,13], injection practices in IDUs are likely to be important, and geographic variations in these may explain the absence of a similar increase in cases in other European countries. However, clinicians should suspect botulism in any patient with an afebrile, descending, flaccid paralysis. Botulinum antitoxin is effective in reducing the severity of symptoms for all forms of botulism if administered early in the course of the disease; this should not be delayed until results of microbiological testing are available. In cases of wound botulism, antimicrobial therapy and surgical debridement are important to reduce the organism load and avoid relapse after antitoxin treatment. *C. botulinum* is sensitive to benzyl penicillin and metronidazole. Advice for responding to suspect wound botulism is available on the HPA website [24]. As well as providing information for health professionals, the HPA website gives advice for preventative measures to IDUs including the following:

- Smoke rather than inject heroin;
- If IDUs must inject, inject intravenously and not intramuscularly or subcutaneously;
- Do not share needles, syringes, cookers, or spoons for injection;
- Use as little citric acid as possible;
- If injecting more than one type of drug, inject in separate places;
- If swelling, redness or pain occurs at injection sites, seek medical advice immediately [24].

At the time of writing (July 2005) a further 20 cases of wound botulism in IDUs had been reported in the UK during 2005.

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References

1. Schoener EP, Hopper JA, Pierre JD. Injection drug use in North America. Infect Dis Clin North Am. 2002;16:535-51.
2. McGiuggan CC, Penrice GM, Gruer L, et al. Lethal outbreak of infection with Clostridium *novyi* type A and other spore forming organisms in Scottish injecting drug users. J Med Microbiol. 2002; 51:971-7.
3. Brett MM, Hallas G, Mpamugo O. Wound botulism in the UK and Ireland. J Med Microbiol. 2004;53:555-61.
4. Hope V, Ncube F, Dennis J, McLauchlin J. Wound botulism: increase in cases in injecting drug users, United Kingdom 2004. Euro Surveill. 2004;9:39-40.
5. Hahne S, Crowcroft N, White J, et *al*. Ongoing outbreak of tetanus in injecting drug users in the UK. Euro Surveill. 2004;9:40-1.
6. Brazier JS, Gal M, Hall V, Morris TE. Outbreak of *Clostridium histolyticum* infections amongst drug users in England and Scotland. Euro Surveill. 2004;9:15-6.
7. Dancer SJ, McNair D, Finn P, Kolsto AB. Bacillus cereus cellulitis from contaminated heroin. J Med Microbiol. 2002; 51:278-81.
8. Arnon SS, Schechter R, Inglesby TV, et *al*. Botulinum toxin as a biological weapon: medical and public health management. JAMA. 2001;285:1059-70.
9. Anon. Case definitions for infectious conditions under public health surveillance. Morb Mortal Wkly Rep. 1997;46 RR10: 1-55.
10. Anon. Botulism in the United States, 1899-1996. Handbook for Epidemiologists, Clinicians and Laboratory Workers, Centres for Disease Control and Prevention Atlanta, GA. 1998.
11. Solomon, HM, Lilly T. *Clostridium botulinum*. FDA Bacteriological Analytical Manual Online, 8th Edition, Revision A, January 2001. Chapter 17, available at: http://www.cfsan.fda.gov/~ebam/bam-17.html#authors. December 2004.
12. Akbulut D, Grant KA, McLauchlin J. Development and application of Real-Time PCR assays to detect fragments of the Clostridium botulinum types A, B, and E neurotoxin genes for investigation of human foodborne and infant botulism. Foodborne Pathog Dis. 2004;1:247-57.

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13. Werner SB, Passaro D, McGee J, Schechter R, Vugia DJ. Wound botulism in California, 1951-1998: recent epidemic in heroin injectors. Clin Infect Dis. 2000;31:1018-24.

14. Holmaas G, Gilhus NE, Gjerde IO, Lund-Tonnessen S, Langorgen J. Wound botulism in heroin addiction. Tidsskr Nor Laegeforen. 1998;118:4357-9.

15. Jensen T, Jacobsen D, von der Lippe E, Heier MS, Selseth B. Clinical wound botulism in injecting drug addicts. Tidsskr Nor Laegeforen. 1998;118:4363-5.

16. Kuusi M, Hasseltvedt V, Aavitsland P. Botulism in Norway. Euro Surveill. 1999 ;4:11-12.

17. Burnens A. Cases of wound botulism in Switzerland. *Eurosurveillance* 2000; 4 http://www.eurosurveillance.org/ew/2000/000203.asp

18. Jermann M, Hiersemenzel LP, Waespe W. Drug-dependent patient with multiple skin abscesses and wound botulism. Schweiz Med Wochenschr 1999;129:1467.

19. Martin C, Schaller MD, Lepori M, Liaudet L. Cranial nerve palsies and descending paralysis in a drug abuser resulting from wound botulism. Intensive Care Med. 1999;25:765.

20. Hiersemenzel LP, Jermann M, Waespe W. Descending paralysis caused by wound botulism. A case report. Nervenarzt. 2000;71:130-3.

21. Sautter T, Herzog A, Hauri D, Schurch B. Transient paralysis of the bladder due to wound botulism. Eur Urol. 2001;39:610-2.

22. Scheibe F, Hug B, Rossi M. Wound botulism after drug injection. Dtsch Med Wochenschr. 2002;127:199-202.Scheibe F. Wundbotulismus Nach Drogeninjektion. Deutsche Medizinische Wochenschrift. 2002;127;199-202.

23. Rundervoort RS, van der Ven AJ, Vermeulen C, van Oostenbrugge RJ. The clinical diagnosis 'wound botulism' in an injecting drug addict. Ned Tijdschr Geneeskd. 2003 ;147:124-7.

24. Botulism, Health Protection Agency. Available at, http://www.hpa.org.uk/infections/topics_az/botulism/menu.htm. August 2004.

ORIGINAL ARTICLES

Euroroundup

PNEUMOCOCCAL VACCINATION POLICY IN EUROPE

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Infection due to *Streptococcus pneumoniae* (Pneumococcus) (Pnc) is an important cause of invasive clinical manifestations such as meningitis, septicaemia and pneumonia, particularly in young children and the elderly. A 23-valent polysaccharide Pnc vaccine (PPV) has been available for many years and a 7-valent conjugate Pnc vaccine (PCV) has been licensed since 2001 in Europe. As part of a European Union (EU) funded project on pneumococcal disease (Pnc-EURO), a questionnaire was distributed to all 15 EU member states, Switzerland, Norway and the 10 accession countries in 2003 to ascertain current pneumococcal vaccination policy. Twenty three of the 27 target countries, constituting the current European Union (plus Norway and Switzerland), completed the questionnaire.

PPV was licensed in 22 of the 23 responding countries and was in the official recommendations of 21. In all the 20/21 countries for which information was available, risk groups at higher risk of infection were targeted. The number of risk groups targeted ranged from one to 12. At least 17 countries recommend that PPV be administered to all those >65 years of age (in three countries, to those over 60 years of age).

Thirteen countries had developed national recommendations for PCV in 2003. No country recommended mass infant immunisation at that time, but rather targeted specific risk groups (between 1 and 11), particularly children with asplenia (n=13) and HIV infection (n=12). PCV use was restricted to children under two years of age in seven countries, and in four countries to children under five years of age.

Future decisions on use of pneumococcal vaccines in Europe will be decided on the basis of several factors including: local disease burden; the predicted impact of any universal programme, particularly the importance of serotype replacement and herd immunity (indirect protection to the unvaccinated population); the effectiveness of reduced dose schedules, and vaccine cost. Indeed, at least one country, Luxembourg, has since implemented a universal infant PCV immunisation policy.

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Introduction

Pneumococcal (Pnc) disease is caused by the bacterium *Streptococcus pneumoniae* of which more than 90 serotypes are now recognised. Pnc is an important cause of morbidity and mortality in Europe [1] – with the observed burden varying geographically, due in part to differences in healthcare factors such as blood culture practice and antibiotic use [2]. With large reductions in the incidence of *Haemophilus influenzae* type b in many European countries, Pnc is now one of the leading causes of meningitis and invasive bacterial disease in children; Pnc is also one of the main aetiological agents for community-acquired pneumonia in adults and for otitis media in children [1]. Furthermore, in recent years antibiotic resistant strains of Pnc have emerged as an increasing problem, with rates of penicillin resistance ranging up to almost 50% of invasive isolates in some European countries [1].

Two types of pneumococcal vaccine are now licensed in Europe, and include a variable number of capsular serotypes: the older 23-valent Pnc polysaccharide vaccine (PPV) and the newer conjugated 7-valent Pnc vaccine (PCV). PPV provides protection against invasive Pnc disease due to 23 serotypes in subjects older than two years [3]. PCV protects against seven serotypes but also in those younger than two years and provides longer lasting immunity against invasive disease. Conjugate vaccine also protects against non-invasive Pnc disease manifestations such as pneumonia [4]. Post-licensure surveillance following introduction of PCV in the United States in 1999 as a universal infant immunisation programme has shown a large reduction in both invasive and non-invasive disease incidence due to vaccine serotypes in both vaccinated and older unvaccinated populations ('herd immunity'). This reduction in disease has also been accompanied by a fall in the rate of penicillin-resistant Pnc [5]. However, a small increase in invasive disease due to non-vaccine serotypes (termed 'serotype replacement') has also been observed [6].

Historically, individuals at higher risk of Pnc infection such as those with immune system impairment, and more recently, the elderly, have been targeted with PPV in Europe. The licensure of the new 7-valent Pnc conjugate vaccine in Europe by the European Medicine Evaluation Agency (EMEA) in 2001 has re-ignited interest in pneumococcal disease and the most appropriate vaccination strategy in a European setting. A number of factors have contributed to this decision making, including the potentially preventable disease burden and the cost and effectiveness of alternative intervention programmes. For European countries to be able to design the most appropriate

future vaccination strategies, it will be important to understand local pneumococcal disease burden in the context of current and past vaccination strategy. This paper summarises the results of a survey of national Pnc vaccine policy undertaken at the end of 2003 across the European Union (EU) and the accession countries that constitute the current EU. This was undertaken within the framework of the EU funded project Pneumococcal Disease in Europe (Pnc-EURO).

Methods

A standardised questionnaire was designed and sent to the national public health institutes of each of the current 25 European Union member states and Switzerland and Norway in late 2003, 10 of them in the accession phase. Data from returned questionnaires were entered and analysed in Excel.

Results

Twenty three of the 27 countries completed and returned the questionnaire. Non-responders were Greece, Hungary, Poland and Spain.

Use of pneumococcal polysaccharide vaccine

A 23-valent PPV vaccine has been licensed in 22 of the 23 responding countries (not in Malta) from the 1980s onwards [TABLE 1], with vaccine from two manufacturers: Sanofi-Pasteur MSD and Wyeth-Lederle. With the exception of Portugal, the remaining countries have developed national recommendations for PPV.

All countries with national recommendations for PPV have implemented strategies to target groups at higher risk of invasive pneumococcal disease [TABLE 1].

The recommended vaccination schedule is generally a single dose, although at least four countries recommend a booster dose after three to six years, at least for certain groups, such as those whose antibody levels decline rapidly.

Country specific risk-group recommendations are outlined in Table 2. The number of risk groups (those individuals at higher risk of invasive disease due to their underlying condition) ranged from one to 12 (median nine groups, n=20) [TABLE 1]. Almost all countries recommended vaccination of individuals with splenic dysfunction (n=19), immunosuppression (n=17), chronic pulmonary disease (CPD)(n=18), chronic cardiac disease (CCF)(n=16) and chronic liver disease (n=15). Seventeen countries recommended that the polysaccharide vaccine be administered to all those >65 years of age: three of these countries made this recommendation for all those over 60 years of age.

TABLE 1

Reported use of 23-valent pneumococcal polysaccharide vaccine in 23 European countries, 2003

	Vaccine licensed	National recommendation for risk groups	Year of introduction	Booster dose recommended	>65 year olds	Number of risk groups [1]	Cost free or refunded
Austria (AUS)	Yes	Yes	2003	na	Yes	9	Yes[5]
Belgium (BEL)	Yes	Yes	1993	na	Yes[6]	11	No[2]
Czech Republic (CZE)	Yes	Yes	-	na	Yes	6	Yes
Cyprus (CYR)	Yes	Yes	na	na	Yes	11	Yes[5]
Denmark (DEN)	Yes	Yes	1980	na	Yes	9	Yes[5]
England (ENG)	Yes	Yes	1992	No[4]	Yes	8	Yes
Estonia (EST)	Yes	Yes	na	na	Yes	9	No
Finland (FIN)	Yes	Yes	na	After 3-5 yrs[7]	Yes	12	No
France (FRA)	Yes	Yes	na	na	No	5	Yes
Germany (GER)	Yes	Yes	1985	After 6 yrs	Yes[6]	7	Yes
Ireland (IRE)	Yes	Yes	1999	na	Yes	11	Yes
Italy (ITA)	Yes	Yes	1999	na	Yes	-	No
Latvia (LAT)	Yes	Yes	2001	na	Yes	2	Yes[5]
Lithuania (LIT)	Yes	Yes	na	na	Yes	9	No
Luxembourg (LUX)	Yes	Yes	1992	na	Yes[6]	12	No
Malta (MAT)	No	No	-	-	-	-	-
Netherlands (NET)	Yes	Yes	na	na	No	5	Yes
Norway (NOR)	Yes	Yes	na	na	Yes	9	Yes[5]
Portugal (POR)	Yes	No	-	-	-	-	-
Slovak Republic (SLK)	Yes	Yes	1999	After 3-5 yrs	na	na	na
Slovenia (SLO)	Yes	Yes	2003	na	Yes	10	Yes[5]
Sweden (SWE)	Yes	Yes	1994	na	No	10	Yes[3]
Switzerland (SWI)	Yes	Yes	2000	After 5 yrs	Yes	9	Yes[5]

1 Of the following 12 risk groups: splenectomised, cardiovascular disease, chronic pulmonary disease, diabetes mellitus, alcoholism, chronic liver disease, cerebrospinal fluid leaks, immunosuppressed, HIV infected, over 65 years of age, nursing home resident and other

2 Except those with insurance

3 Varies between regions

4 Unless a rapid decline in antibody levels

5 Some risk groups

6 >60 year olds targeted

7 For immunocompromised only

na= not available

TABLE 2

Country-specific recommendations for use of pneumococcal polysaccharide vaccine by risk group in 19 European countries

	AUS	BEL	CZE	CYP	DEN	ENG	EST	FIN	FRA	GER	IRE	LAT	LIT	LUX	NET	NOR	SLO	SWE	SWI
Splenic dysfunction	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes[1]	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Chronic cardiovascular disease	Yes	Yes[2]	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Chronic pulmonary disease	Yes	Yes[2]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Diabetes mellitus	Yes	Yes[2]	No	Yes	Yes	Yes	Yes	Yes	No	Yes	No	No	Yes	Yes	No	No	Yes	Yes	Yes
Alcoholism	Yes	Yes[2]	No	Yes	No	No	No	Yes	Yes	No	Yes	No	na	Yes	No	No	No	Yes	No
Chronic liver disease	Yes	Yes[2]	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes
CSF fluid leak	Yes	No	No	Yes	Yes	No	No	Yes	No	Yes	Yes	No	na	Yes	No	Yes	Yes	Yes	Yes
Immunodeficiency	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
HIV infected	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes
> 65 years of age	Yes[4]	Yes[4]	Yes[3]	Yes	Yes	Yes[5]	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes[4]	No	Yes	Yes	Yes[3]	Yes
In nursing home	No	Yes	Yes	Yes	No	No	Yes	Yes	No	No	No	No	na	Yes	No	Yes	Yes	No	No

1 Children only
2 >45 years old
3 In some regions
4 >60 years old
5 Phased introduction from 2003 onwards
6 Under consideration
na= not available
Information not available for Slovak Republic

A variety of other risk groups were also targeted including individuals with cochlear implants (England), chronic renal disease (Finland, Germany, Luxembourg and Ireland), travellers with certain chronic conditions (Lithuania), those with repeated pneumococcal infections (Norway) and those with Down's syndrome (Sweden).

For those countries where the vaccine was recommended, in most instances (n=14) the vaccine was either free or the cost refunded, at least for some risk groups [TABLE 1]

Use of Pneumococcal conjugate vaccine

Twenty of the 23 responding countries had a pneumococcal conjugate vaccine officially licensed, but not Estonia, Malta, or Slovenia [TABLE 3]. In all cases, this was the 7-valent vaccine manufactured by Wyeth-Lederle (*Prevenar*). No other PCV was commercially available at that time. By 2003, 13 of these 20 countries had developed and implemented national recommendations for use of this vaccine since 2001. For seven countries, mainly in central Europe and Scandinavia, the vaccine is licensed but national recommendations are not yet in place or are being developed (Czech Republic, Denmark, Latvia, Lithuania, Netherlands, Portugal and Sweden). The recommended schedule is enerally three doses one to two months apart from the second or third month of life. At least nine countries recommend a booster dose after the age of one year.

TABLE 3

Reported use of pneumococcal conjugate vaccine in 23 European countries, 2003

	Vaccine licensed	National recom-mendation	Universal strategy	Risk group policy	Year of intro-duction	Primary schedule (age in months)	Booster dose (age in months)	Target groups*	Child <2 years	Cost refunded or free of charge
Austria	Yes	Yes	No	Yes	2003	3, 4, 5	24	9	Yes	Yes[2]
Belgium	Yes	Yes	No	Yes	na	na	na	6	Yes[1]	##
Czech Republic	Yes	No	-	-	-	-	-	-	-	-
Cyprus	Yes	Yes	No	Yes	2003	2, 4, 6	12-15, 24	11		Yes
Denmark	Yes	No	No	Yes	-	3, 5, 7	15	7	Yes	Yes[2]
England	Yes	Yes	No	Yes	2003	2 to 24, 2-3 doses		9	Yes[1]	Yes
Estonia	No	No	-	-	-	-	-	-	-	-
Finland	Yes	Yes	No	Yes	2002	2, 4, 6	24		Yes[1]	No
France	Yes	Yes	No	Yes	2003	2, 3, 4	24	8	Yes	Yes
Germany	Yes	Yes	No	Yes	2002	2, 3, 4	>12	9	Yes	Yes
Ireland	Yes	Yes	No	Yes	2002	12	24	10	Yes	Yes
Italy	Yes	Yes	No	Yes	2002	2 to 24, 2-3 doses		9	Yes	Yes[2]
Latvia	Yes	No	No	Yes	-	na	na	1	na	Yes[2]
Lithuania	Yes	No	No	-	-	-	-	-	-	-
Luxembourg	Yes	Yes	Yes	No	2004	2, 3, 4	12-15	-	-	Yes
Malta	No	No	-	-	-	-	-	-	-	-
Netherlands	Yes	No	-	-	-	-	-	-	-	-

(continued Table 3)

	Vaccine licensed	National recom-mendation	Universal strategy	Risk group policy	Year of intro-duction	Primary schedule (age in months)	Booster dose (age in months)	Target groups*	Child <2 years	Cost refunded or free of charge
Norway	Yes	Yes	No	Yes	2001	na	na	2	na	Yes[2]
Portugal	Yes	No	-	-	-	-	-	-	-	-
Slovak Republic	Yes	Yes	No	Yes	2003	2 to 24, 2-3 doses		0	Yes	No
Slovenia	No	No	-	-	-	-	-	-	-	-
Sweden	Yes	No	-	-	-	-	-	-	-	-
Switzerland	Yes	Yes	No	Yes	2001	2, 3, 4	12	8	Yes#	Yes

* Of the following 12 risk groups: splenectomised, chronic cardiovascular disease, chronic pulmonary disease, diabetes mellitus, alcoholism, chronic liver disease, cerebrospinal fluid leaks, immunosuppressed, HIV infected, over 65 years of age, nursing home residents and others

1 Under 5 years of age
2 Applies to some risk groups
Not yet determined
na= not available
Information not available for Slovak Republic

At the time of the original questionnaire in 2003, no European country recommended mass infant immunisation. In 2004, at least one country (Luxembourg) recommended PCV for all children under 24 months of age (universal infant immunisation). In all countries with national recommendations, conjugate vaccine was targeted at specific risk groups. In many countries (at least seven), use in target groups is restricted to children less than two years of age, and in four countries to those under five years of age (Belgium, England, Finland and Switzerland). The number of risk groups range from one to 11 (median 8, n=13) [TABLE 3]: the most common are individuals with asplenia (n=13), CCF (n=11), CPD (n=11), diabetes (n=11), immune deficiency (n=11) and HIV infection (n=12). Use in all persons over 65 years of age is recommended in one country, Cyprus.

Other risk groups targeted include those with chronic renal disease (Finland, Ireland, England and Germany) and children with ventilatory tubes inserted (France). In France, young children in families with more than three pre-school children or children attending daycare are also targeted.

In the majority of countries where PCV is recommended (n=12), the vaccine is reported to be free or the cost refunded, at least for some risk groups [TABLE 4].

Discussion

This article provides a summary of pneumococcal vaccine policy in Europe at the end of 2003 and illustrates differences in national pneumococcal policy across Europe ranging from no licensure of any pneumococcal vaccine to the more recent introduction of a universal Pnc conjugate vaccine programme in infancy in 2004 in at least one country. These variations in national vaccination policy have been previously well documented for other vaccine programmes [7].

The Pnc polysaccharide vaccine, PPV, has been widely recommended in some European countries for over two decades for groups perceived to be at higher risk of invasive disease. The evidence base for the true risk of Pnc in these groups may vary from country to country, but has not been systematically collated. We demonstrate that by 2003, the number of risk groups actually targeted ranges dramatically across the countries of the EU. Furthermore, we found that a large number of countries recently implemented programmes for all individuals older than 65 years. There is limited published evidence of the effectiveness of PPV targeted at populations at higher risk of invasive infection [3,8], whereas a 'universal' elderly PPV programme has been shown to be both effective [9] and cost-effective [10] against

TABLE 4

Country-specific recommendations for use of pneumococcal conjugate vaccine by risk-group in 14 European countries

	AUS	BEL	CYP	DEN	ENG	FIN	FRA	GER	IRE	ITA	LAT	NOR	SLK	SWI
Splenic dysfunction	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
Chronic cardiovascular disease	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	No	Yes
Chronic pulmonary disease	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	No	Yes
Diabetes mellitus	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	No	Yes
Alcoholism	No	No	Yes	No	No	No	na	No	No	No	No	No	No	No
Chronic liver disease	Yes	No	Yes	No	Yes	No	na	No	Yes	Yes	No	No	No	Yes
CSF fluid leaks	No	No	Yes	Yes	na	Yes	Yes	Yes	Yes	Yes	No	No	No	Yes
Immunodeficiency	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	No	Yes
HIV infected	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	Yes
>65 Years of age	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No
Nursing home	No	No	Yes	No	No	No	No	No	No	Yes[1]	No	No	No	No
Other groups	Yes	-	-	-	Yes	Yes	Yes[2]	Yes	Yes	-	-	-	-	-
Free of charge	Yes[5]	$	Yes	No	Yes[3]	No	No	Yes	Yes	Yes[3]	Yes[3]	Yes[3]	No	Yes[3]
Refunded	Yes[5]	$	No	Yes[4]	-	Yes[5]	Yes[3]	Yes[5]	Yes	-	No	No	No	Yes[3]

1 Some regions
2 Additional target groups in France are children <2 Years old & breastfed < 2mts, belonging to families with 3 or more pre-school children, being taken care of with others (>2) more than 4 hrs per week
3 All recommended groups
4 Splenectomised persons only
5 In some circumstance e.g. privately insured
$ Decision not yet taken
na= not available

invasive Pnc disease (at least in the United Kingdom). We did not collate information on the uptake of these various programmes, but ad hoc studies have suggested that targeted high-risk programmes often have difficulty achieving high levels of coverage [11], whereas 'universal' programmes such as those targeting all those over 65 years of age may be easier to implement. It will be important to ensure surveillance systems are in place to monitor the coverage, impact and effectiveness of these various PPV programmes in Europe.

Following the recent licensure of the 7-valent PCV in Europe, we found that the majority of countries have now included the new vaccine in their national recommendations. In 2003, PCV was targeted at certain groups of children under two years of age who are at higher risk of invasive infection (under five years in some countries), with the number of recommended risk groups varying dramatically from country to country from very limited to very extensive indications including children attending daycare, such as in France. In this article, we have gathered information only on national recommendations: the coverage and impact of these programmes has not been collated and remain largely unreported. The factors that influence the coverage achieved (and thus the eventual impact) in any one country are manifold. However, it is important to note that in a number of countries, a large proportion of all vaccination may be administered through the private sector, where insurance schemes may (or may not) reimburse cost of vaccination. Clearly, this raises issues of equity and access to healthcare. It will be important to ensure that national surveillance schemes fully capture the programmatic impact of PCV administered through both the public and private sectors.

No country in the European Union had implemented a universal PCV programme at the time of the original questionnaire in 2003. Future decisions on the use of pneumococcal vaccines in Europe, in particular PCV, will be decided on the basis of a number of factors: disease burden and the effectiveness and cost effectiveness of alternative interventions. The Pnc disease burden in European settings is recognised to vary across the continent [2] due both to differences in healthcare factors affecting observed rates of disease (such as use of antibiotics and blood culture [12,13]), and also to real differences in pneumococcal epidemiology (such as Pnc serotype distribution and the prevalence of antibiotic resistance [2,14]). High quality pre-vaccination surveillance data will be critical for informed national decision making for local vaccination policy. Secondly, the impact of the universal PCV programme in North America is increasingly evident, particularly the size of the herd immunity effect with evidence of significant protection for older, unvaccinated populations (together with evidence of serotype replacement – the emergence of non-vaccine serotypes, for instance, as observed in acute otitis media [15]). Finally, the cost-effectiveness of any PCV programme (compared to PPV programme) will be influenced by recent clinical trial evidence of the effectiveness of alternative primary immunisation schedules involving fewer doses of vaccine [16]. Indeed, at least one European country, Luxembourg, introduced a universal infant immunisation programme in 2004, with a three dose primary course and a booster dose in the first year of life.

We have demonstrated a diversity of Pnc vaccination programmes in Europe, and these are rapidly evolving. It will be critical for countries to ensure that high quality surveillance systems are in place to monitor the impact and effectiveness of these programmes and to ensure future interventions, particularly in relation to possible introductions of PCV, are undertaken in an informed fashion based on local Pnc disease epidemiology.

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References

1. Cartwright K. Pneumococcal disease in Western Europe: burden of disease, antibiotic resistance and management. Eur J Pediatr 2002; 161: 188-95.
2. Hausdorff WP, Siber G, Paradiso PR. Geographic differences in invasive pneumococcal disease rates and serotype frequency in young children. Lancet 2001; 357: 950-52.
3. Jackson LA, Neuzi KM, Yu O, Benson P, Barlow WE, Adams AL et al. Effectiveness of pneumococcal polysaccharide vaccine in older adults. N Engl J Med. 2003; 348(18):1747-55.
4. Poehling KA, Lafleur BJ, Szilagyi PG, et al. Population-Based Impact of Pneumococcal Conjugate Vaccine in Young Children. Pediatrics 2004;114(3):755-61.
5. Black S, Shinefield H, Baxter R, Austrian R, Bracken L, Hansen J et al. Post licensure surveillance for pneumococcal invasive disease after use of heptavalent pneumococcal conjugate vaccine in Northern California Kaiser Permanente. Pediatr Infect Dis J 2004; 23: 485-89.
6. Whitney CG, Farley MM, Hadler J, Harrison LH, Bennett NM, Lynfield R et al. Decline in invasive pneumococcal disease after the introduction of protein-polysaccharide conjugate vaccine. N Engl J Med. 2003; 348(18):1737-46.
7. EUVAX report. Scientific and technical evaluation of vaccination programmes in the European Union.
8. Fedson DS, Liss C. Precise answers to the wrong question: prospective clinical trials and the meta-analyses of pneumococcal vaccine in elderly and high-risk adults. Vaccine 2004;22(8):927-46.
9. Melegaro A, Edmunds WJ. The 23-valent pneumococcal polysaccharide vaccine. Part I. Efficacy of PPV in the elderly: a comparison of meta-analyses. Eur J Epidemiol. 2004;19(4):353-63.
10. Melegaro A, Edmunds WJ. The 23-valent pneumococcal polysaccharide vaccine. Part II. A cost-effectiveness analysis for invasive disease in the elderly in England and Wales. Eur J Epidemiol. 2004;19(4):365-75.
11. Wahid ST, Nag S, Bilous R, Marshall S, Robinson A. Audit of influenza and pneumococcal vaccination uptake in diabetic patients attending secondary care in the Northern Region. Diabet Med 2001; 18(7): 599-603.
12. Washington JA. An international multicentre study of blood culture practices. Eur J Clin microbial Infect Dis 1992; 11(12): 1115-1128.
13. Huchon GJ, Gialdroni-Grassi G, Leophonte P, Manresa F, Schaberg T, Woodhead M. Initial antibiotic therapy for lower respiratory infection in the community: a European study. Eur Respir J 1996; 9: 1590-95.
14. Hausdorff WP. Invasive pneumococcal disease in children: geographic and temporal variations in incidence and serotype distribution. Eur J Pediatr. 2002 Dec;161 Suppl 2:S135-9.
15. McEllistream MC, Adams J, Mason EO, Wald ER. Epidemiology of acute otitis media caused by Streptococcus pneumoniae before and after licensure of the 7-valent pneumococcal protein conjugate vaccine. J Infect Dis 2003;188: 1679-84
16. Goldblatt D, Ashton L, Southern J, Burbidge P, Burrage M, Morris R et al. Immunogenicity and boosting following a reduced number of doses of a Pneumococcal conjugate vaccine in infants and toddlers. ISPPD 4, Helsinki, May 2004.

THE EPIDEMIOLOGY OF SEVERE *STREPTOCOCCUS PYOGENES* ASSOCIATED DISEASE IN EUROPE

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Several European countries reported outbreaks of severe disease caused by *Streptococcus pyogenes* in the late 1980s. This marked a departure from the previous decades, where very few such outbreaks were noted. These changes in disease occurrence formed part of a global phenomenon, the reasons for which have yet to be explained. Results of surveillance activities for invasive *S. pyogenes* infection within Europe over the past fifteen years identified further increases in many countries. However, variations in surveillance methods between countries preclude robust comparisons being made, illustrating the need for a unified surveillance strategy across Europe. This was finally embodied in the Strep-EURO programme, introduced in 2002.

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Background

Invasive infections due to the Lancefield group A *Streptococcus* (iGAS), *Streptococcus pyogenes*, have attracted increasing levels of attention since the late 1980s. Reports from the United States (US), Norway, Sweden and Denmark in the mid- to late 1980s warned of a possible re-emergence of severe clinical manifestations of *S. pyogenes*, and non-suppurative sequelae such as rheumatic fever [1-4]. M1 serotype, and to a lesser extent M3, were implicated in these rises [3-6], serotypes which have since become synonymous with outbreaks and fatal outcome.

During the early 1980s, reports emerged from the then Czechoslovakia and the US describing a hitherto unrecognised complication of *S. pyogenes* infection, termed the 'streptococcal toxic shock-like syndrome' [7-10]. A review of these reports by a working group from the Centers for Disease Control and Prevention led to the establishment of a case definition for streptococcal toxic shock-like syndrome (STSS) [11]. The diverse spectrum of invasive diseases recognised as being caused by *S. pyogenes* included puerperal sepsis, necrotising fasciitis, septic arthritis, pneumonia, STSS and bacteraemia (without primary focus).

One of the most defining events for iGAS surveillance activity occurred in 1994 when a cluster of necrotising fasciitis cases was detected in the South West of England (Gloucestershire) [12]. This event acted as an important catalyst for a host of activity within and outside the United Kingdom (UK). Enhanced surveillance for iGAS was immediately implemented in the UK, with several European and other countries following suit. This response resulted in a small number of countries obtaining for the first time measures of disease-specific incidence, risk factors and outcome.

The impetus generated during the mid-1990s led to the establishment of an ad hoc World Health Organization (WHO) working group on *S. pyogenes*, comprised of representatives from streptococcal reference centres in the Czech Republic, Italy, New Zealand, UK, US and Canada. The main recommendation of the WHO consultations that followed was to support member countries in initiating comprehensive public health programmes for the control of GAS infections. The key priorities that emerged from the 1998 consultation included the urgent need to develop a mechanism to strengthen microbiological capacity and provide sustained support to an international network of laboratories, the need to evaluate the tools available for surveillance, and the need to include streptococcal infections in national public health priorities [13]. However, no definitive network across Europe was formed, and collaborations between European countries were undertaken on a largely informal basis, if at all. A formal European network was not established until 2002 [14].

Advances in microbiological characterisation of *S. pyogenes*

The application of molecular techniques within the last decade has contributed significantly to our understanding of the epidemiology and pathogenesis of *S. pyogenes* disease. The development and application of a wide range of methods for *S. pyogenes* characterisation led to a new era in typing and have also highlighted the importance of establishing standardised methods and agreed criteria for the interpretation and verification of types. External quality assurance (EQA) among international centres has therefore become recognised as essential for accurate epidemiological and microbiological surveillance of disease.

The *emm* gene which encodes the major virulence factor, the M protein, is used as the basis for the characterisation of GAS within the majority of international typing centres, although conventional serotyping is also used in some centres. A total of 93 validated M-types have been identified to date [15]. Most GAS isolates that are deemed non-typable by serological methods can be genotyped through *emm* sequence determination. The extensive N-terminal variability of *emm* genes forms the basis for the distinction of more than 170 designated *emm*-types described to date[16]. Marked changes in the distribution of M-types circulating in Europe were noted from the late 1980s onwards [17,18]. Observations of both severe and non-severe GAS manifestations suggest cyclical patterns of dominance between certain serotypes [18-20].

Molecular methodologies have allowed us to examine iGAS pathogenesis from a new perspective. *S. pyogenes* has a repertoire of pathogenic mechanisms that assure its success as a colonising and invading organism. Molecular technologies have also provided us with more subtle tools to help identify, distinguish and ultimately understand both the bacterial and the host mechanisms mediating pathogenesis.

Surveillance of iGAS disease in Europe

In the absence of an iGAS surveillance network, or informally agreed protocol, different countries within Europe have been undertaking surveillance of iGAS disease according to their own criteria. However, common methodological approaches emerged, allowing some degree of comparability of results.

Very few countries within Europe list iGAS disease manifestations among their notifiable diseases. In Norway cases of iGAS have been notifiable since 1975, and all severe GAS (i.e., including isolates from

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non-sterile sites, when accompanied by severe clinical presentation) since 1995 [21]. Finland similarly made iGAS disease notifiable in 1995. Ireland added iGAS infections in their recent review of infectious disease notifications, effected in 2004 [22]. With the exception of these countries, surveillance activities are therefore predominantly reliant on voluntary reporting systems. The Table summarises national or multi-site surveillance activity results identified from WHO European Region countries. Most operate through the capture of routine local microbiological diagnoses into a central data bank [TABLE]. The quality of data available through such systems is variable, both in terms of the breadth of information collected and completeness of reporting. Many such systems do not routinely capture clinical information, which is a particular shortfall for iGAS infection given the plethora of associated conditions.

TABLE

Invasive group A streptococcal infection surveillance in Europe, 1990 onwards

Country	Surveillance methods				Latest estimates		References
	Surveillance period*	Coverage	Surveillance method/s	Clinical information available	Incidence per 100 000 (year)	Macrolide resistance (year)	
Belgium	1994-	National	Microbiology laboratory reports	No	1.0 (2003)	na	[34;67]
	1994-	National	Isolates submitted to reference laboratory	No	na	8.9% (1997)	
Czech Republic	1994-98	National	Isolates submitted to reference laboratory	Yes	0.40 (1994-96)	na	[56]
Denmark	1969-	National	Isolates submitted to reference laboratory	Yes	3.30 (1998)	1.8% (2003)	[32;68]
Finland	1988-96	National	Isolates submitted to reference laboratory	No	na	4.5% (1996)†	[27;69]
	1995-	National	Microbiology laboratory notifications + isolates submitted to reference laboratory	No	2.27 (2003)†	na	
France	1998-	National	Isolates submitted to reference laboratory (invasive & non invasive GAS)	Yes	na	23% (2002)†	[40] [33;70;71]
	1987-	National	Microbiology laboratory reports	No	1.7 (2002)†	na	
Hungary	1975-	National	Microbiology laboratory reports (invasive & non invasive GAS)	No	1.3 (2002)†	na	[72]
Iceland	1975-	National	Microbiology laboratory reports	No	3.8 (1996-02)	na	[36]
Israel	1980-	Regional	Clinical & microbiology laboratory reports	Yes	4.8 (1990-94)	2.2% (1987-94)	[61]
Italy	1993-	National	Microbiology laboratory reports (invasive & non invasive GAS)	Yes	0.06 (1994-96)	32% (1994-96)	[39]
Netherlands	1992-03	National	Isolates submitted to reference laboratory	Yes	3.1 (2002)	na	[17]
Norway	1975-	National	Notification through laboratory	Yes	3.3 (2002)	na	[30]
Portugal	1998-99	Sentinel sites	Isolates submitted to reference laboratory	No	na	11% (1998-99)	[42]
Russia	2000-01	Sentinel sites	Isolates submitted to reference laboratory (invasive & non invasive GAS)	Yes	na	11% (2000-01)	[41]
Sweden	1989-	National	Microbiology laboratory reports + isolates submitted to reference laboratory	Yes	2.9 (2000)	na	[28;29;55]
United Kingdom	1975-	England, Wales, Northern Ireland	Microbiology laboratory reports	No	3.5 (2003)†	4% (2003)	[24;25;73] [54]
	1988-	Scotland	Microbiology laboratory reports	No	3.6 (2002)†	na	
	1980-	National	Isolates submitted to reference laboratory	Yes	na	5% (1994-97)	

* The dash indicates still ongoing

† Blood ± CSF only

na= not available/applicable

As many countries within Europe have a recognised national reference centre for microbiological identification and typing of streptococci, surveillance activities have commonly used isolate submission for surveillance purposes. This provides information on microbiological characteristics of strains circulating within these countries, such as serotype (based on T and M proteins), sequence typing of the *emm* gene (*emm*ST) and antibiotic susceptibility. A potential drawback can be referral bias, depending on which criteria are applied in choosing isolates or inviting isolate submission. Isolates that are sent primarily for 'epidemiological purposes', usually referring to the determination of strain relatedness for outbreak control purposes, will be unlikely to represent the primarily sporadic bulk of iGAS cases. Referral on the basis of atypical microbiological characteristics or clinical features would also present a biased group of isolates. However, some countries attempt to circumvent these problems of biased sampling by requesting submission of all iGAS isolates. Many countries in Europe are using isolate referral-based and laboratory report-based surveillance systems in parallel.

Regardless of the methods used to obtain cases for surveillance purposes, routine sources of information have been periodically supplemented through invoking a period of enhanced surveillance, primarily to gain additional patient, clinical, microbiological and outcome measures. In accordance with the aim of Strep-EURO, eleven countries are now undertaking enhanced surveillance (see Forming a European network - Strep-EURO). Belgium also began enhanced surveillance in 2004 following an observed sudden increase in iGAS cases detected through their laboratory surveillance system [23].

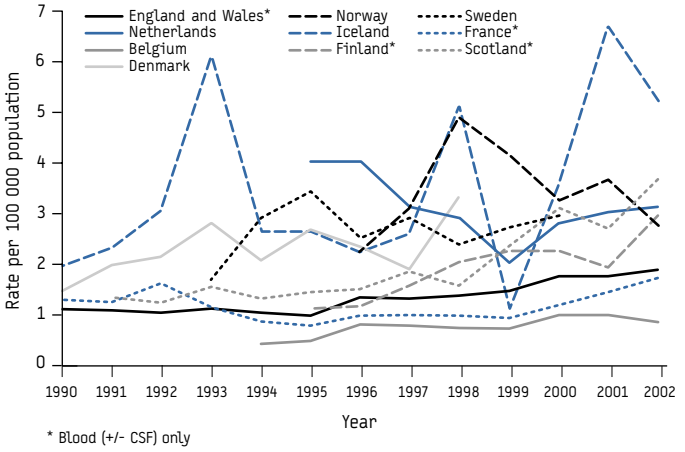
Trends in iGAS disease in Europe in the 1990s

Some interesting parallels emerge when comparing results from surveillance activities across Europe over the last decade. Surveillance data from countries who have published five or more consecutive

years' results are shown in Figure 1. Results from these primarily Northern European countries show some interesting and not entirely uniform trends, although most left the 1990s with higher rates of iGAS reports than they entered the decade. Data from the Netherlands in particular contrast with those from other countries, with rates of iGAS halving between 1995 (4.0 per 100 000) and 1999 (2.0/100 000), although an upturn was subsequently observed [17]. Most of the other countries examined showed reasonably consistent results suggestive of an overall increase in incidence during the 1990s and into the 2000s, although trend patterns varied markedly from near linear to marked peaks and troughs. Data from Scotland are among the most compelling, showing marked year-on-year rises from the mid-1990s onwards when rates of GAS bacteraemia rose from 1.49/100 000 in 1996 to 3.66/100 000 in 2002, averaging at a 41% increase per year [24;25]. A more diluted rise in reports was also seen in England and Wales throughout the 1990s[26]. Data from Finland also showed a similar pattern, rising sharply from 1996 (1.17) to 2002 (2.95) [27]. Surveillance data from neighbouring Sweden (1993-1997) showed a less clear cut pattern, rising sharply between 1993 and 1996 before dropping back again to a more stable annual rate between 2.3 - 2.9/100 000 [28,29]. Following the initial reports of a marked rise in severe clinical manifestations of GAS infection in the mid-1980s [2], rates in Norway showed an initial fall only to re-escalate around 1993 [21]. More recent web-published data indicate further sharp rises in rates of iGAS in Norway between 1996 and 1999 when rates of reports more than doubled to reach 4.9/100 000 [30]. Even more pronounced changes are apparent in Iceland, the smallest of the countries examined, where rates of iGAS have swung from lows of around 1-2 per 100 000 to peaks above 6/100 000, the highest rates observed in any European country over this period. Published data from Denmark showed further increases in the early 1990s to those identified towards the end of the previous decade [3,31], with the latest estimate from 1998 standing at 3.3/100 000 [32].

FIGURE 1

Country-specific annual rates of invasive group A streptococcal infection, 1990-2002



* Blood (+/- CSF) only

Surveillance data from France from the early 1990s were suggestive of a downward trend in iGAS infections, although recent reports indicate a rise between 1999 and 2002 [33]. Annual reporting rates in Belgium show marked rises between 1994 and 2000[34], from less than 0.5 iGAS cases per 100 000 in the mid-1990s to approaching 1/100 000 in early 2000s. The subsequent downturn after 2000 may have been short-lived: recent indications suggested a resurgence in early 2004, triggering the initiation of enhanced surveillance activities [23].

It is interesting to note the pattern of the changes in rates of iGAS reports within countries. Whereas countries such as Norway, Sweden, Iceland and the Netherlands showed quite marked up- and downswings in their rates of disease, other countries such as the UK and France have not seen such marked changes. It may be that any potential outbreaks of GAS disease are masked in national data given the larger size of these countries. Regional analyses and further microbiological characterisation of isolates would need to be undertaken to confirm if this is the case. Regardless of the patterns of iGAS disease, there is general suggestion of increasing iGAS across Europe over the past two decades. The reasons behind this change remain unclear and warrant further investigation.

In comparing estimates of the overall burden of iGAS disease between countries, it is important to take into account the different case definitions used for surveillance purposes. Whereas routinely available data from the UK, Finland and France are based on blood culture isolates only (+/- CSF), most other countries monitor all sterile site isolates. The majority of iGAS disease result in bacteraemia, however, non-disseminated invasive infections have been found to account for around 10% of cases [9,35,36], although estimates as high as 24% have been documented [37]. This would in part account for the differences in rates shown in Figure 1, with countries including all sterile sites reporting generally higher rates than others. Some countries, such as Norway, also monitor cases where the clinical presentation indicates a severe infection but without a sterile site isolate being obtained, increasing case numbers by around a quarter if included [21]. Surveillance in Belgium is somewhat unusual in including deep ear sites within its routine case definition, adding approximately two thirds more cases, although data for sterile site isolates are also available separately, as reproduced in this paper [34]. Also of note are differences in coverage within each country. Although typically all laboratories are invited to report cases or submit isolates, in many countries such as Belgium and Hungary, coverage is known to be less than complete. In the UK, coverage is very good, although under-reporting by active laboratories is also known to occur [38]. With these factors borne in mind, there is a degree of congruence between countries over this period, with rates of GAS bacteraemia between 1.7 and 2.95/100 000 in the early 2000s, and rates of iGAS (all sterile sites) between 2.7 and 3.6/100 000. Exceptions to this are the recent peaks seen in Iceland (over 5/100 000) and earlier estimates from Italy and the Czech Republic (mid-1990s), both of which measured incidence of less than 0.5 per 100 000, considerably lower than contemporaneous estimates from other countries. To what extent these lower estimates reflect true differences in incidence or other influencing factors, such as differences in common clinical practice in microbiological sampling, is unclear.

Antimicrobial resistance of iGAS isolates in Europe

Unlike other streptococci, *S. pyogenes* has to date remained universally susceptible to the first line treatment of choice, penicillin. Given the development of penicillin-resistance in other members of the genus, continued monitoring of penicillin susceptibility of *S. pyogenes* remains essential. Aside from beta-lactams, monitoring of GAS isolate susceptibility to other classes of antibiotics is also important. Latest estimates of macrolide resistance in iGAS from across Europe are given in the Table. Substantial variations in prevalence of macrolide resistance are apparent, with no clear geographical association. Results from enhanced surveillance in Italy identified 32% of iGAS isolates as exhibiting resistance to macrolides, the highest among European countries during this period [39]. France has reported a steady escalation of erythromycin resistance since the mid-1990s, reaching 23% of iGAS isolates in 2002 [40]. Analysis of small collections of invasive strains from Russia and Portugal identified 11% as resistant to macrolides [41,42]. It is conceivable that some bias in the choice of isolates reported or referred may have influenced these results, although they may equally reflect the true level of macrolide resistance among strains circulating in those countries. A further possibility is that treatment with antibiotics prior to microbiological sampling is selecting for the more resistant strains. Results from other countries during the 1990s fall between 1% and 7% macrolide resistance in iGAS.

Prevention and control of iGAS disease

The overwhelming majority of iGAS cases arise in the community, 4%-13% of infections being acquired in hospital [5,37,43]. Of community-acquired cases, the vast majority are thought to arise sporadically [43,44], limiting opportunities for implementation of control measures. Although many clusters linked in time and place have been reported, many involve strains belonging to different M-types and/or cases with no apparent epidemiological link [12,45,46]. Where household clusters occur, their presentation can often be almost simultaneous, limiting the potential for effective intervention [47,48]. Attempts have been made in the US and Canada to quantify the risk of secondary or 'subsequent' cases, a third party often being the source of infection [43,44]. No European country has yet to publish any full guidance on the management of iGAS in the community, although France and the UK have begun this process [49].

Of the cases that arise in hospitals, clusters are not uncommon [50,51]. Cases of puerperal fever still occur, occasionally resulting in the death of otherwise healthy young women [21,29,52]. Reviews of maternal death both in the UK and the Netherlands identified increases in maternal sepsis involving *S. pyogenes* over the past decade [52,53].

Few countries within Europe undertake continuous surveillance in sufficient depth to be able to monitor trends according to specific risk factors or modes of acquisition. Enhanced surveillance data obtained during the 1990s in European countries confirmed the following as risk factors for iGAS disease: alcoholism, malignancy, diabetes, skin lesions, recent childbirth, steroid use and chickenpox [5,54,55]. However, in a substantial proportion of cases there is no evidence of any particular risk or predisposing factors, between 17-31% [3,56,57]. Risk factor information accompanying isolates referred to the national reference laboratory in the UK has yielded some startling trends in iGAS associated with injecting drug use (IDU). Of the isolates referred to the reference laboratory between 1995 and 2002, the proportion emanating from IDUs has risen dramatically from <5% to 15% [58]. Early results from the Strep-EURO programme in the UK have substantiated the importance of IDUs as a risk group for iGAS disease [35]. Analysis of *S. pyogenes* strains circulating in Switzerland between 1993 and 1997 identified the spread of distinct clones among IDUs [59], further supported by the results of a case-control study which identified a common place of drug purchase as strongly associated with iGAS disease [60].

Some countries in Europe have reported higher incidence of iGAS disease in particular ethnic groups. A study from southern Israel found a significantly higher risk of iGAS disease in its Bedouin population compared to the Jewish population [61]. Without adjustment for key variables that could explain these differences, it remains unclear to what extent this is attributable to genetic factors, frequency of underlying illnesses or living arrangements. Interestingly, a study from north London found higher rates of pharyngeal carriage of GAS in orthodox Jewish children and adults attending primary care services than other attendees, regardless of sore throat symptoms [62].

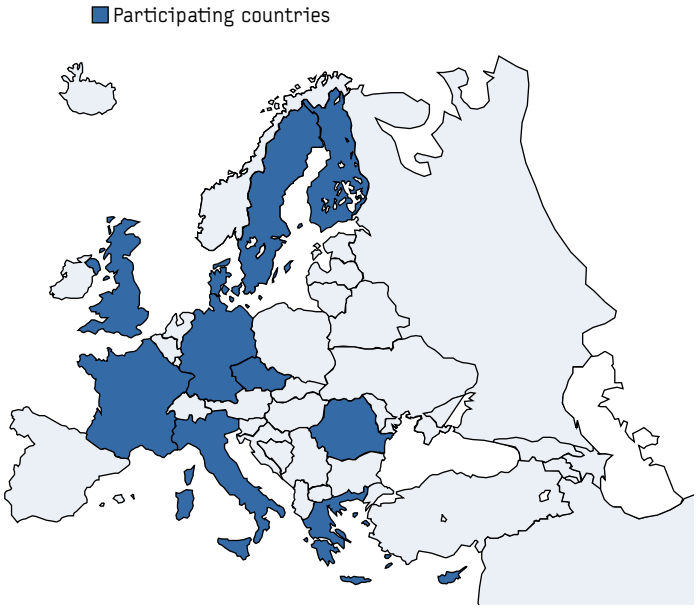
That iGAS disease occurs more commonly in late winter-early spring is a fairly ubiquitous finding across Europe [2,3,17]. Similar patterns are seen for scarlet fever and streptococcal pharyngitis [63,64]. The degree to which these seasonal patterns in GAS disease manifestations reflect climate-induced vulnerability to respiratory pathogens, or a sequel to viral respiratory infections remains unclear.

Forming a European network - Strep-EURO

In light of recent reports suggesting global changes in the epidemiology of severe clinical manifestations of GAS infection, and given the disparate and disconnected surveillance activities across Europe, leading microbiologists from across Europe have formed a unified network to take forward a programme of work relating to iGAS. Funded by the Fifth Framework Programme of the European Commission's Directorate-General for Research, the Strep-EURO network was launched in September 2002 (www.strep-euro.lu.se). Eleven countries are participating in Strep-EURO [FIGURE 2], with overall coordination coming from the University of Lund in Sweden. The programme of work is divided into seven work packages. Central to these work packages is the collection of enhanced surveillance data, which each country undertook for a period of two years (1 January 2003 – 31 December 2004) using a standardised questionnaire for the capture of patient, clinical, risk factor and outcome data. Cases were defined through isolation of *S. pyogenes* from a site that is normally sterile or from a non-sterile site where accompanied by clinical symptoms indicative of STSS[11].

FIGURE 2

Countries participating in the Strep-EURO severe *Streptococcus pyogenes* disease network



Each country undertook to capture information on all cases arising within their country, or within a geographical area with a definable catchment population. Some countries, such as the UK and Finland, maximised case ascertainment through linkage of microbiological reports and isolates referred to the national reference centre [65]. Isolates were sought from each case and sent to a central laboratory, usually the national reference laboratory. These strains will be subject to the same microbiological characterisation, primarily M serotyping and/or *emm* sequence typing (*emm*ST). Detection of toxin and antibiotic resistance genes will also be performed on a subset of strains. A selection of strains will be characterised further by multilocus sequence typing (MLST) and pulsed-field gel electrophoresis (PFGE).

Three external quality assessment studies are included within the remit of the Strep-EURO programme, for serological and molecular (*emm*) typing, PFGE subtyping and antimicrobial susceptibility determination using phenotypic and genotypic methods.

Collection of these data should allow some meaningful and robust comparisons of cases arising in each country, in particular clinical manifestations, risk factors and strain characteristics. Results are also being pooled into a single Strep-EURO database held in Helsinki. Amalgamation of these diverse clinical, epidemiological and microbiological data promises to provide a powerful tool for examining the interrelation between these factors. Given the number of different M-types, and the diverse range of clinical manifestations associated with invasive GAS disease, pooling of data is essential to gain statistical power for the identification of significant associations, for example between virulence markers and pathogenicity or mortality.

It is hoped that results from Strep-EURO will substantially improve our understanding of the epidemiology of iGAS disease in Europe. This should in turn yield findings of public health value. Identification and quantification of clusters of iGAS will help direct prevention guidance, with early results already showing success in using Strep-EURO data for such purposes [49,66]. Efforts to enhance or initiate a system for the capture of iGAS cases are also proving successful in many countries. Evaluation of serotype distribution could be of benefit in the evaluation of the possible impact of polyvalent vaccines.

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References

1. Veasy LG, Wiedmeier SE, Orsmond GS, Ruttenberg HD, Boucek MM, Roth SJ et al. Resurgence of acute rheumatic fever in the intermountain area of the United States. N Engl J Med. 1987; 316(8):421-427.
2. Martin PR, Høiby EA. Streptococcal serogroup A epidemic in Norway 1987-1988. Scand J Infect Dis. 1990; 22(4):421-429.
3. Andersen MM, Rønne T. Group A streptococcal bacteraemias in Denmark 1987-89. J Infect. 1995; 31(1):33-37.
4. Strömberg A, Romanus V, Burman LG. Outbreak of group A streptococcal bacteremia in Sweden: an epidemiologic and clinical study. J Infect Dis. 1991; 164(3):595-598.
5. Bucher A, Martin PR, Høiby EA, Halstensen A, Ødegaard A, Hellum KB et al. Spectrum of disease in bacteraemic patients during a *Streptococcus pyogenes* serotype M-1 epidemic in Norway in 1988. Eur J Clin Microbiol Infect Dis. 1992; 11(5):416-426.
6. Schwartz B, Facklam R, Breiman RF, GAS Study Group. The changing epidemiology of group A streptococcal infections in the United States: association with serotype. Int J Med Microbiol. 1992; 277-8(Supp 22):17-19.
7. Hribalova V. *Streptococcus pyogenes* and the toxic shock syndrome. Ann Intern Med. 1988; 108(5):772.
8. Cone LA, Woodard DR, Schlievert PM, Tomory GS. Clinical and bacteriologic observations of a toxic shock-like syndrome due to *Streptococcus pyogenes*. N Engl J Med. 1987; 317(3):146-149.
9. Hoge CW, Schwartz B, Talkington DF, Breiman RF, MacNeill EM, Englender SJ. The changing epidemiology of invasive group A streptococcal infections and the emergence of streptococcal toxic shock-like syndrome. A retrospective population-based study. JAMA. 1993; 269(3):384-389.
10. Fanta J, Drabkova J, Rehak F, Smat V, Votocek K, Frankova K. Primary peritonitis imitating the toxic shock syndrome (TSS). Prakt Lek (Prague). 1984; 64:674-676.
11. Defining the group A streptococcal toxic shock syndrome. Rationale and consensus definition. The Working Group on Severe Streptococcal Infections. JAMA. 1993; 269(3):390-391.
12. Cartwright K, Logan M, McNulty C, Harrison S, George R, Efstratiou A et al. A cluster of cases of streptococcal necrotizing fasciitis in Gloucestershire. Epidemiol Infect. 1995; 115(3):387-397.
13. The WHO Programme on Streptococcal Diseases Complex. Report of a consultation, Geneva, 16-19 February 1998. EMC/BAC/98.7. 1998. Geneva, World Health Organization.
14. Schalén C. European surveillance of severe group A streptococcal disease. Eurosurveillance weekly. 2002; 6(35): 25/8/2004 (http://www.eurosurveillance.org/ew/2002/020829.asp)
15. Facklam R, Beall B, Efstratiou A, Fischetti V, Johnson D, Kaplan E et al. *emm* typing and validation of provisional M types for group A streptococci. Emerg Infect Dis. 1999; 5(2):247-253.
16. Beall B. *Streptococcus pyogenes emm* sequence database. CDC. 2004: 10/11/2004 (http://www.cdc.gov/ncidod/biotech/strep/emmtypes.htm)
17. Vlaminckx BJ, van Pelt W, Schouls LM, van Silfhout A, Mascini EM, Elzenaar CP et al. Long-term surveillance of invasive group A streptococcal disease in The Netherlands, 1994-2003. Clin Microbiol Infect. 2005; 11(3):226-231.
18. Colman G, Tanna A, Gaworzewska ET. Changes in the distribution of serotypes of *Streptococcus pyogenes*. Int J Med Microbiol. 1992; 277-8(Supp 22):14-16.
19. Kaplan EL, Wotton JT, Johnson DR. Dynamic epidemiology of group A streptococcal serotypes associated with pharyngitis. Lancet. 2001; 358(9290):1334-1337.
20. Siljander T, Toropainen M, Muotiala A, Hoe NP, Musser JM, Vuopio-Varkila J. *emm*-typing of invasive T28 group A streptococci, 1995-2004, Finland. 15th European Congress of Clinical Microbiology and Infectious Diseases; Apr. 2005; Copenhagen. Clin Microbiol Infect. 11(Suppl 2):567.
21. Hasseltvedt V, Høiby EA. Severe invasive group A streptococcal disease, Norway, 2000. Eurosurveillance weekly. 2001; 5(44).
22. Health Protection Surveillance Centre. Weekly infectious disease report: week 39 2004. National Disease Surveillance Centre. 2004: 12/11/2004 (http://www.ndsc.ie/IDStatistics/WeeklyIDReport/)
23. Hanquet G, IPH, ID Team. Severe disease due to group A streptococcus infections in Belgium: an update. Infect Dis Spotlight. 2004: 12/11/2004 (http://www.iph.fgov.be/epidemio/epien/plaben/idnews/index_en.htm)
24. Scottish Centre for Infection & Environmental Health. Outbreaks of group A streptococcal infection. SCIEH. Weekly Rep 2001; 35(2001/22):144-148.
25. Scottish Centre for Infection & Environmental Health. Bacteraemias reported to SCIEH in 2001 and 2002. SCIEH. 2003: 21/10/2004 (http://www.show.scot.nhs.uk/scieh/)
26. HPA. Pyogenic streptococcal bacteraemia laboratory reports: England and Wales, 1992 – 2003. HPA. 2004: 1/11/2004 (http://www.hpa.org.uk/infections/topics_az/strepto/pyogenic/data_pyogenic_labrep.htm)
27. KTL. National infectious diseases register. KTL. 2004: 26/10/2004 (http://www3.ktl.fi/stat/)
28. Carrique-Mas J, Nygård K, Romanus V. Increased cases of invasive Group A streptococcal infections in Sweden. Eurosurveillance weekly. 2001; 5(21).
29. Eriksson BK, Norgren M, McGregor K, Spratt BG, Normark BH. Group A streptococcal infections in Sweden: a comparative study of invasive and noninvasive infections and analysis of dominant T28 emm28 isolates. Clin Infect Dis. 2003; 37(9):1189-1193.
30. Folkehelseinstituttet. Streptokokkinfeksjon, gruppe A. *MSIS* 2003: 26/10/2004 (http://www.fhi.no/artikler/?id=28695)
31. Henrichsen J, Konradsen HB. Invasive infections caused by *Streptococcus pyogenes* in Denmark 1990-1994. Adv Exp Med Biol. 1997; 418:201-205.
32. Johansen KE, Konradsen HB. Group A streptococcal T-protein in Invasive and Non-invasive Isolates in Denmark 1987-98. In: Martin DR, Tag.J.R., editors. Streptococci and streptococcal diseases; entering the new millenium. Proceedings of the XIV Lancefield International Symposium on Severe Streptococcal Diseases.; 1999 Oct 11-15; Auckland, New Zealand. Porirua: Securacopy; 2000. p 823-825.
33. Georges S, Perrocheau A, Laurent E, Lévy-Bruhl D, les bactériologistes du réseau Epibac. [Invasive infections from *H. influenzae, L. monocytogenes, N. meningitidis, S. pneumoniae, S. agalactiae* and *S. pyogenes* in France in 2001-2002]. Bull Epidemiol Hebdo. 2004; 34: 29/10/2004 (http://www.invs.sante.fr/beh/2004/34/BEH_34_2004.pdf)
34. Ducoffre G. Rapport annuel sur la surveillance des maladies infectieuses par un réseau de laboratoires vigies, 2002 + Tendances Epidémiologiques 1983-2001. Institut Scientifique de Santé Publique, Section d'Epidémiologie; 2004.
35. Lamagni TL, Neal S, Alhaddad N, Efstratiou A. Results from the first six months of enhanced surveillance of severe *Streptococcus pyogenes* disease in England and Wales. 14th European Congress of Clinical Microbiology and Infectious Diseases; May 2004; Prague. Clin Microbiol Infect. 10(Suppl 3):34.
36. Erlendsdottir M, Gottfredsson K, Kristinsson KG. Epidemiology of invasive group A streptococcal infections in Iceland during a 28 year period, 1975-2002. Abstracts of the forty-fourth Interscience Conference on Antimicrobial Agents and Chemotherapy.; 2004 Oct 30-Nov 2; Washington DC, USA. Washington DC: American Society for Microbiology; 2004. p 381.
37. Efstratiou A, George RC, Gaworzewska ET, Hallas G, Tanna A, Blake WA et al. Group A streptococcal invasive disease in England and Wales. Adv Exp Med Biol. 1997; 418:207-210.
38. HPA. *Staphylococcus aureus* bacteraemia: England, Wales, and Northern Ireland: January to December 2003. Commun Dis Rep CDR Wkly [serial online]. 2004; 14(16):Bacteraemia.
39. Suligoi B, von Hunolstein C, Orefici G, Scopetti F, Pataracchia M, Greco D. Surveillance of systemic invasive disease caused by group A *Streptococcus* in Italy 1994-1996. Euro Surveill. 1998; 3(2):11-14.
40. Bouvet A, Aubry-Damon H, Péan Y. [Emergence of the resistance to macrolides of Streptococcus pyogenes]. Bull Epidemiol Hebdo. 2004; 32: 29/10/2004 (http://www.invs.sante.fr/beh/2004/32_33/beh_32_33_2004.pdf)
41. Kozlov RS, Bogdanovitch TM, Appelbaum PC, Ednie L, Stratchounski LS, Jacobs MR et al. Antistreptococcal activity of telithromycin compared with

→→→

seven other drugs in relation to macrolide resistance mechanisms in Russia. Antimicrob Agents Chemother. 2002; 46(9):2963-2968.

42. Melo-Cristino J, Fernandes ML. *Streptococcus pyogenes* isolated in Portugal: macrolide resistance phenotypes and correlation with T types. Portuguese Surveillance Group for the Study of Respiratory Pathogens. Microb Drug Resist. 1999; 5(3):219-225.
43. Robinson KA, Rothrock G, Phan Q, Sayler B, Stefonek K, Van Beneden C et al. Risk for severe group A streptococcal disease among patients' household contacts. Emerg Infect Dis. 2003; 9(4):443-447.
44. Davies HD, McGeer A, Schwartz B, Green K, Cann D, Simor AE et al. Invasive group A streptococcal infections in Ontario, Canada. Ontario Group A Streptococcal Study Group. N Engl J Med. 1996; 335(8):547-554.
45. Barnham M, Weightman N, Chapman S, Efstratiou A, George RC, Stanley J. Two clusters of invasive *Streptococcus pyogenes* infection in England. Adv Exp Med Biol. 1997; 418:67-69.
46. El Bouri KW, Lewis AM, Okeahialam CA, Wright D, Tanna A, Joynson DH. A community outbreak of invasive and non-invasive group A beta-haemolytic streptococcal disease in a town in South Wales. Epidemiol Infect. 1998; 121(3):515-521.
47. Smolyakov R, Riesenberg K, Schlaeffer F, Borer A, Gilad J, Peled N et al. Streptococcal septic arthritis and necrotizing fasciitis in an intravenous drug user couple sharing needles. Isr Med Assoc J. 2002; 4(4):302-303.
48. Oliver I, Smith A, Lamagni TL, Efstratiou A, George R, Morgan M et al. UK guidance for close community contacts of invasive group A streptococcal infection. Health Protection Agency Annual Conference. 2004; Sept. 2004; Warwick.
49. Health Protection Agency Group A Streptococcus Working Group. Interim UK guidelines for management of close community contacts of invasive group A streptococcal disease. Commun Dis Public Health. 2004; 7(4):354-361.
50. Raymond J, Schlegel L, Garnier F, Bouvet A. Molecular characterization of *Streptococcus pyogenes* isolates to investigate an outbreak of puerperal sepsis. Infect Control Hosp Epidemiol. 2005; 26(5):455-461.
51. Detcheva AD, Savoia D, Bianco S, Beall B, Facklam R, Djigosheva E et al. Three epidemiologically related cases of invasive infection caused by *Streptococcus pyogenes emm65*. 3rd Balkan Conference of Microbiology; Sept. 2003; Istanbul.
52. National Institute for Clinical Excellence, Scottish Executive Health Department, Department of Health SSaPSNI. Why mothers die 1997-1999. The confidential enquiry into maternal deaths in the United Kingdom. 2001. London, RCOG Press.
53. Schuitemaker N, van Roosmalen J, Dekker G, van Dongen P, van Geijn H, Gravenhorst JB. Increased maternal mortality in The Netherlands from group A streptococcal infections. Eur J Obstet Gynecol Reprod Biol. 1998; 76(1):61-64.
54. George RC, Efstratiou A, Monnickendam MA, McEvoy MB, Hallas G, Johnson AP et al. Invasive group A streptococcal infections in England and Wales. Abstracts of the thirty-ninth Interscience Conference on Antimicrobial Agents and Chemotherapy.; 1999 Sep 26-29; San Francisco, USA. Washington DC: American Society for Microbiology;1999. p 658.
55. Svensson N, Öberg S, Henriques B, Holm S, Kallenius G, Romanus V et al. Invasive group A streptococcal infections in Sweden in 1994 and 1995: epidemiology and clinical spectrum. Scand J Infect Dis. 2000; 32(6):609-614.
56. Kriz P, Motlova J. Analysis of active surveillance and passive notification of streptococcal diseases in the Czech Republic. Adv Exp Med Biol. 1997; 418:217-219.
57. O'Brien KL, Beall B, Barrett NL, Cieslak PR, Reingold A, Farley MM et al. Epidemiology of invasive group a streptococcus disease in the United States, 1995-1999. Clin Infect Dis. 2002; 35(3):268-276.
58. Efstratiou A, Emery M, Lamagni TL, Tanna A, Warner M, George RC. Increasing incidence of group A streptococcal infections amongst injecting drug users in England and Wales. J Med Microbiol. 2003; 52(Pt 6):525-526.
59. Lechot P, Schaad HJ, Graf S, Tauber M, Muhlemann K. Group A streptococcus clones causing repeated epidemics and endemic disease in intravenous drug users. *Scand* J Infect Dis. 2001; 33(1):41-46.
60. Bohlen LM, Muhlemann K, Dubuis O, Aebi C, Tauber MG. Outbreak among drug users caused by a clonal strain of group A streptococcus. Emerg Infect Dis. 2000; 6(2):175-179.
61. Chiobotaru P, Yagupsky P, Fraser D, Dagan R. Changing epidemiology of invasive *Streptococcus pyogenes* infections in southern Israel: differences between two ethnic population groups. Pediatr Infect Dis J. 1997; 16(2):195-199.
62. Spitzer J, Hennessy E, Neville L. High group A streptococcal carriage in the Orthodox Jewish community of north Hackney. Br J Gen Pract. 2001; 51(463):101-105.
63. Briko NI, Filatov NN, Zhuravlev MV, Lytkina IN, Ezhlova EB, Brazhnikov AI et al. [Epidemiological pattern of scarlet fever in recent years]. Zh Mikrobiol Epidemiol Immunobiol. 2003;(5):67-72.
64. Gubbay L, Ellis A, Lopez HG, Galanternik L. Streptococcal pharyngitis in Argentina. A four-year study. Adv Exp Med Biol. 1997; 418:49-52.
65. HPA. First year of the enhanced surveillance of invasive group A streptococcal infections. Commun Dis Rep CDR Wkly [serial online]. 2004; 14(16).
66. Smith A, Lamagni TL, Oliver I, Efstratiou A, George RC, Stuart J. Invasive group A streptococcal disease: should close contacts routinely receive antibiotic prophylaxis? Lancet Infect Dis. 2005;5(8):494-500.
67. Descheemaeker P, Chapelle S, Lammens C, Hauchecorne M, Wijdooghe M, Vandamme P et al. Macrolide resistance and erythromycin resistance determinants among Belgian *Streptococcus pyogenes* and *Streptococcus pneumoniae* isolates. J Antimicrob Chemother. 2000; 45(2):167-173.
68. Statens Serum Institut, Danish Veterinary and Food Administration, Danish Medicines Agency, Danish Institute for Food and Veterinary Research. DANMAP 2003 – Use of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from food animals, foods and humans in Denmark. 2004. Denmark, Statens Serum Institut.
69. Seppälä H, Klaukka T, Vuopio-Varkila J, Muotiala A, Helenius H, Lager K et al. The effect of changes in the consumption of macrolide antibiotics on erythromycin resistance in group A streptococci in Finland. Finnish Study Group for Antimicrobial Resistance. N Engl J Med. 1997; 337(7):441-446.
70. Mehl-Auget I, Vaillant V, Goulet V. Invasive streptococcal disease (group A, B, and *Streptococcus pneumoniae*) in France 1987-1994. Adv Exp Med Biol. 1997; 418:75-78.
71. Perrocheau A, de Benoist, A.C., Laurent E, Goulet V, Lévy-Bruhl D. Infections invasives a *Haemophilus influenzae, L. monocytogenes, N. meningitidis, S. pneumoniae, S. agalactiae* et *S. pyogenes* en France en 2000. Epidemiologie des maladies infectieuse en France. Situation en 2000 et tendences récentes. 2004. p 281-286.
72. National Center for Epidemiology. The 2002 yearly report of the "Johan Béla" National Center for Epidemiology, Budapest, Hungary. 2002.
73. HPA. Pyogenic and non-pyogenic streptococcal bacteraemias, England, Wales, and Northern Ireland: 2003. Commun Dis Rep CDR Wkly [serial online]. 2004; 14(16):Bacteraemia.

Original Articles

Outbreak report

Real or media-mediated outbreak of coxsackie infections in 2002 in Greece ?

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The purpose of this study was to provide evidence about the existence of a coxsackie B outbreak in Greece in 2002 by comparing data of laboratory confirmed coxsackie B recent infections in northern Greece between 1998-2001 with data from 2002, supposedly an epidemic year.

The infections were confirmed serologically, using the indirect immunofluorescence method detecting IgM antibodies for coxsackie B1-B6 viruses. Sera from 2701 patients residents of northern Greece who were suspected to be suffering from coxsackie B virus infections were examined: 2056 between 1998 and 2001, and 645 in 2002.

The comparison between the results of laboratory confirmed cases and data available at the laboratory between the two periods showed that:
- The total number of patients examined per year was higher in 2002 (645 versus an annual average of 514 in 1998-2001).
- The proportion of laboratory confirmed recent infections was lower in 2002 (27.8% versus 32.7%) and the estimated incidence was 0.66/10 000 for 2002 and 0.32-0.84/10 000 for 1998-2001.
- The age distribution differed: the proportions of cases in children versus cases in adults were reversed in 2002 compared with 1998-2001, with a higher proportion among children in 2002. The difference between the two periods was statistically significant. Children aged 3-5 years were the age group most affected in 2002.
- Seasonal distribution remained the same for both periods (peaks in spring and autumn). In 2002, three fatal cases occurred in April, but no deaths were reported in 1998-2001.
- The clinical syndromes involved also differed: cases of respiratory infections, mainly pneumonia, rose from 5.75% to 24.3% in children in 2002 and cases of myopericarditis rose in adults from 13% in 1998-2001 to 29.5% in 2002.
The last finding, combined with the involvement of the media (because of the three fatal cases) and the panic in the general public that followed suggested that an outbreak had occurred, but we conclude that there was no outbreak.

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Key words : Coxsackie, Greece, outbreak, media

Introduction

In early April 2002, several cases of acute respiratory infections with myocarditis and pericarditis were initially reported from Crete, followed by two deaths in women aged 45 and 48 years. More cases were later reported from Ioannina in northwest Greece followed by one death in a 32 year old woman. Postmortem examination showed that all three deaths were attributable to myocarditis. Several other reports of non-fatal cases of myopericarditis following respiratory infections were then reported to the Hellenic Center for Infectious Disease Control (HCIDC) from all over Greece. The media coverage of these cases exaggerated the severity of the situation, and the government decided to close all schools throughout Greece three days before the start of the scheduled Easter holidays.

Reports of the cases and laboratory findings at the time have already been published [1,2] and suggest that coxsackie B viruses were the causative agents.

This study aims to find evidence for the existence of an outbreak and, if this is found, to assess the extent of the outbreak.

Materials and methods

To compare data from our laboratory for coxsackie B infections diagnosed between 1998-2001 and in 2002, sera from 2701 patients admitted to hospital for suspected coxsackie B infections between 1998-2002 were examined. The sera were sent directly to the laboratory from hospitals in northern Greece between 1998-2002.

Although there is no established network for reporting coxsackie B infections in Greece, the clinical virology unit of our university microbiology laboratory performed serological tests to confirm these infections for all hospitals in northern Greece since 1998, because enteroviral infections are not included in the routine diagnostic panel of hospital laboratories in northern Greece.

A case of recent coxsackie B infection was defined as any person with clinical symptoms compatible with coxsackie B infection and detectable IgM antibodies during the entire period under study.

The method used was indirect immunofluorescence for the detection of IgM antibodies to coxsackie B1-B6 viruses (Bios GmbH Labordiagnostik).

The sera were divided into two groups. Group I consisted of 2056 sera from patients for the period 1998-2001, a mean of 514 patients per year, and group II consisted of 645 patients for the year 2002. The features compared were:
a. The total annual number of sera examined
b. The proportion of confirmed recent infections
c. The age distribution of confirmed cases
d. The seasonal distribution of confirmed cases
e. The clinical syndromes involved

Statistical analysis was performed using the SPSS software (version 11.5). Descriptive statistics and the 2 test were used to estimate different frequencies and the incidence of confirmed infections per year, and to compare the two groups for all the years studied (1998-2002).

Results

The total number of sera examined was 2056 for group I and 645 for group II. Three hundred and twelve samples were examined in 1998, 534 in 1999, 644 in 2000 and 566 in 2001, a mean of 514 per year for group I [TABLE 1].

TABLE 1

Examined samples and recent infections during 1998-2002, Greece

Year	Examined samples	Recent infections	Incidence (per 10^5)
1998	312	86 (27.6%)	3.2
1999	534	226 (42.3%)	8.4
2000	644	212 (32.9%)	7.8
2001	566	147 (26.0%)	5.4
Average per year	**514**	**168 (32.7%)**	**6.3**
2002	645	179 (27.8%)	6.6

For group I, 32.7% of all samples were confirmed to be recent coxsackie B infections (mean annual number of 168 cases). For group II, this proportion was 27.8% (179 cases) [TABLE 2]. The exact rates of confirmed cases for the years 1998, 1999, 2000 and 2001 were 27.6%, 42.3%, 32.9% and 26%, respectively. The population of northern Greece for the period studied was 2 684 663, and so the estimated incidence of confirmed coxsackie B infections for each of the years 1998-2002 was 3.2, 8.4, 7.8, 5.4 and 6.6 per 100 000 inhabitants, respectively [TABLE 1].

TABLE 2

Sera examination from patients suspected as suffering from Coxsackie B infections during 1998-2002, Greece

Patients	No. of examined samples		No. (%) of recent infections	
	1998-2001*	2002	1998-2001*	2002
Children	225	417	57 (11.1%)	145 (22.5%)
Adults	289	228	111 (21.5%)	34 (5.3%)
Total	**514**	**645**	**168 (32.7%)**	**179 (27.8%)**

*Average per year

In the period 1998-2001, 33.9% of all confirmed cases were diagnosed in children (57/168), compared with 81% in 2002 (145/179). A total of 66.7% (111/168) of all confirmed cases were diagnosed in adults, compared with 19% (34/179) in 2002. Thus, the proportions of cases in children versus adults were reversed in 2002 compared with 1998-2001.

The age distribution of recent coxsackie B infections for both groups is shown in Figure 1. A statistically significant rise is found ($p < 0.001$) for group II in children aged 3-5 years old, while there is a considerable decrease (p 0.017) of recent infections in children aged 6-10 years for group II. As for adults, over the age group most affected was >60 years, while morbidity decreased in the 41-60 year group in 2002.

FIGURE 1

Age distribution of Coxsackie B infections in 1998-2001 and 2002, Greece

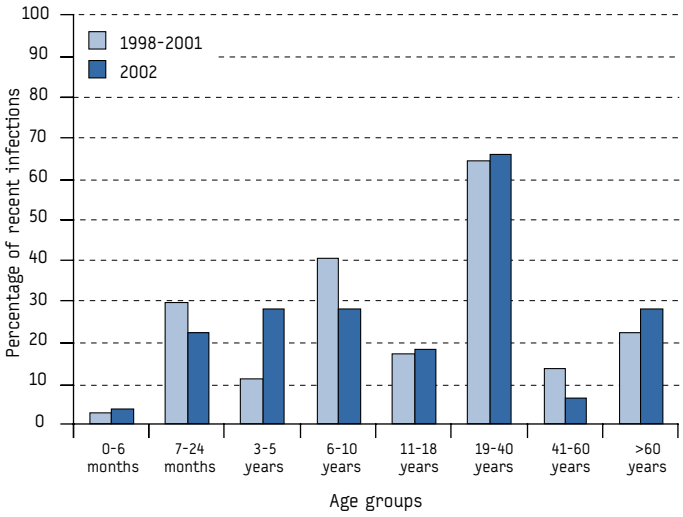


Figure 2 presents the seasonal distribution of these infections for both groups. No difference was found between the two groups. Coxsackie B infections seem to peak in spring and autumn.

FIGURE 2

Comparative seasonal distribution of recent Coxsackie B infections in 1998-2001 and in 2002, Greece

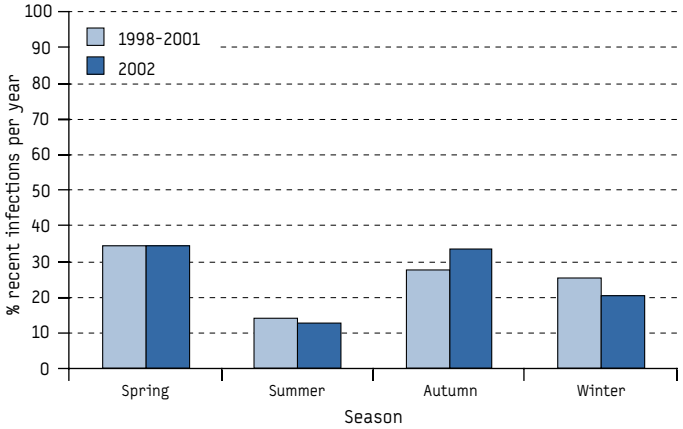
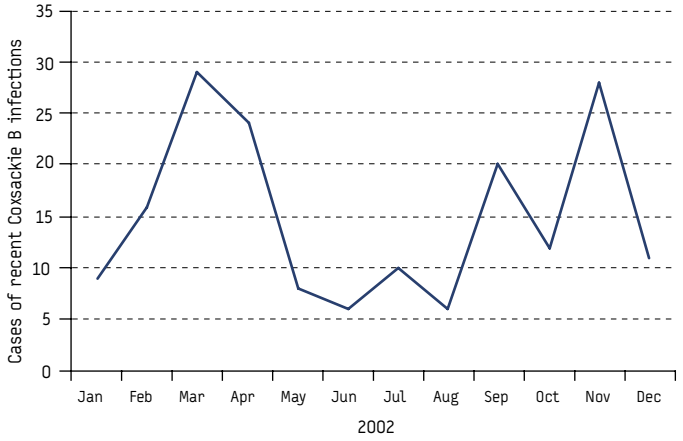


Figure 3 shows the epidemic curve of all confirmed coxsackie B infections in 2002. Two peaks were observed: one in March-April (53 cases) and one in November (28 cases).

FIGURE 3

Monthly distribution of Coxsackie B infections in 2002, Greece



A correlation between recent coxsackie B infections and clinical syndromes appears in Figure 4 for children and in Figure 5 for adults. It seems that the proportions of fever and rash (p 0.002), meningitis (p 0.005) and gastrointestinal infections (p 0.001) decreased in group II while the proportion of respiratory infections increased considerably (p 0.002) for the same group. As for adults, the only remarkable change between the two groups is the considerable increase of the proportion of myopericarditis cases in 2002 (p 0.029).

FIGURE 4

Correlation between Coxsackie B infection and clinical syndromes in children, 1998-2001 and 2002, Greece

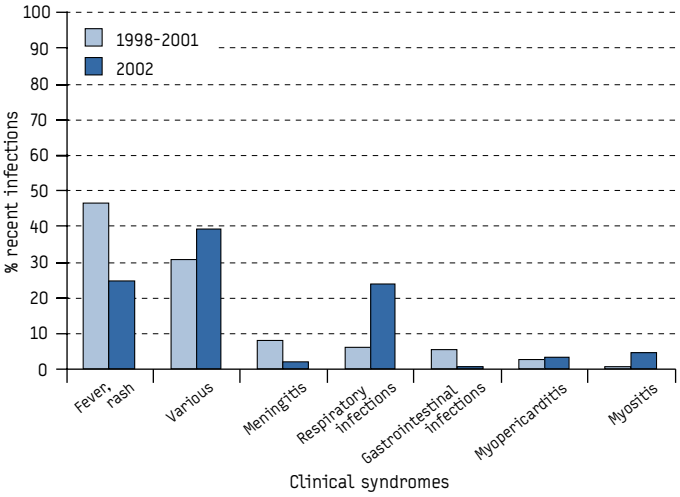
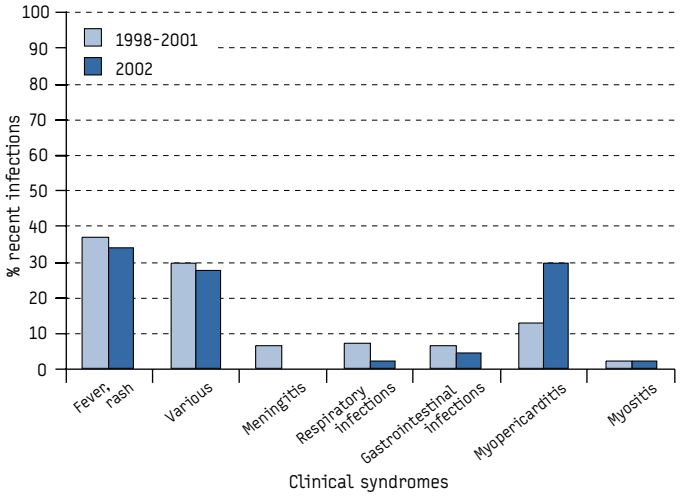


FIGURE 5

Correlation between Coxsackie B infection and clinical syndromes in adults, 1998-2001 and 2002, Greece



Discussion and conclusions

The coxsackie B viruses, members of the Picornaviridae family, are known as causative agents of infections occurring in humans with different clinical features, such as rash, fever, epidemic myalgia, aseptic meningitis, myositis, myocarditis, pericarditis, dilated cardiomyopathy, respiratory and gastrointestinal infections [3].

Despite the fact that coxsackie viruses are endemic in many countries, outbreaks do occur [4-6].

Comparison of data available in this laboratory with the results of the tests which were performed seems to show that the total number of suspected cases did not increase dramatically in 2002, despite the alertness of the clinicians (645 cases in 2002 compared with an annual mean of 514 between 1998 and 2001). In fact, the proportion of laboratory confirmed cases decreased in 2002 (27.8% compared

32.7%), which is understandable if one considers the pressure felt by clinicians to ask for laboratory confirmation even for cases that they normally would not have tested.

Children were predominantly affected in 2002. More cases were identified in children (145 cases compared with a mean annual number of 57 cases from 1998-2001) and fewer cases in adults (34 compared with a mean annual number of 111 for the period 1998-2001). A smaller proportion of examined sera from adults tested positive in 2002 (5.3%) than in 1998-2001 (21.5%).

There was a statistically significant movement of the morbidity to younger children (3-5 years old) followed by reduced morbidity in the next age group (6-10 years old) in 2002.

Throughout the 1998-2002 period, seasonal distribution showed more cases in spring and in autumn, although in other countries enteroviruses circulate more frequently in summer [7]. No difference in the proportion of confirmed cases between the two groups studied was found. In 2002, there were peaks (March-April and November), and the three fatal cases occurred in April.

The comparison of clinical syndromes in cases of coxsackie B infections in both periods showed that respiratory infections, mainly pneumonia cases, predominated among children in 2002, while in adults the only remarkable change was a higher proportion of cases with myopericarditis although absolute numbers of myopericarditis cases were actually lower than in the period 1998-2001. Such cases do occur from time to time [8,9]. No fatal cases were reported in the years 1998-2001.

Therefore, the impression of a severe outbreak of coxsackie B infections in Greece in 2002 seems to have been the result of the combination of three different factors:

1. The increased proportion of myopericarditis cases, probably due to more cardiotropic strains of the circulating viruses in 2002,
2. The three fatal events which attracted the attention of the media,
3. The panic in the general public following headline news about the fatal cases in the media.

In conclusion, there is no evidence for a large outbreak of coxsackie B infections in Greece in 2002, though there was an increased number of cases in young children with more severe infections.

References

1. Panagiotopoulos T, Tsiodras S, Spala G, Kourbeti I, Triantafyllou E, Michailidi D, Spilioti A, Katsibris K, Baka A, Saroglou G, Lionis Ch, Philalithis A, Pediaditis J, Tselentis Y. Update – cases of acute respiratory infection with myocarditis and pericarditis in Greece. Eurosurveillance Weekly, 3 May 2002; 6(18)
2. Cases of Acute Respiratory Infection with Myocarditis and Pericarditis in Greece, April 2002. Epi-Insight, June 2002; Vol. 3; 6(1)
3. Pallansch A M and Roos P R. Enteroviruses: Polioviruses, Coxsackieviruses, Echoviruses, and Newer Enteroviruses. In: Fields Virology. 4th ed. Lippincott Williams & Wilkins; 2001. Vol. 1, pp. 723-768.
4. Druyts-Voets E, Van Renterghem L, Gerniers S. Coxsackie B virus epidemiology and neonatal infection in Belgium. J Infect. 1993 Nov; 27(3): 311-316.
5. Girin VN, Boiko II, Kirilenko VA, Gabura VV, Plugatyr' VM. An outbreak of Coxsackie B enteroviral infection in children. Lik Sprava. 1994 Feb; (2): 79-81.
6. Alexander JP Jr, Chapman LE, Pallansch MA, Stephenson WT, Torok TJ, Anderson LJ. Coxsackie B infection and aseptic meningitis: a focal outbreak among members of a high school football team. J Infect Dis. 1993 May; 167(5): 1201-1205.
7. Maguire HC, Atkinson P, Sharland M, Bendig J. Enterovirus infections in England and Wales: laboratory surveillance data: 1975 to 1994. Commun Dis Public Health. 1999 Jun; 2(2): 122-125.
8. Schoub BD, Johnson S, McAnerney JM, Dos Santos IL, Klaassen KI. Epidemic Coxsackie B virus infection in Johannesburg, South Africa. J Hyg (Lond). 1985 Oct; 95(2): 447-455.
9. Dechkum N, Pangsawan Y, Jayavasu C, Saguanwongse S. Coxsackie B virus infection and myopericarditis in Thailand, 1987-1989. Southeast Asian J Trop Med Public Health. 1998 Jun; 29(2): 273-276.

ORIGINAL ARTICLES

Outbreak report

OUTBREAK OF TINEA CORPORIS GLADIATORUM, A FUNGAL SKIN INFECTION DUE TO *TRICHOPHYTON TONSURANS*, IN A FRENCH HIGH LEVEL JUDO TEAM

DM Poisson[1], D Rousseau[2], Defo Defo[3], E Estève[3]

An outbreak of 49 cases of tinea corporis gladiatorum due to *Trichophyton tonsurans* infection occurred in a high level judo team of 131 members in Orléans, central France, between October 2004 and April 2005. The team was divided into 5 groups: cadet-junior boys (n=44), cadet-junior girls (n=33), male university students (n= 15), female university students (n=21), and a group called 'pôle technique' made up of high level judokas who have finished academic study (n=18). The outbreak involved 86% of the cadet-junior boys, but only 6 men in the 'pôle technique' (33%) and only 5 of the 69 other team members (7%) (cadet-junior girls and university students). We describe the outbreak and the results of a survey that found a known risk factor for the 'pôle technique': sharing an electric shaver. Personal hygiene practices were found to be very good among the cadet-junior boys. The high attack rate in this group may be linked to the poor shower facilities in the gymnasium where they practiced that led them to have their showers several hours after the end of daily practice.

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Key words : Tinea, Trichophyton, judoka, wrestling, athlete.

Introduction

Tinea corporis gladiatorum is a fungal infection due to *Trichophyton tonsurans*, well known in wrestlers and widespread among wrestling teams worldwide [1,2]. Judokas were considered free of this fungal skin infection until Shiraki et al described cases in judokas at a university in Japan in 2004 [3].

We were involved in the treatment and the investigation of an outbreak of 49 cases of tinea corporis gladiatorum that took place between October 2004 and April 2005 among the 131 high level judokas who were members of the Pôle France Orléans, a sport-study

programme based in Orléans, a city of 113 000 inhabitants located in the centre of France [4]. This article describes the evolution of the outbreak, with the aim of raising awareness across Europe. This fungal infection is transmitted through close skin-to-skin contact, and the athletes involved in this outbreak, like those described by Shiraki et al, are involved in international competitions [3].

Methods

In France, mixed sport-study programmes known as 'pôles' are offered to high level athletes throughout the country. For judokas, one of the five such structures is located in Orléans (Pôle France Orléans) and divided in 5 groups (each one known as a 'pôle'): the cadet-junior boys (n=44; age 15-18), the cadet-junior girls (n=33, age 15-18), the male university students (n=15; age 18-24), the female university students (n=21), and a group called 'pôle technique' for high level judokas who have finished academic study and may be in employment (n=18; age 16-24). The programme members are coached by 7 adult trainers. For sport-related medical care, team members may consult a staff of 11, including physicians, masseurs, physiologists, school nurses and dieticians.

The judokas in the 'pôle technique' lived together in La Source, a suburb in the south of the city, and shared a bathroom. The cadet-junior boys and girls boarded at night in different schools in the city centre. Each group had its own practice facility where 3 hours of daily training took place: cadet-junior boys trained in the city centre, while cadet-junior girls and university students trained in La Source. All five groups practiced together for several hours each Wednesday.

Each team member participated in between five and seven national and international competitions a year, and several local challenges.

The team members travelled to their homes in other parts of France on the few weekends when they were not competing.

Case reports

Clinical examinations were carried out by a single dermatologist. A confirmed case of tinea corporis gladiatorum was defined as a team member presenting with clinically typical lesions. A suspect case was a transient definition for a team member with suspect skin lesions. Both confirmed and suspect cases were sampled and cultured for fungus. After a 30 day incubation, a suspect case growing the *fungus Trichophyton* tonsurans became a confirmed case, and a suspect case without fungal growth was discarded.

An episode was defined as a confirmed case of tinea corporis gladiatorum from symptom onset to healing of lesions and completion of treatment.

A new case was defined as the first episode in a given individual following our investigations.

Re-infection was defined as the occurrence of second or third episode in a given individual involving other anatomical sites than the previously known ones.

Throughout the period of the study, suspect cases were reported by team members and their coaches; and on two occasions by the dermatologist who examined the athletes in the gymnasium during a training session. When suspicious lesions were seen, hospital appointments were scheduled for the following day, where the lesions were mapped and samples were taken for microbiological testing.

The following data were collected for each case: date, sex, group, judo level, name, date of birth, address, number of visit, anatomical locations of lesions seen by patient, and of additional lesions discovered by clinician, anatomical location of sampled lesions, current self-medication, and prescribed treatment.

One of two treatments was offered: all cases received topics and oral terbinafine 250 mg/d for 1 month, and the case was withdrawn from judo practice for 7 days if 5 or fewer lesions were seen, and for 14 days if more than 5 lesions were seen.

Environmental and microbiological investigation

For the environmental investigation, five 20 cm x 20 cm squares of the practice mat (4 corners and 1 middle) were sampled on 6 January with wet cotton compresses cultured for fungi.

Mycological cultures were carried out on Sabouraud Chloramphenicol Gentamicin Agar, Sabouraud Chloramphenicol Actidion Agar and Dermatophyte Agar incubated at 30°C for at least 30 days. Staphylococci and enterococci were looked for on Chapman Agar and Bile Esculin Azid Agar incubated at 37°C for 2 days. (All media from BioMérieux – France).

Hygiene survey

A hygiene habits survey was conducted with a three page questionnaire distributed by the coaches to each team member on their personal hygiene habits.

Results

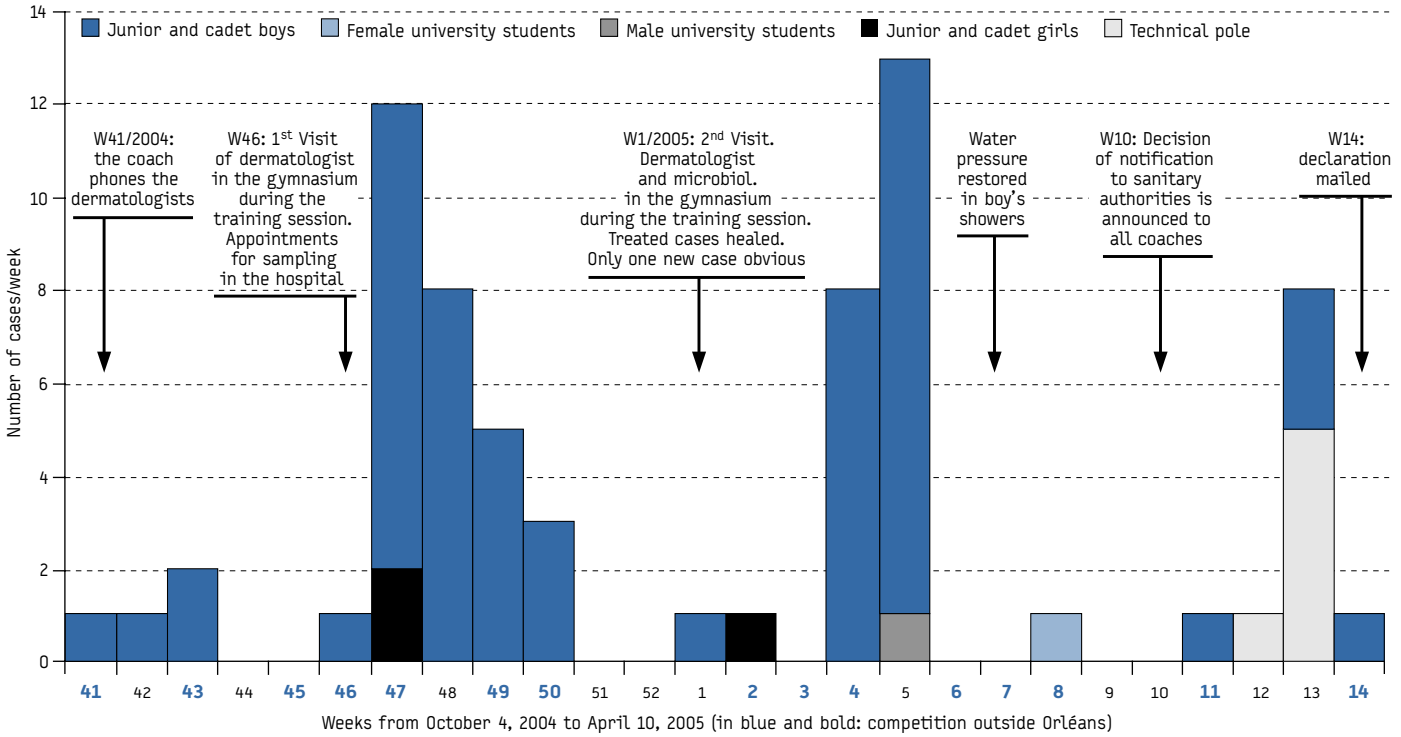
Cases reports

The first case was identified at the beginning of term by the cadet-junior boys' coach, who recognised lesions he had seen during the season 2003-2004 and that each boy had presented with to his own physician when visiting his family. The coach decided to refer every team member to a single dermatologist in Orléans.

The outbreak then evolved in three phases [Figure 1]. The first phase was from 6 October 2004 (week. 41/2004) until 6 January 2005 (week.1/2005) and involved 29 boys in the cadet-juniors group (29/44) and two girlfriends of cadet-junior boys, who belonged to the cadet-junior girls. Two of the boys were infected twice. On 6 January 2005, all cases had fully recovered and only two new cases were discovered, in one boy and one girl (week 2). The second phase began in week 4. In weeks 4 and 5 there were 5 new cases and 15 re-infections among the cadet-junior boys,bringing the total number of cases to 35/44. At this point, no cases had been reported in members of the 'pôle technique' and there were only 3 new cases in the remaining groups. The third phase began in week 11: the 'pôle technique' reported 6 new cases (6/18), while the cadet-junior boy referred 3 more new cases (total cases 38/44, 86%) and 2 re-infections. In week 12 the Fédération Française de Judo sent a notification to the local health authorities (Direction Départementale de l'Action Sanitaire et Sociale du Loiret). The epidemic curve was calculated up to week 14. A few cases occurred after that time, including the only case in a person who did not belong to the programme, a girlfriend of one of the last team members to be infected. Although she did not belong to the programme, she practiced judo at a private club whose members had recently competed against the Pôle France Orléans.

FIGURE

Epidemic curve of *tinea corporis gladiatorum* outbreak among judo team, in Orléans, October 2004-April 2005



In total, 81 athletes were referred to the dermatologist and 68 episodes of tinea were observed: 49 new cases and 19 re-infections (eighteen second episodes and one third episode). Forty five of the infected athletes were male and 4 were female, and the mean age was 17.3 years (range 15.4 to 23.9).

The outbreak affected 86% of the cadet-junior boys (38/44), who practiced judo in Orléans city centre. In La Source, 6 cases occurred among the 18 athletes of the 'pôle technique'; whereas very few members of the other groups – cadet-junior girls and the university students - were involved (5/69, 7%).

Environmental and microbiological investigation

One sample taken from the practice mat used by the cadet-junior boys grew the fungus *Trichophyton tonsurans*. None grew *Enterococcus sp.* or *Staphylococcus aureus*.

The distribution of lesions on the body was as follows: 31 on forearm, 25 on anterior trunk, 24 on scalp, 23 on face and neck, 14 on arm, 12 on back, 2 on buttock, 9 on lower leg and thigh, and only 2 on feet. The mean number of lesions was 2.1 per person per episode (range 1-15). Mycological confirmation of the fungus was obtained by culture in 48/68 episodes (70%). Every 48 isolates were *T. tonsurans var sulfureum*.

Hygiene survey

The 18 judokas in the 'pôle technique' were not included in computations since their case histories revealed that all cases in this group were in men who shared an electric shaver : all presented with at least one scalp lesion, and 85% of lesions in this group were on the scalp.

For the 113 other athletes, 102 questionnaires were returned by the coaches (90%), and no problems with personal hygiene practice were identified. In fact, cases were significantly associated with preventive attitudes such as showering twice a day, daily hairwashing using shampoo, and using one's own towel. The only significant risk factor was one which concerned the cadet-junior boys, who all had showers several hours after the end of practice.

Discussion

Our study revealed an outbreak that began in 2003-2004, according to the cadet-junior boys, but each of them had consulted a physician when visiting his family: since the team members' families lived in many different locations across France, each physician saw only one case and the outbreak was unrecognised. The outbreak was only recognised when a single dermatologist was called in by a coach to deal with all cases.

High contact sports are a well known cause of transmission of viruses, bacteria, parasites, and fungi causing skin infections, and the best documented infection transmitted in this way is herpes simplex [5]. Fungi are considered a benign risk in comparison with herpes, though more widely spread : during the 1998-1999 season in the United States, Kohl et al found that 84% of wrestling teams had at least one case of tinea corporis gladiatorum. The causative agent is always the fungus *T. tonsurans* [6]. Until year 2004, reports of outbreaks of tinea corporis gladiatorum were seemingly restricted to wrestling teams [1,2,6].

The first cases among judokas were described by Shiraki et al from the Juntendo University School of Medicine in an unnamed university in Japan in 2004, a year in which a large number of high level judokas were brought together in one place by the Olympic Games [3]. This observation may have been made more acute because of the epidemic situation in the team at the authors' university, the Juntendo University School of Medicine. This paper was soon followed by others in early 2005, showing that the epidemic had already spread across Japan more quickly than expected. It was shown to have been present in judo teams since 2001, and in wrestlers since 1994 or 1995 [7,8,9]. Two genotypes of *T. tonsurans* have been isolated in wrestlers, and only one in judokas, which probably signifies a more recent introduction of the fungus among judokas [7].

Although the infection has been widespread among wrestlers for some time now, risk factors and prevention strategies are not yet well defined. Fomites were identified in previous studies of tinea capitis due to *T. tonsurans* in the elderly [10] and practice mats were statistically suspected by Kohl et al for wrestlers [6], but they probably do not play a major role in our study: neither faecal nor cutaneous contaminants were found, and lesions were rare on feet. Most lesions appeared on upper extremities, neck and head; these are the zones where judokas

hold on to their opponents. Therefore, prevention should address person-to-person contacts. Asymptomatic carriage may exist on the scalp or around healed lesions. The delay we identified between the end of practice time and having a shower may be an interesting risk factor. It could allow deeper colonisation of the skin by the fungus through small wounds that are usually self-healing.

The water supply in the gymnasium used by the cadet-junior boys lacked pressure, and it was impossible for all 44 athletes to use the showers at the same time. As a result, the boys used to practice until the last minute, then change out of their practice clothes, travel back to the dormitory for dinner, study for 1-2 hours, and then have their showers. The water pressure at the gymnasium has now been restored and showers are taken immediately after practice.

In our investigation, the clinical aspects of lesions raised two problems:
1. lesions can mimic mat-burns or skin grazes, frequent in team members above the protuberances of bones on wrists or elbows,
2. the number of lesions is frequently underestimated by the individual, and not only when they occur on the scalp or back.

This may be why skin lesions are considered to be benign problems, and may also explain the failure of self-medication with topical treatments: not all lesions receive the treatment. Oral treatment was therefore indicated. Itraconazole and fluconazole are always efficient [3,11,13,14]. Terbinafine worked well in our study.

T. tonsurans is highly contagious: 40% of Parisian cases of tinea in 1910 were due to *T. tonsurans* and temporary exclusion from school has long been a compulsory part of treatment. Despite this long history, treatment guidelines for tinea corporis have failed to produce the desired goals in the particular population of contact sports practitioners. Specific problems appear when dealing with such an outbreak in such a team [12]. First of all, cases must be withdrawn from practice, but discontinuation of practice disrupts individual and team goals and is therefore difficult to accept. Athletes can be tempted to hide their lesions until competitions are over. Second, these patients are minors, and prevention of infection requiring a daily screening of the entire skin surface raises ethical problems if this screening is to be carried out by a room mate or an adult coach.

These problems probably played a role in the sequencing of the outbreak: the first cases were referred to the dermatologist by one of the coaches. This coach made possible the recognition of the outbreak and the treatment of ongoing cases. The second phase began when teams had resumed their competition tours across France: it is likely that most of cadet-junior boys were re-contaminated when fighting at locations outside of Orléans, and we hypothesised a nationwide outbreak. However, it is also likely that some of the cadet-junior boys had lesions, but did not want to be withdrawn from practice and competitions, and so hid their lesions with adhesive wound coverings that are widely used for ordinary mechanical abrasions, and waited until the end of competitions to seek the help of a coach or the dermatologist. We hypothesise that this behaviour also led to the third phase: the 'pôle technique' only sought medical advice after the decision was made to officially notify the health authorities.

Recent results from Hirose et al suggest that discontinuation of practice is not required to prevent the spread of the fungus, provided that the asymptomatic carriers, detected by scalp sampling every two months, are treated with, according to these authors, one week pulse oral itraconazole 400mg and miconazole shampoo, and that the whole group accepts the implementation of infection prevention measures. This procedure will be tested during the next term of our judo programme, although there are differences with the sports clubs in the study of Hirose et al, where training only occurred once a week and did not seem to include external competitions [14]. Our athletes train every day and participate in national and international competitions. There are sexual relationships between some of the athletes and the cadet-junior sleep in dormitories.

As mentioned by Kohl et al in year 2000, the majority of the literature has described outbreaks in isolated contact sport teams [12]. More recently, in Japan, a case of *T. tonsurans* infection was observed in a boy in a nursery school who was a member of judo club [7]. In our study, transmission could be observed between the different teams, and the case described outside the programme practiced judo in a club that had challenged the Pôle France Orléans during the season. From these results we may also consider the outbreak as limited to judo practice, but the contamination of the first two cadet-junior girls was also linked to sexual relationships. Therefore we consider this to be an artefact: cases must occur outside contact sport teams, but since they are not seen by the same physician, they remain outside the published descriptions.

The observations of both this and the Japanese study together suggest that the infection has been diffused through high level judo teams worldwide. Since contamination is specifically inter-human, eradication is achievable if the reservoirs are extensively investigated and treated simultaneously. This paper has been written with the aim of raising the alert.

References

1. Stiller MJ, Klein WP, Dorman RI, Rosenthal S. Tinea corporis gladiatorum: an epidemic of Trichophyton tonsurans in student wrestlers. J Am Acad Dermatol 1992; 27:632-3
2. Beller M, Gessner BD. An outbreak of tinea corporis gladiatorum on a high school wrestling team. J Am Acad Dermatol 1994; 31:197-201
3. Shiraki Y, Soda N, Hirose N, Hiruma M. Screening examination and management of Dermatophytosis by Trichophyton tonsurans in the judo club of a university. Jpn J Med Mycol 2004; 45:7-12
4. Estève E, Defo D, Rousseau D, Poisson DM. Epidémie de trichophyties cutanées chez les judokas du pôle France d 'Orléans : septembre 2004 - avril 2005. Bull Epidémiol Hebd 2005;34 :171-2
5. Brian B. Adams. Dermatologic disorders of the athlete. Sports Med 2002; 32:309-321
6. Kohl TD, Giesen DP, Moyer J Jr, Lisney M. The Pensylvania experience. Clin J Sport Med. 2002 May;12(3):165-71
7. Mochizuki T, Tanabe H, Kawasaki M, Anzawa K, Ishizaki H. Survey of Trichophyton tonsurans infection in the Hokoriku and Kinki regions of Japan. Jpn J Med Mycol 2005; 46: 99-103
8. Kasai T. Epidemiological survey of Trichophyton tonsurans infection in Tohoku district and its clinical problems. Jpn J Med Mycol 2005; 46: 87-91
9. Hiruma M, Shiraki Y, Nihai N, Hirose N, Suganami M. Questionnaire investigation of incidence of Trichophyton tonsurans infection in dermatology clinics in the Kanto area. Jpn J Med Mycol 2005; 46: 93-97
10. Frieden IJ, Howard R. Tinea capitis: epidemiology, diagnosis, treatment, and control. J Am Acad Dermatol. 1994 Sep;31(3 Pt 2):S42-6
11. Kohl TD, Martin DC, Berger MS. Comparison of topical and oral treatments for Tinea gladiatorum. Clin J Sport Med. 1999; 9:161-6
12. Kohl TD, Lisney M. Tinea Gladiatorum. Wrestling's emerging foe. Sports Med 2000; 29:439-47
13. Nishimoto K, Honma K, Shinoda H, Ogasawara Y. Survey of Trichophyton tonsurans infection in Kyushu Chugoku and Shikoku areas of Japan. Jpn J Med Mycol 2005; 46: 105-108
14. Hirose N, Shiraki Y, Hiruma M, Ogawa H. An investigation of Trichophyton tonsurans infection in university students participating in sports clubs. Jpn J Med Mycol 2005; 46: 119-123

AN OUTBREAK OF MUMPS IN SWEDEN, FEBRUARY-APRIL 2004

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Between 24 February and 26 April 2004, Västra Götaland county in Sweden reported 42 cases of suspected mumps. A descriptive study of the cases was undertaken. A questionnaire was administered by telephone and vaccine effectiveness was calculated using the screening method. Seventy four per cent (31/42) of the suspected cases were interviewed by telephone. Eight out of the 42 serum samples were positive or equivocal for mumps IgM by ELISA. Mumps virus genome was identified in 21/42 (50%) saliva samples. Eleven were selected for sequencing and all were confirmed to be mumps virus. Cases were predominantly from 2 small towns. Eighteen out of 19 cases that developed bilateral swelling could be linked to one small town. The median age of interviewed cases was 43 years (range 5 to 88). Six cases were admitted to hospital, 5 of which were older than 30 years. The highest incidence occurred in the 35 to 44 years age group. Vaccine effectiveness was estimated to be 65% for 1 dose and 91% for 2 doses.

This descriptive study shows the increasing age of mumps cases with increasing vaccine coverage. Vaccine effectiveness was particularly high for 2 doses. Second-dose uptake must be ensured, as primary vaccine failure is well documented in mumps. Stronger precautions must be taken to avoid pools of susceptible older individuals accumulating due to the increased risk of complications.

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Key words: mumps, outbreak, vaccine effectiveness

Introduction

Mumps is an acute viral disease, of which the commonest symptom is painful swelling of one or both parotid glands. Mumps in childhood tends to be mild and around 30% of infections are asymptomatic [1,2]. Transmission occurs through inhalation of respiratory droplets or by direct person-to-person contact.

Vaccination against mumps in Sweden began in 1982 with the introduction of combined mumps, measles and rubella (MMR) vaccine in the national immunisation programme at 18 months and 12 years. Coverage rates quickly exceeded 90% and have been kept at this level for the past 20 years [3]. The annual incidence of mumps in Sweden was about 435 cases per 100 000 in the pre-vaccine era (1977-1979), and dropped to less than 1 per 100 000 in the post-vaccine era (1993-1995). This represented a reduction of more than 99%.

Mumps is a notifiable disease in Sweden. Between 24 February and 26 April 2004, Västra Götaland county reported 42 suspected cases of clinical parotitis. This number of cases was well above expected for this county (about 10 cases per year) and most were in adults. The Department of Epidemiology at the Swedish Institute for Infectious Disease Control (SMI) was invited by the County Medical Office to investigate the outbreak. The aims were to describe the outbreak, identify any risk groups as well as complications and evaluate vaccine effectiveness.

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Methods

Case finding and definition

All physicians in the area were requested to report suspected mumps cases. A description of the outbreak was also posted in EPI-aktuellt (the weekly national epidemiological bulletin published by SMI) with a request for further cases to be notified. A probable case was defined as painful swelling of one or more salivary glands for at least 2 days; occurring after 10 February 2004 in a person who either lived or worked in Västra Götaland between 1 February and mid-April 2004. A confirmed case was defined as the above plus serological confirmation of IgM mumps antibodies and/or isolation of mumps virus genome in saliva by PCR.

Questionnaire design and administration

A questionnaire was developed and administered by telephone, asking for case age and sex, place of work or study, household members (age and profession/school), recent travel, drugs taken, allergies, vaccination status, symptoms/complications, possible contacts and previous mumps-like illness.

Laboratory methods

Mumps-specific IgM (inhouse ELISA and Behringwerke, Germany) and IgG (Behringwerke, Germany) were detected in serum by ELISA. Mumps virus RNA was extracted from saliva samples using QIAamp RNA extraction kit (Qiagen). The extracted RNA was reverse transcribed to cDNA using Superscript III reverse transcriptase and random primers. The cDNAs generated were amplified in two consecutive PCR reactions (nested PCR) using Platinum Taq DNA Polymerase (Invitrogen) and two sets of primers specifically for conserved regions of the nucleocapsid gene. Primers used for the nested PCR were: mumps-of 5'AGTGTACTAATCCAGGCTTG 3' and mumps-or 5' ACCCACCATTGCATAGTATC 3' for the first round of PCR and the primers mumps- if 5' GTATGACAGCGTACGACCAAC and mumps-ir GATAGGAACCCCTGCCGTCT 3'for the second round of PCR. The nested PCR amplificates were analysed by agarose gel (2%) electrophoresis and bands of about 220 base pairs were considered positive for the nucleocapsid gene. Eleven out of 22 of the PCR positive products were verified by DNA sequence analysis and were shown to be mumps virus when compared with published sequences in GenBank.

Vaccine effectiveness

Patients or parents of patients were questioned about their mumps vaccination status. Vaccine effectiveness (VE) was calculated for individuals aged less than 24 years (who would have been included in the vaccination programme started in 1982) using the screening method [4,5,6,7,8]. The formula of VE is VE = (PPV-PCV)/(PPV*[1 PCV]), where PPV equals the proportion of the population vaccinated and less than 24 years of age and PCV equals the corresponding proportion among cases. A seroprevalence survey for vaccine preventable diseases was undertaken in Sweden in 1997 [9]. This provided a background rate of natural immunity in the population and was used in certain denominator calculations. Vaccine coverage rates were obtained from Statistics Sweden (SCB).

Results

Laboratory findings, response rate and case classification

Forty two suspected clinical cases were reported by Västra Götaland county. Serological analysis indicated that 8 of 42 samples were positive or equivocal for mumps IgM. PCR identified mumps virus genome in 21 of 42 (50%) saliva samples. In total, 22 cases were either positive for mumps IgM or mumps virus genome was identified. In total, 31 patients (74%) were interviewed (11 patients were therefore not interviewed, despite repeated phone calls). According to our case definition, 17 cases were defined as probable and 14 as confirmed.

Symptoms and admission to hospital

All 31 patients had parotitis: 19 patients (61%) reported bilateral swelling, 11 patients (35%) unilateral swelling and 1 reported swelling but information on symmetry was missing. 11 patients (35%) had fever, 19 patients (61%) reported pain in the parotid area, 12 patients (39%) headache and 6 patients (19%) reported dryness of the mouth. The reported complications were orchitis in 1 case. Five out of 6 patients who were admitted to hospital were unvaccinated and over 25 years old. Twenty patients (all unvaccinated) indicated that they had had mumps in the past (median age=52 years, range 34 to 88), 9 patients (7 vaccinated patients) indicated that they had not had mumps (median age=20 years, range 5 to 50) and 2 patients (1 vaccinated patient) did not know.

Age and sex distribution

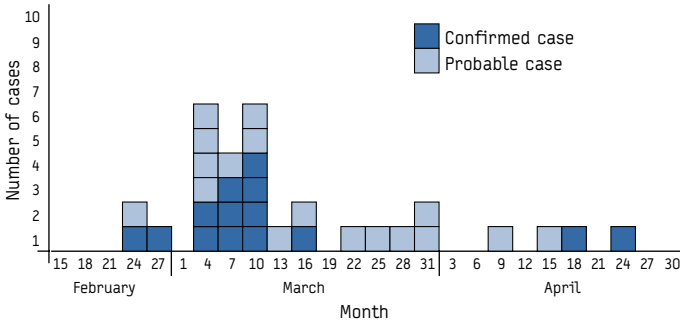
Overall median age was 38.3 years (range 5 to 88) and 23 (55%) patients were female. The median age of the 31 interviewed patients was 43 years (range 5 to 88) and 25 out of 31 were 24 years or older. Median age of those not interviewed (n=11) was 21 years (range 5 to 76). The 35 to 44 years age group had the highest incidence (2.87 / 10 000) followed by the 25 to 34 years age group (2.32 / 10 000). Incidence decreased with older age groups.

Epidemic curve

Figure 1 shows the epidemic curve for this outbreak. The first cases were reported on 24 February 2004 with the majority reporting onset of symptoms between 4 and 11 March 2004. Thereafter, the number of cases decreased steadily.

FIGURE 1

Epidemic curve showing date of onset (by 3-day interval) of illness, 2004, Sweden

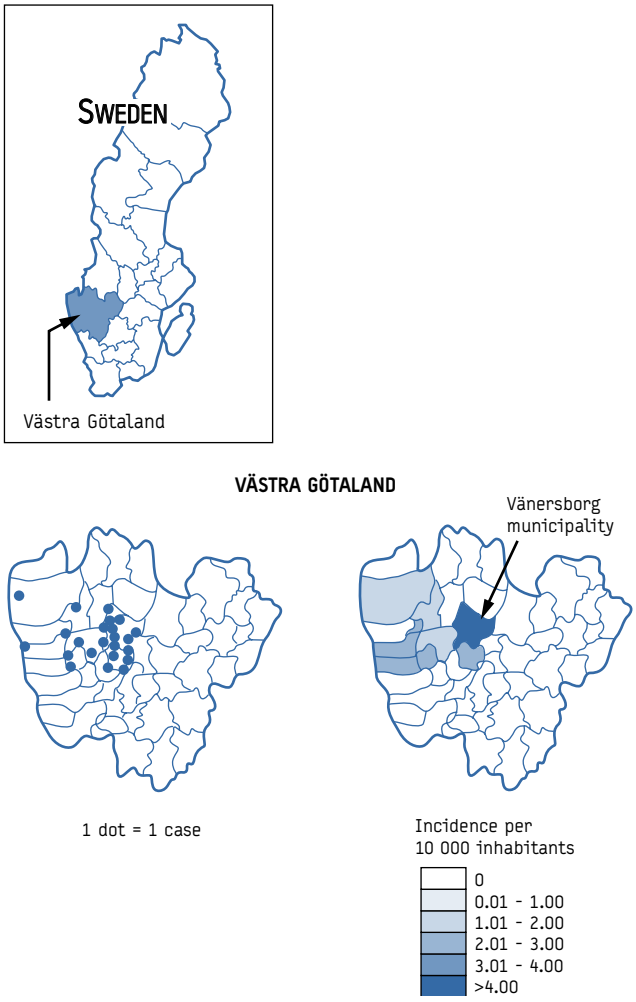


Geographical distribution

While the outbreak did spread to other municipalities in Västra Götaland county, it was not particularly widespread, nor did it appear to show any distinct pattern of spread over time. Figure 2 shows that the distribution and incidence of cases was very limited geographically and temporally. Vänersborg municipality had the highest incidence (4.05 per 10 000) and a significantly higher risk (RR=4.86; 95% CI: 1.77-13.36) when compared to municipalities with only 1 case.

FIGURE 2

Dot density (n=31) and incidence map of mumps outbreak by municipalities in Västra Götaland County, Sweden, 2004



Vaccine effectiveness

All 6 patients under 24 years old indicated that they had been vaccinated against mumps at least once. Among patients older than 23 years, 2 indicated that they had been vaccinated. VE (ascertained by self-reported immunisation status) was 65% for 1 dose and 91% for 2 doses. Patients with unknown vaccination status (n=7) or unknown dosage (n=1) were excluded in the calculation of VE, as recommended [10].

Discussion

This study illustrates the impact of the vaccination programme: higher median age of mumps cases with increasing vaccine coverage. The outbreak's greatest effect was on age cohorts (particularly 35-44 years) that were not included in existing vaccination programmes and that had had fewer opportunities to acquire natural infection. The slightly lower incidence in the 25-34 years age group is because many in this group were vaccinated, although they were not the right age to be included in the vaccination programme when it started [9]. The incidence decreased with age due to acquired immunity. Large numbers of unvaccinated and susceptible adults were probably being exposed to circulating virus in schools through their children (many adult patients indicated that they had children at home). Similar outbreaks in individuals too old to receive the MMR vaccine have been observed in the United Kingdom in 2004, particularly in students aged 14-22 years [10].

Several limitations are recognised in this study. Firstly, due to the nature of the investigative response, this study did not include a control group needed to make more conclusive findings. Secondly, vaccination status of cases in this study relied upon self-reported status and was not confirmed. The small number of vaccinated individuals also makes the VE estimate imprecise. Thirdly, individuals not interviewed had a lower median age. If it is the case that a high proportion of these non-interviewed patients have been vaccinated, then it is likely that the VE estimated here is too high. Lastly, up to 30% of mumps infections can be asymptomatic. Subclinical cases would therefore have been missed and their role in the transmission of the virus in these communities cannot be assessed. This problem needs to be addressed if future contact tracing is to be more successful in person-to-person outbreaks involving infectious agents with a high asymptomatic rate.

The screening method will indicate whether there is a need for more careful evaluation, and should not be relied upon for precise estimation of VE [11]. We infer that the VE was high, particularly if the person had indicated having received 2 doses. Five out of seven vaccinated patients indicated only having received 1 dose of MMR vaccine. Secondary vaccination must be ensured, as primary vaccine failure with mumps is well documented [12]. There also appeared to be more severe illness in older, unvaccinated individuals. We recommend using the data obtained from the seroprevalence surveys conducted in Sweden every 5 years, to check that pools of susceptible older individuals are not accumulating due to the increased risk of complications.

Acknowledgements

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References

1. Bum SG, Litman N. Mumps virus. In: Mandell GL, Douglas RG, Bennett JE, *Principles and practice of infectious disease*. New York: Churchill Livingstone. 1995: Chapter 135: 1260-65.
2. Weible RE. Mumps vaccine. In: Plotkin SA, Mortimer EA, editors. *Vaccines*. Philadelphia: Saunders Company. 1988.
3. Galazka A, Robertson S & Kraigher A. Mumps and mumps vaccine: a global review. Bulletin of the World Health Organisation. 1999; 77[1]: 3-14.
4. Malfait P, Jataou I, Jollet M, Margot A, de Benoist A & Moren A. Measles epidemic in the urban community of Niamey: transmission patterns, vaccine efficacy and immunization strategies, Niger, 1990 to 1991. Perdiatr Infect Dis J 1994; 13: 38-45.
5. Orenstein WA, Bernier RH, Dondero TJ, Hinman AR, Marks JS, Bart KJ, Sirotkin B. Field evaluation of vaccine efficacy. Bull World Health Organ. 1985; 63:1055-68.
6. Cutts FT, Smith PG, Colombo S, Mann G, Aschero A, Soares AC. Field Evaluation of measles vaccine efficacy in Mozambique. Am J Epidemiol. 1990; 133: 349-55.
7. Halloran ME, Haber M, Longini IM Jr, Struchiner J. Direct and indirect effects in vaccine efficacy and effectiveness. Am J Epidemiol. 1991; 133: 323-31.
8. Farrington C. Estimation of vaccine effectiveness using the screening method. International Journal of Epidemiology. 1993; 22[4]: 742-746.
9. Olin P, Carlsson R, Johansen K, Hallander H, Ljungman M & Svensson Å. Vaccinationsuppföljning seroepidemiologisk tvärsnittsstudie 1997, Slutrapport. Smittskyddsinstitutet rapportserie NR 3: 2004.
10. Medical News Today. UK-wide outbreak of mumps among students. ProMed mail [2004], Archive number: 20041103.2974
11. Orenstein WA, Bernier RH, Dondero TJ, Hinman AR, Marks JS, Bart KJ & Sirotkin B. Field evaluation of vaccine efficacy. Bulletin of the World Health Organisation 1985; 63 [6]: 1055-1068.
12. Briss PA, Fehrs LJ, Parker RA, Wright PF, Sannella EC, Hutcheson RH, Schaffner W. Sustained transmission of mumps in a highly vaccinated population: assessment of primary vaccine failure and waning vaccine-induced immunity. J Infect Dis. 1994; 169[1]: 77-82.

A NATIONWIDE OUTBREAK OF MULTIRESISTANT *SALMONELLA* TYPHIMURIUM VAR COPENHAGEN DT104B INFECTION IN FINLAND DUE TO CONTAMINATED LETTUCE FROM SPAIN, MAY 2005

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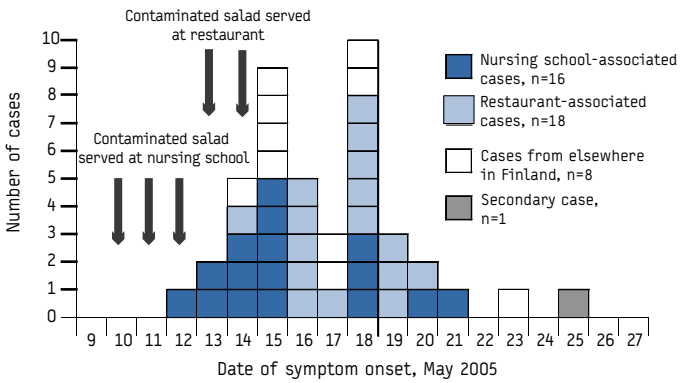
A rare multiresistant *Salmonella* Typhimurium DT 104B has caused an outbreak of 60 microbiologically confirmed cases in May 2005, widely distributed across southern and western Finland. The isolates have an identical pulsed field gel electrophoresis (PFGE) and antimicrobial resistance pattern (ACSSuT). Of the 56 cases confirmed so far, 80% were in females and 45% were in people aged between 15-24 years (range 7 to 53). Before this outbreak, there were between two and four *S.* Typhimurium var Copenhagen DT104B cases annually in Finland. None of the previous PFGE types share exactly the same profile with the isolates in the current outbreak.

A cluster occurred among students of a nursing school in southeast Finland in mid-May 2005. The nursing school has around 800 healthcare students and teaching staff. A questionnaire was sent to the students and staff by the local health authorities. A private company operates the cafeteria providing lunch at the school. The kitchen had kept frozen food samples from the dishes served each day, in accordance with the Hazard Analysis Critical Control Points (HACCP) risk management system [1]. *S.* Typhimurium DT 104B was detected in samples of salad made from lettuce, other vegetables and/or noodles from three successive days, served between 10 and 12 May. Three salad isolates have been genotyped so far, and are indistinguishable from the isolates obtained from the patients.

In western Finland, the cases were geographically widespread, but the great majority of the patients had eaten at the same restaurant on 13 or 14 May. Between 280 and 570 customers ate at the restaurant on those days. The preliminary epidemic curve shows that for the restaurant-associated cases, two peaks occurred on 15 and 18 May 2005, supporting the microbiological and descriptive epidemiological evidence that the contaminated salad was served in the restaurant over a three day period (Figure).

FIGURE

***Salmonella* Typhimurium var Copenhagen DT104B, cases by date of first symptoms in Finland, Laboratory of Enteric Pathogens, KTL (n=43)**



A traceback investigation showed that the nursing school and the restaurant had both purchased iceberg lettuce, the only kind of lettuce served on the implicated days, with a documented trail leading back to a supplier in Spain. Thousands of kilograms of this iceberg lettuce have been imported from Spain and distributed throughout Finland. However, the limited outbreaks observed to date suggest that only a small proportion of lettuce was contaminated. The traceback investigation is ongoing. A press release was sent out to the healthcare settings and environmental authorities on 21 June. An alert was sent out through the European Early Warning and Response System (EWRS) on 21 June and the Rapid Alert System for Food and Feed (RASFF) on 22 June 2005 [2].

References

1. www.foodsafety.gov [homepage on the Internet]. Gateway to Government Food Safety Information [updated 4 May 2005; cited 29 June 2005]. Industry Assistance. Hazard Analysis and Critical Control Point (HACCP) Systems. (http://www.foodsafety.gov/~fsg/fsghaccp.html)
2. European Commission. Rapid Alert System for Food and Feed (RASFF). Week 2005/26. (http://europa.eu.int/comm/food/food/rapidalert/reports/week26-2005_en.pdf)

OUTBREAK OF *CLOSTRIDIUM DIFFICILE* INFECTION IN AN ENGLISH HOSPITAL LINKED TO HYPERTOXIN-PRODUCING STRAINS IN CANADA AND THE US

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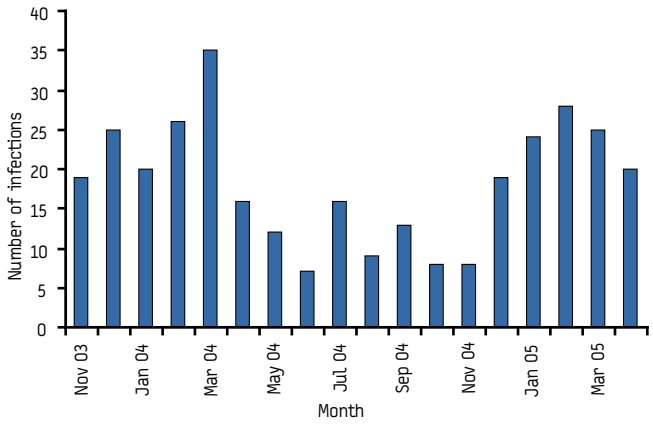
(http://www.eurosurveillance.org/ew/2005/050630.asp#2)

An outbreak of *Clostridium difficile* infections in an acute hospital in southeast England is currently being investigated. Laboratory tests have confirmed that 59% of the *C. difficile* isolates from this outbreak belong to PCR ribotype O27, which is unusual in the United Kingdom (UK), and which has also been associated with outbreaks in Canada and the United States (US) [1,2].

When *C. difficile* infects vulnerable patients, often the elderly who have been treated with antibiotics, it can produce symptoms ranging from diarrhoea to severe inflammation of the bowel, which can be life-threatening. Within the affected hospital, there were 85 positive tests for *C. difficile* toxin in the 12 months between April 2003 and March 2004 and this rose to 209 during the following 12 month period. An outbreak was declared in November 2003. A period of control was achieved in mid-2004 (Figure).

FIGURE

Number of new cases of hospital-acquired *C. difficile* within the acute hospital by month of report, hospital in southeast England, November 2003 to April 2005 (n=330)



Control measures

The following control measures were implemented:

- affected patients were isolated or cohorted within the hospital
- the isolation policy was reviewed and implemented

- 'diarrhoea' was clearly defined using a stool chart (based on Bristol Stool Form Scale) to help with bed management
- patient transfers within the hospital were restricted
- there was increased use of disinfectants containing detergent and hypochlorite for environmental cleaning, and more frequent environment and equipment cleaning in the affected clinical areas
- a rigorous programme of hand hygiene using liquid soap and hot water was implemented (alcohol gels are used routinely by healthcare staff between treating patients, but only if their hands are not visibly soiled)
- protective clothing, e.g. gloves and aprons, was used
- the hospital restricts the use of broad-spectrum antibiotics, and this policy was monitored for compliance.

Suspicion that the clinical presentation of *C. difficile* infection was changing (increased severity of disease) resulted in isolates being referred to the UK Anaerobe Reference Laboratory for investigation. Typing revealed that the majority of the isolates belonged to PCR ribotype O27, a previously very unusual type in the UK. Similar strains belonging to PCR ribotype O27 have been reported recently in Quebec, Canada, and across six states of the US. Outbreaks with such a strain in Canada were associated with more severe infection and an increase of the case-fatality ratio.

The UK isolates are being further characterised and compared with Canadian and US outbreak strains. Examples of UK type O27 isolates have also been sent to the US Centers for Disease Prevention and Control for comparison of their toxin-liberating capacities in the CDC in vitro toxin assay. Preliminary pulsed-field gel electrophoresis (PFGE) and repetitive extragenic palindromic-PCR (REP-PCR) subtyping investigations have revealed that some of the UK type O27s examined so far, while not identical, are very closely related to some of the North American isolates.

Investigations in North America have shown that some of the O27 isolates there are hypertoxin producers due to a deletion in a toxin regulating gene tcdC that results in a 16 to 20 fold increase in toxins A and B production respectively. The O27 strains mainly liberate toxins in the logarithmic growth phase, whereas comparator strains liberate toxins mainly in the stationary phase. The strain investigated has been characterised as belonging to toxinotype III which produces the binary toxins A and B, and is resistant to certain new fluoroquinolones. All type O27 isolates from the UK examined so far are also in vitro hypertoxin producers and have the same *tcdC* gene deletion. Further examples are currently being examined.

Meanwhile, healthcare workers in England and Wales are being requested to note any increases in severity of cases of *C. difficile* disease, higher mortality than expected, or an increase of cases associated with the use of certain fluoroquinolones.

References

1. Health Protection Agency. Outbreak of Clostridium difficile infection in a hospital in south east England. Commun Dis Rep Wkly 2005: 15(25): 23/06/2005 (http://www.hpa.org.uk/cdr/archives/archive05/News/news2405.htm#cdiff).
2. Pépin J, Valiguette L, Alary M-E, Villemure P, Annick Pelletier A, Forget K et al. Clostridium difficile-associated diarrhoea in a region of Quebec from 1991 – 2003 : a changing pattern of disease severity. Can Med Assoc J 2004;171:466-72.

Outbreak of rubella in the Madrid region, Spain, 2005

Red de Vigilancia Epidemiológica de la Comunidad de Madrid (Epidemiological Surveillance Network of the Autonomous Region of Madrid)

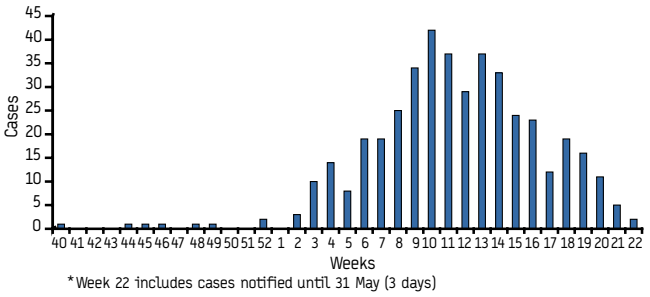
Published online 7 July 2005
(http://www.eurosurveillance.org/ew/2005/050707.asp#2)

There was an unexpected increase in the number of confirmed rubella cases notified in the autonomous region of Madrid during the first weeks of 2005. Between 1 January and 31 May 2005, 431 suspected cases of rubella were notified to regional health authorities. Young adults of Latin American origin made up a high proportion of patients. Because of the unexpectedly high number of cases, which is similar to what occurred in the region in 2003 [1], measures to reinforce rubella surveillance were implemented. These included awareness campaigns for health professionals, urgent notification of suspected cases, serological confirmation of cases in the regional public health reference laboratory, identification of potential secondary cases and close contacts, and vaccination of susceptible contacts.

Of the cases notified between January and March, 360 (84%) were confirmed, either by serology or by epidemiological link with a confirmed case. Cumulative incidence of rubella during this period was 7.5 cases per 100 000 inhabitants. This incidence was 15.6 times higher than the expected annual mean observed from 1998-2004 (0.48 cases/100 000 inhabitants).The increase in notifications began in the third week of January and reached a peak in the second week of March (Figure 1). Since mid-April, there has been a steady decrease in the number of notified cases.

Figure 1

Notified rubella cases by week of onset of symptoms between 3 October 2004 and 31 May 2005. Source: Mandatory notification system, Autonomous Region of Madrid



*Week 22 includes cases notified until 31 May (3 days)

Most patients were between 20 and 29 years old. The majority of the patients (58%, 251) were of foreign, mainly Latin American, origin. One hundred and eighty-five (43%) patients were female and 170 (92%) were of childbearing age. Immigrants made up 39% of male patients and 84% of female patients. Thirty-three percent of cases were in immigrant women of childbearing age compared with 6% in Spanish women of childbearing age. Only 5% of patients recalled being previously vaccinated against rubella. A total of 95 cases (22%) were identified as part of 42 clusters of between two and four cases each. Regional health services notified three voluntary abortions because of congenital rubella syndrome risk (CRS) since 1 January 2005.

CRS can affect up to 90% of newborns if their mothers were infected during the first 11 weeks of pregnancy, and up to 20% if the infection occurs during the first 20 weeks [2]. Thus, rubella control measures were especially targeted at women of child bearing age, stressing the importance of vaccination and improving access to vaccination for immigrant women.

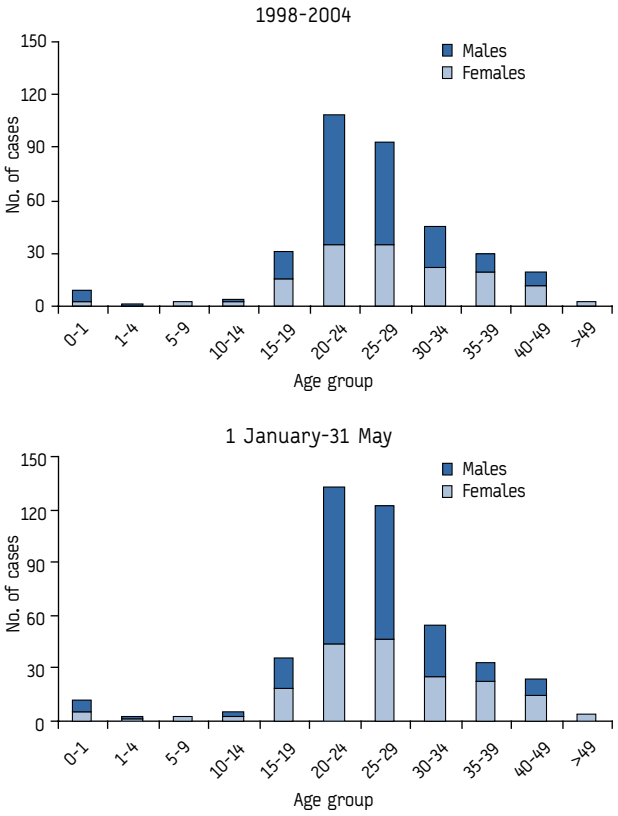
Rubella is a mandatorily notifiable disease in Spain [3,4]. Data should be sent to the regional surveillance institute every week. Rubella vaccination was introduced in the late 1970s in Spain, with campaigns targeting 11 year old school girls. In 1980, the trivalent vaccine against measles, mumps and rubella (MMR) for 15 month old children was included in the national child vaccination programme. A second dose of MMR vaccine for 11 year olds was introduced in 1996. In 1999, the second dose was rescheduled for children aged four.

Results of the III Encuesta de Serovigilancia de la Comunidad de Madrid, 1999-2000 [5] (III Serosurveillance survey of the Autonomous Region of Madrid, 1999-2000) showed rubella antibody prevalence to be above 95% in every age group from 2 to 60 years old. However, there are gender differences: close to 99% of women aged 16 to 20 years old have a positive serology, compared with 93% of the men in the same age group. Seroprevalence in women 16 to 45 years old is

98.6% (95% CI: 96.8% – 99.4%). These differences in susceptibility could explain the different distribution by sex of patients of Spanish origin. Adults living in Madrid born in countries where vaccination against rubella is not included in the vaccination schedule or has been introduced recently, could be more susceptible to rubella infection as has been shown in different seroprevalence studies [6]. The risk of CRS is probably higher in this population group.

FIGURE 2

Notified rubella cases by age group and sex from 1998-2004 and between 1 January and 31 May 2005. Autonomous Region of Madrid



OVER 2000 CASES SO FAR IN *SALMONELLA* HADAR OUTBREAK IN SPAIN ASSOCIATED WITH CONSUMPTION OF PRE-COOKED CHICKEN, JULY-AUGUST, 2005

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Published online as an e-alert 9 August 2005 (http://www.eurosurveillance.org/ew/2005/050811.asp#1)

As of 8 August 2005, 2138 cases of salmonella gastroenteritis have been reported to the Centro Nacional de Epidemiología (National Centre for Epidemiology, CNE) in Spain. The reported cases have been epidemiologically and microbiologically linked to a single brand of pre-cooked, vacuum-packed roast chicken (brand A) which was commercially distributed throughout Spain.

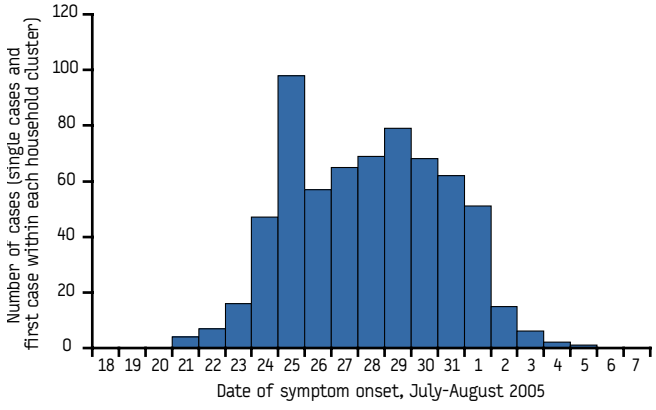
On 28 July 2005, the Centro Nacional de Epidemiología (National Centre for Epidemiology, CNE) received a report from the autonomous region of Valencia of the detection of eight household clusters of gastroenteritis involving a total of 25 cases, all with clinical presentation of salmonella infection. On the same day, two more autonomous regions reported similar outbreaks and Agencia Española de Seguridad Alimentaria (Spanish Food Safety Agency, http://www.aesa.msc.es) started investigating the source. On 29 July, an alert was sent to the health authorities throughout Europe via the Early Warning and Response System (EWRS) and Enter-net (http://www.hpa.org.uk/hpa/inter/enter-net_menu.htm).

Descriptive Epidemiology

A total of 1983 cases were part of household clusters. Of the people at risk, 74% developed symptoms (1011 cases out of 1363 people at risk in 373 clusters and single cases for which we have this information). Seventeen out of 19 autonomous regions have been affected by this outbreak with Valencia, Murcia, Andalucia and Castilla La Mancha accounting for 60% of all cases. A total of 234 patients have been admitted to hospital and one death has been recorded (in a man aged 90 years). Symptom onset per household cluster or single case ranges from 21 July to 5 August, with peaks on 25 and 29 July (Figure). However, as the implicated brand A chicken product is vacuum-packed and has a shelf-life of at least 3 weeks, it is expected that cases will continue to be reported during August. At present, the CNE has information on age and sex distribution for 253 cases (12% of total). Fifty five per cent of these cases are in men and 45% are in women. The age group most affected is 25-34 years (24% of all cases) followed by 35-44 years (17%) and 45-54 years (13%). In the age group 0-4 years and >74 years, 9 and 6 cases have been recorded respectively. A retrospective case-control study is ongoing.

FIGURE

Date of symptom onset for 651 household clusters and 155 single cases of *Salmonella* Hadar infection in 17 autonomous regions of Spain, 21 July-8 August 2005*



*For household clusters, only the first case is included. Data updated 8 August 2005.

Microbiological and environmental investigations

The National Reference Laboratory for Salmonella and Shigella (LNRSSE) has received 90 salmonella isolates from patients and 6 from chicken samples. Results of the 35 strains studied so far (30 human, 5 chicken) confirm the identification of *Salmonella enterica*, subspecies *enterica*, serotype Hadar, and in 34 strains phage type 2 has been identified. The isolates are resistant to ampicillin, cefalotine, streptomycin, nalidixic acid and tetracycline. The pulsed field gel electrophoresis (PFGE) profiles of human and chicken samples are indistinguishable.

The day the report was received by the CNE, local health authorities conducted an environmental inspection of the factory producing brand A chicken. Official results from this investigation are still pending.

Control measures

• On 28 and 29 July, all brand A chicken products were recalled from commercial outlets

• On 28 July, a mass media campaign to ensure people avoided consuming brand A chicken that they have already bought was launched throughout Spain.

There have been daily information updates sent to the Ministry of Health and all local epidemiological services, in order to evaluate the impact of the control measures undertaken.

Conclusion

In Spain, salmonella infection is the most common cause of bacterial gastroenteritis [1]. The outbreak reported here has been the largest outbreak of salmonella infection in recent Spanish history. The outbreak is attributable to the mass commercial sale of contaminated brand A chicken. Control measures were effective in preventing new infections from appearing, as demonstrated by the rapid decline in cases after the date of recall of brand A chicken.

References

1. Hernández-Pezzi GA, Torres P, Ordóñez, Cevallos C. Brotes de enfermedades transmitidas por alimentos. España, 1993-2002 (excluye brotes hídricos). Boletín Epidemiológico Semanal 2004; 12(52): 289-291.(http://193.146.50.130/htdocs/bes/bes0452.pdf)

Salmonellosis outbreak linked to carpaccio made from imported raw beef, Denmark, June-August 2005

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Published online 22 September 2005
(http://www.eurosurveillance.org/ew/2005/050922.asp#3)

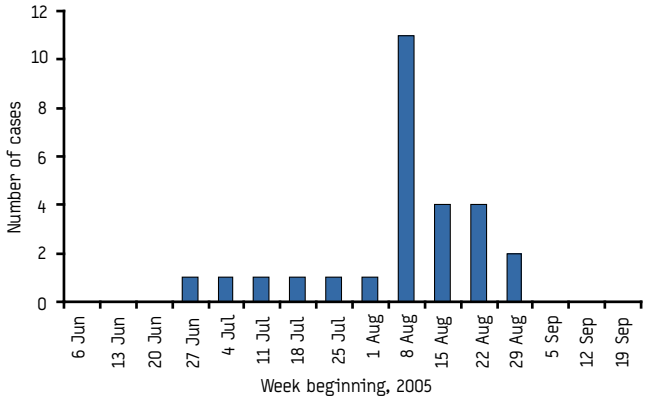
An outbreak of multiresistant *Salmonella* Typhimurium DT104 infections associated with beef imported from Italy has recently occurred in Denmark. So far, 22 laboratory confirmed cases have been detected via the national passive laboratory surveillance system, as well as a number of probable cases identified via patient interviews.

The Italian beef, from an Italian company, was imported into Denmark on two different occasions in summer 2005. One batch was tested on import and found to be positive for *S.* Typhimurium DT104, was immediately destroyed and therefore not consumed (Denmark has a zero-tolerance policy towards multiresistant DT104). The strain isolated from this meat matched the outbreak strain by all typing methods.

The second batch was used for carpaccio, a dish made from thinly sliced, marinated raw beef or veal, by a restaurant serving Italian food. Before their illness onset, most of the patients had eaten separately at the restaurant over a period of more than 5 weeks (from 16 July to 23 August). A few patients who were infected at the very beginning of the outbreak did not eat at the restaurant, and the source of their infections is unclear.

Figure

Outbreak curve - week of sample arrival at laboratory, *Salmonella* Typhimurium DT104 linked to carpaccio, Denmark



Almost all the patients remembered eating carpaccio from the restaurant buffet. As a raw food product, it is high-risk if contaminated with salmonella. The carpaccio was not available for analysis, but was identified as the probable source of the outbreak based on interviews with patients and the finding of the outbreak strain in the previously imported batch of beef. As a result of the epidemiological investigation, the beef from this batch was recalled by the importer, which at that time, had only been used at this one restaurant. The restaurant stopped using the beef from this batch at the end of August.

Several of the patients whose infections were laboratory-confirmed reported gastrointestinal symptoms in friends or family who also ate at the restaurant. Based on this knowledge, and taking into account the fact that the restaurant is popular and that the carpaccio was served over several weeks, the real number of patients infected at the restaurant may have been substantially higher.

The outbreak strain was defined by multilocus VNTR analysis (MLVA; VNTR stands for variable number of tandem repeats) in combination with pulsed-field gel electrophoresis (PFGE). MLVA is a PCR-based typing method using differences in the number of short tandem repeats in several loci of the bacterial genome. The method is routinely used for surveillance of *S.* Typhimurium in Denmark. The outbreak strain was phage type DT104 and was resistant to ampicillin, chloramphenicol, tetracycline, sulphonamide, spectinomycin, and streptomycin, with additional intermediary resistance to florfenicol. The PFGE type of the strain was distinct from the DT104 type commonly seen in Denmark. The strain isolated from the beef matched the outbreak strain both by PFGE, MLVA, phage type and resistance type.

The outbreak has been the subject of two alerts on the Rapid Alert System for Food and Feed (RASFF), a warning on the European Early Warning and Response System, and an Enter-net (http://www.hpa.org.uk/hpa/inter/enter-net_menu.htm) urgent enquiry. A short report will be published in EPI-NEWS , the Danish national infectious diseases bulletin. There is a possibility that other cases associated with this beef may be found in other European countries.

ISOLATION OF *CLOSTRIDIUM DIFFICILE* RIBOTYPE 027, TOXINOTYPE III IN THE NETHERLANDS AFTER INCREASE IN *C. DIFFICILE*-ASSOCIATED DIARRHOEA

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(http://www.eurosurveillance.org/ew/2005/050714.asp#1)

Clostridium difficile ribotype 027, toxinotype III, which has caused outbreaks in North America and has recently been reported in the United Kingdom, has been detected in the Netherlands. In the St. Jansdal Hospital in Harderwijk, in the east central region of the Netherlands, the incidence of *C. difficile*-associated diarrhoea (CDAD) increased from 4 per 10 000 patient admissions in 2004 to 83 per 10 000 in the months April to July 2005.

At 8 July 2005, 33 patients had been infected, and two of the 33 had died due to complications of CDAD and their underlying condition. Four patients had a relapse. The strain was further characterised as *C. difficile* ribotype 027 and toxinotype III by the Department of Medical Microbiology at the Leids Universitair Medisch Centrum (Leiden University Medical Center). As has been reported previously in Canada, physicians noticed an absence of clinical response to metronidazole, whereas the isolate was susceptible in vitro as determined by E-test (minimal inhibitory concentration less than 0.1 mg/L) [1].

The hospital has taken additional measures on top of the existing hospital guidelines for infection control of CDAD. These include isolation of all patients with diarrhoea, cohorting of all *C. difficile*-infected patients on a separate ward, limiting the use of certain antibiotics known to be associated with CDAD, like cephalosporins and clindamycin and banning all fluoroquinolone use.

A second cluster occurred in another hospital 30 km from the first hospital and is probably related to the outbreak in Harderwijk through a transferred patient. Five isolates have been obtained and were indistinguishable from the isolates from Harderwijk and the UK reference 027 strain (Dr Jon Brazier, Anaerobe Reference Laboratory, Cardiff, United Kingdom, personal communication, 7 July 2005).

A third cluster of 3 patients at a third hospital, not related to the first two outbreaks, has also been confirmed as ribotype 027 (toxin typing is still ongoing). Two more clusters in other hospitals and nursing homes elsewhere in the Netherlands are under investigation.

The incidence of CDAD in the Netherlands is low compared with many other countries. This is probably related to the relatively low use of antibiotics in the Netherlands. A Dutch interdisciplinary working group on antibiotic use has published guidelines on the internet [2]. Recently, an overview of this working group showed that the antibiotic consumption in the Netherlands is the lowest of all European countries [3]. Low antibiotic use correlates with less antibiotic resistance [4].

In response to the cases, the Landelijke Coördinatiestructuur Infectieziektebestrijding (national coordination centre for infectious disease control LCI) organised a meeting with experts in the fields of microbiology, infection control, and epidemiology. The team agreed to:

- publish the existing national hospital guidelines for infection control relevant for CDAD on the internet [5];
- increase diagnostic facilities and make them accessible for hospital microbiologists;
- register new incidents nationally;
- inform relevant professionals through the various scientific societies and by using the email service of the coordination centre (Inf@ct at http://www.infectieziekten.info);
- publish short Q&A for the public on the same website, and to begin developing Q&A for professionals;
- use national and international experience in drawing up guidelines for hospitals and nursing homes that are experiencing CDAD problems.

References

1. Pepin J, Valiquette L, Alary ME, Villemure P, Pelletier A, Forget K, et al. Clostridium difficile-associated diarrhea in a region of Quebec from 1991 to 2003: a changing pattern of disease severity. CMAJ 2004; 171(5):466-72. (http://www.cmaj.ca/cgi/content/full/171/5/466)
2. www.swab.nl [homepage on the internet]. Amsterdam: Stichting Werkgroep Antibiotica Beleid [Working Party on Antibiotic Policy]; 2005. Various guidelines available. (http://www.swab.nl)
3. SWAB. NethMap 2005 – Consumption of antimicrobial agents and antimicrobial resistance among medically important bacteria in the Netherlands. 47 pp. (http://www.swab.nl)
4. Goossens H, Ferech M, Vander Stichele R, Elseviers M, and the ESAC Project Group. Outpatient antibiotic use in Europe and association with resistance. Lancet 2005; 365: 579-587.(http://www.ua.ac.be/main.aspx?c=*ESAC2&n=21600)
5. Stichting Werkgroep Infectie Preventie. INFECTIEPREVENTIE MAATREGELEN BIJ CLOSTRIDIUM DIFFICILE [Draft hospital hygiene guidelines, Clostridium difficile]. Leiden: Stichting Werkgroep Infectie Preventie [Dutch Workingparty on Infection Prevention]; July 2005. (http://www.wip.nl/free_content/ClostriumdifficileWIP1.pdf)

LARGER THAN USUAL INCREASE IN CASES OF HANTAVIRUS INFECTIONS IN BELGIUM, FRANCE AND GERMANY, JUNE 2005

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(http://www.eurosurveillance.org/ew/2005/050721.asp#4)

An exceptionally large increase in hantavirus infections has been detected simultaneously in Belgium, Germany and France since spring 2005. From 1 January to 15 June 2005, 120 cases were reported in Belgium (Figure 1) and 115 cases in France (Figure 2). In Germany, 258 laboratory confirmed hantavirus cases were reported between 1 January and 30 June, and in contrast to previous annual trends, the increase in cases has occurred earlier in the year (Figure 3).

FIGURE 1

Human hantavirus cases, Belgium, 1 January 1996-15 June 2005

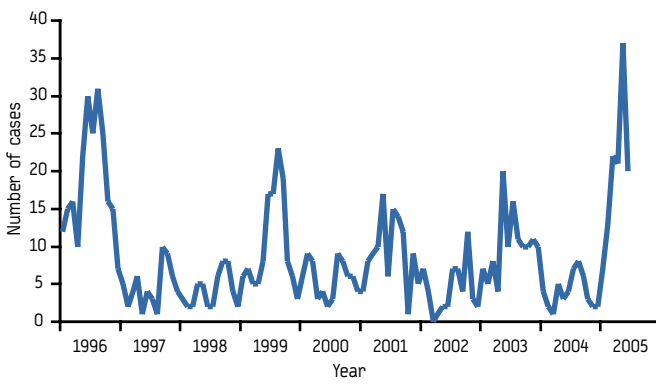


FIGURE 2

Human hantavirus cases, France, 1 January 2001-15 June 2005

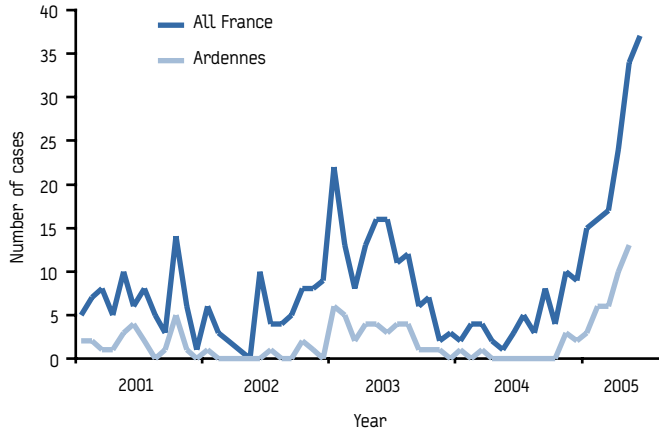
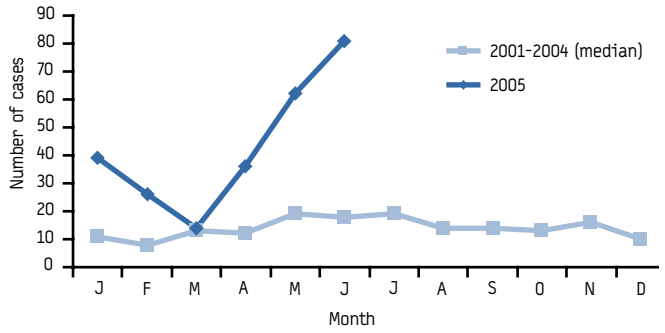


FIGURE 3

Human hantavirus cases (n=258), January-June 2005, compared with median number of cases in 2001-2004, Germany



The total number of cases for 2003 and 2004 was respectively 122 and 47 in Belgium, 128 and 55 in France. In Germany the number of reported cases for 2003 and 2004 from 1 January to 30 June was 72 and 64 respectively.

In 2005, most cases have been in men; the male:female sex ratio was 3.0 in Belgium, 3.4 in France and 2.5 in Germany. Their mean age was around 41 years in all 3 countries: 42.9 (range: 11-82 years) in Belgium, 42.8 (range: 16-83 years) in France and 40.9 (range: 5-75 years) in Germany. In Germany, most infections were caused by the hantavirus species Puumala (n=212, 82%), 5 infections (2%) were caused by Dobrava and for 41 cases the causative virus was not specified (16%).

Belgium

In Belgium, the area most affected in this outbreak is Luxembourg province, where there have been 34 cases, an incidence of 2.0/100 000 inhabitants, followed by Liège province (27 cases, 2.6/100 000 persons) and the Namur province (25 cases, 5.5/100 000 persons) (figure 4). A large number of cases in Liège province was observed in 2003. In Belgium, hantavirus epidemics are characterised by a minor spring peak and a major summer peak, and so a further increase in the registered number of cases is anticipated for 2005. According to local health professionals, part of this increase is due to a greater awareness among health professionals and a higher recourse to hantavirus testing. Risk factors for Belgian cases are not yet available.

Since 1980. over 1200 cases have been diagnosed in Belgium, and outbreaks of hantavirus infections in humans have been described in 1985, 1990, 1991, 1993, 1996, 1999, 2001 and 2003, with most cases having onset in summer. Known endemic areas are the provinces of Hainaut, Namur and Luxembourg.

In Belgium, the national reference laboratory for hantavirus infections and the IPH sentinel laboratory network report data to the Scientific Institute of Public Health (IPH).

France

Most of the 2005 cases in France are in the Ardennes (40 cases, 13.8/100 000 persons) and the Aisne administrative départements (18 cases, 6.9/100 000 persons) in northern France, bordering on Belgium. The département of Jura bordering on Switzerland is also an epidemic area, with 13 cases to 15 June 2005 (5.2/100 000 persons) (Figure 4).

Since 1980, over 1000 cases of hantavirus infection have been diagnosed in France. Hantavirus outbreaks have been described in 1985, 1990, 1991, 1993, 1996, 1999, and 2003, with most cases having onset in summer. The known endemic areas in previous years have been northeastern France, along the Belgian and German borders (in the administrative départements of Ardennes, Aisne, Nord and the administrative regions of Lorraine, Picardie and Franche-Comté). Clusters of hantavirus infections have rarely been reported in the Jura before 2005.

In France, the national reference laboratory for hantavirus infections is in charge of surveillance of human infections.

Germany

The increase of hantavirus infections in Germany between 1 January and 30 June 2005 has also been seen in federal states such as Nordrhein-Westfalen, Niedersachsen and Hessen, that have not had high hantavirus prevalence in previous years. The federal states most affected are Nordrhein-Westfalen (92 cases, 0.5/100 000 persons), Niedersachsen (51 cases, 0.6/100 000 persons), Baden-Württemberg (46 cases, 0.4/100 000), Hessen (23 cases, 0.4/100 000 persons) and Bayern (23 cases, 0.2/100 000 persons) (Figure 4).

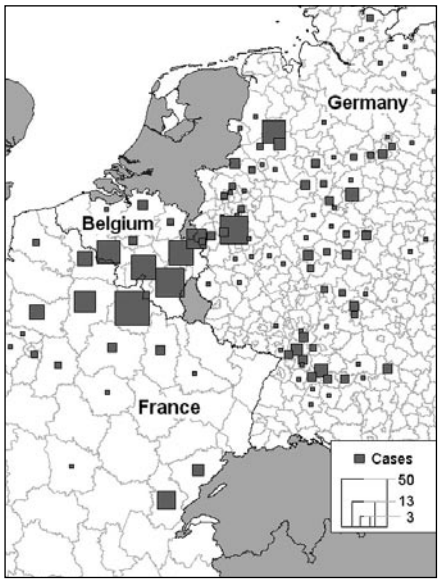
In Germany, the average incidence for hantavirus infections over the time period 2001-2004 was 0.25/100 000 persons. An increase in hantavirus infections was observed in 2002 and 2004. In both years the increase was due to outbreaks in a known endemic area of Baden-Württemberg, and an outbreak of 38 cases also occurred in Niederbayern in 2004. In Germany, the known regions with higher prevalence of human hantavirus infections are Schwäbische Alb in Baden-Württemberg and parts of Unterfranken in Bayern (Bavaria).

Hantavirus infection became a notifiable disease in Germany with the introduction of the Infektionsschutzgesetz (the Protection against Infection Act) in 2001. Reports of laboratory confirmed Hantavirus infections are transmitted to the Robert Koch-Institut (RKI) based on a case definition [1].

In many forest and agricultural regions of Belgium, France and Germany, a significant increase in the population density of rodents, especially voles, has been observed since the autumn of 2004, with no sign of this increase abating.

FIGURE 4

Geographical distribution of human hantavirus cases in 2005, from 1 January to 15 June for Belgium and France and 1 January to 30 June for Germany



Control measures and recommendations

An alert was sent out from France through the European Early Warning and Response System (EWRS) on 21 June, and subsequent messages were sent through this system from Germany (22 June) and Belgium (5 July).

General recommendations for avoiding hantavirus infection include preventing rodent access to houses or buildings. Any factor that could attract rodents inside, such as keeping uncovered food, should be avoided. When cleaning a previously unoccupied building where rodents may have settled, soil and surfaces should be sprayed with a disinfectant before dust is removed. People living in endemic areas should be informed about the risk factors and clinical symptoms of the disease, and advised to seek medical attention and report their risk exposure if they develop symptoms consistent with haemorrhagic fever with renal syndrome (HFRS).

A case-control study including Belgian and French cases identified the main risk factors as living less than 50 m from a forest and seeing rodents in or around the home, digging, spending long periods in the forest and being in contact with wood or disturbed earth or dust [2].

Information has been released to the general public in Liège province in Belgium, and general information is available on the website of the Scientific Institute of Public Health (IPH), Brussels (http://www.iph.fgov.be/epidemio) and the national reference laboratory's website (http://www.smd.be/rlvbd). An update of the situation on 24 June 2005 is also available on the IPH website [3]. Printed versions of the leaflet have been widely distributed and more copies can be obtained from the IPH.

In France, information about the disease and recommendations for avoiding infection have been issued in the national media to alert the resident population in affected areas and tourists. A leaflet is being printed by the ministry of health describing the clinical features of hantavirus infection and general recommendations protecting homes from rodents and avoiding infection when working or spending leisure time outdoors, and this will be soon available in camping sites, leisure centres and tourist information offices. The InVS has published a press release [4] and more information is available at the websites of the ministry of health (http://www.sante.gouv.fr) and the Institut Pasteur (http://www.pasteur.fr).

In Germany, a further increase in human cases is expected during the following months. Healthcare professionals around Germany are increasingly aware of the disease, and guidelines for preventing hantavirus infection are available on the RKI website [5]. In collaboration with the federal and local health departments, the RKI is conducting a nationwide case-control study to identify more specific risk factors for human hantavirus infections in Germany [6]. There are plans to trap rodents in affected areas to test for hantavirus infection.

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Germany: Muna Abu Sin and Judith Koch, Department of Infectious Disease Epidemiology, Robert Koch-Institut, Berlin; the Federal and Local Health Departments of Germany.

References

1. Falldefinitionen des Robert Koch-Instituts zur Übermittlung von Erkrankungs- oder Todesfällen und Nachweisen von Krankheitserregern Ausgabe 2004. Berlin: Robert Koch-Institut; 2004. (http://www.rki.de/cln_011/nn_225576/DE/Content/Infekt/IfSG/Falldefinition/IfSG/Falldefinition,templateId=raw,property=publicationFile.pdf/Falldefinition)
2. Crowcroft NS, Infuso A, Ilef D, Le Guenno B, Desenclos JC, Van Loock F, Clement J. Risk factors for human hantavirus infection: Franco-Belgian collaborative case-control study during 1995-6 epidemic. BMJ 1999; 318(7200):1737-8. (http://bmj.bmjjournals.com/cgi/content/full/318/7200/1737)
3. IPH. Seasonal increase of hantavirus infections in Wallonia. Infectious Diseases in the Spotlights 2005; 24 June. (http://www.iph.fgov.be/epidemio/epien/plaben/idnews/ID050624.pdf)
4. Recrudescence des infections à Hantavirus, Nord Est de la France. Point au 30 juin 2005. Institut de veille sanitaire, press release 30 June 2005. (http://www.invs.sante.fr/display/?doc=presse/2005/le_point_sur/hantavirus_300605/index.html)
5. Hantavirus-Infektionen. Robert Koch-Institut website. Updated 8 July 2005. (http://www.rki.de/nn_225576/DE/Content/InfAZ/H/Hantavirus/hantavirus.html)
6. Zum vermehrten Auftreten von Hantavirus-Erkrankungen. [note] Epidemiologisches Bulletin 2005; (27): 236. (http://www.rki.de/cln_011/nn_335538/DE/Content/Infekt/EpidBull/Archiv/2005/27__05,templateId=raw,property=publicationFile.pdf/27_05)

Large decrease in incidence of invasive *Haemophilus influenzae* b disease following introduction of routine vaccination in the Czech Republic

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Routine vaccination of infants against *Haemophilus influenzae* b (Hib) was introduced in the Czech Republic in July 2001, based on an updated regulation from the ministry of health. The vaccine schedule consists of four doses. Infants over 9 weeks of age are vaccinated with three doses of combined diphtheria, tetanus, pertussis (DTP) and conjugated Hib vaccine at 1-2 months interval, so that the third dose is given before the end of the first year of life. The fourth dose is given to toddlers aged 18-20 months.

A nationwide enhanced surveillance system for invasive diseases caused by Hib was established two and a half years earlier (January 1999). The system covered the entire population (10.3 million). Consequently, an excellent opportunity arose to assess the impact of routine vaccination against Hib. The case definition of invasive Hib disease in the Czech Republic includes meningitis, epiglottitis, bacteraemia and/or sepsis, pneumonia and arthritis. Based on laboratory results, cases of Hib are classified as confirmed, probable or suspected. After the introduction of routine Hib vaccination in infants, the surveillance was extended to include reporting of Hib vaccination failure, classified into three categories (as used in the United Kingdom): true vaccine failure (TVF), apparent vaccine failure (AVF) and possible vaccine failure (PVF). The Czech Republic participates in the European Union Invasive Bacterial Infections Surveillance Network (EU-IBIS, http://www.euibis.org/).

Routine notification of Hib meningitis began in the Czech Republic in 1987. The incidence of Hib meningitis for the entire population ranged between 0.5 and 0.7/100 000 person-years in the period 1987-1998. Enhanced surveillance since 1999 found a higher incidence of Hib invasive disease that year (Figure 1), but incidence of Hib meningitis remained similar to previously recorded notification data, indicating good quality of notification data. The total incidence rates of Hib invasive disease was observed as 1.0/100 000 and 1.1/100 000 during the two years before introduction of routine Hib vaccination. Incidence decreased after the introduction of routine Hib vaccination of infants in July 2001 and reached 0.5/100 000 and 0.2/100 000 in 2003 and 2004, respectively [1].

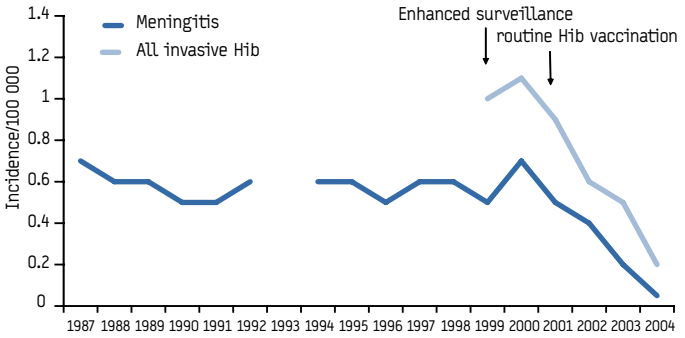
TABLE 1

Hib invasive disease, Czech Republic, 1999-2004. Age distribution and age specific incidence/100 000. Surveillance data

Age group	1999		2000		2001		2002		2003		2004	
	No.	Incidence	No.	Incidence	No.	Incidence	No.	Incidence	No.	Incidence	No.	Incidence
0-11 m	16	17.1	14	15.6	14	15.6	3	3.3	3	3.3	1	1.1
1-4 y	69	17.4	78	20.9	63	17.4	43	11.8	26	7.3	8	2.2
5-9 y	11	1.7	16	2.6	9	1.5	10	1.7	12	2.3	8	1.6
10-14 y	-	-	2	0.3	1	0.1	2	0.3	-	-	2	0.3
15+ y	5	0.1	7	0.1	7	0.1	8	0.1	11	0.1	4	0.05
Total	**101**	**1.0**	**117**	**1.1**	**94**	**0.9**	**66**	**0.6**	**52**	**0.5**	**23**	**0.2**

FIGURE 1

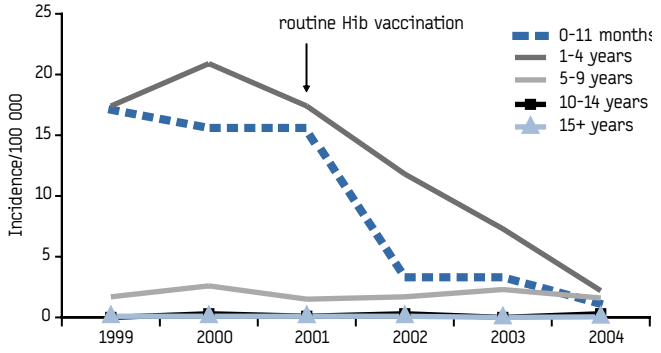
Invasive Hib disease in the Czech Republic, 1987-2004



In 1999 and 2000, the highest incidence rates of Hib invasive disease were found in the age groups 0-11 months (17.1/100 000 and 15.6/100 000, respectively) and 1-4 years (17.4/100 000 and 20.9/100 000, respectively). The most noticeable decrease in Hib incidence after the introduction of routine Hib vaccination of infants in July 2001 was found in the youngest age group, which is the population target group for routine Hib vaccination. The surveillance data for 2001 – 2004 show a clear downward trend in Hib incidence in the Hib vaccination target age group (0-11 months). Within two years after vaccine introduction, the incidence of Hib in children under 1 year of age decreased by 81% (from 17.1 to 3.3/100 000) and within 3 years by 94% (from 17.1 to 1.1/100 000) (Table 1, Figure 2). The highest age specific incidence remained in the age group 1-4 years, but decreased to 7.3/100 000 and 2.2/100 000 in 2003 and 2004, respectively.

FIGURE 2

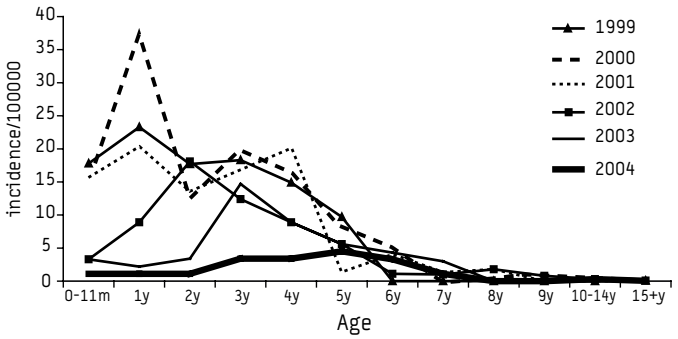
Age specific incidence of invasive Hib disease, Czech Republic, 1999-2004



For a better illustration of the effect of routine Hib vaccination, the Hib incidence rates at one year intervals of age for children 0-9 years old were calculated for the period 1999-2004. Figure 3 shows that when the routine Hib vaccination was introduced, the age specific incidence rates in 2001 were similar to 1999 and 2000, that is, before the introduction of routine Hib vaccination. The effect of routine Hib vaccination on Hib incidence in children began to be noticeable in 2002. The peak of incidence, which was observed in 1 year old children before routine immunisation (23.3/100 000 in 1999, 37.9/100 000 in 2000 and 20.3/100 000 in 2001) has moved gradually to an older age group, and has decreased: the peak of incidence was in 2 years olds (18.1/100 000) in 2002, in 3 years olds (14.7/100 000) in 2003 and in 5 years olds (4.5/100 000) in 2004.

FIGURE 3

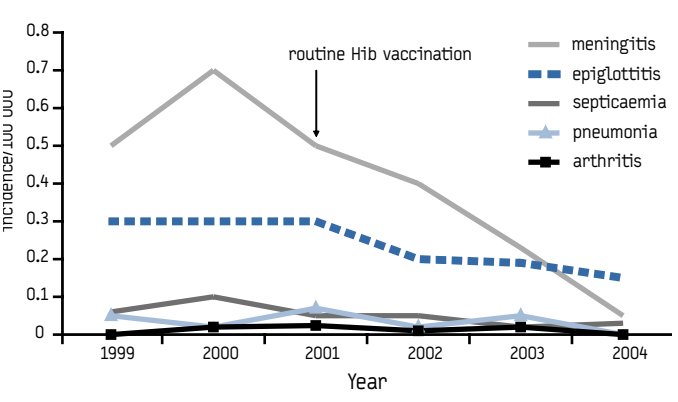
Age specific incidence of Hib invasive disease in one year intervals of age, Czech Republic, 1999-2004



Meningitis followed by epiglottitis was the most frequent clinical form of invasive Hib disease. Bacteremia and/or sepsis, pneumonia and arthritis were rare. No case of epiglottitis was reported in infants under 1 year of age over the whole period 1999-2004. The most noticeable decrease in Hib-related disease after the introduction of routine Hib vaccination was seen for meningitis (FIGURE 4). In 2004, the frequency of Hib meningitis fell to lower than that for epiglottitis (0.05/100 000 and 0.15/100 000, respectively).

FIGURE 4

Clinical symptoms of Hib invasive disease - all age groups, Czech Republic, 1999-2004



The total case fatality rate was 2.6% for the whole period (1999-2004). Differences in the case fatality rates between age groups and/or clinical pictures were not statistically significant (Table 2). Case fatality rate was stable by year.

TABLE 2

Case fatality rate of Hib invasive disease, Czech Republic, 1999-2004. Surveillance data.

Category of case fatality rate	Number of deaths/ number of cases	Case fatality rate (%)
Total	**12/453**	**2.6**
Hib meningitis	8/240	3.3
Hib epiglottitis	4/152	2.6
0-11 m	1/51	2.0
1-4 y	7/287	2.4
5-9 y	2/66	3.0
1999	1/101	1.0
2000	3/117	2.6
2001*	1/94	1.1
2002	2/66	3.0
2003	4/52	7.7
2004	1/23	4.3

* Routine vaccination introduced in July

Only six vaccine failures were observed in the period 2001-2004 among about 360 000 vaccinees: four TVF (3 in 2003 and 1 in 2004), one AVF (in 2001) and one PVF (in 2004).

Changes have been reported in other countries in the observed incidence of other types of Hib disease, and of disease in non-vaccinated age groups, after the introduction of vaccine [2,3]. During the first four years of routine Hib vaccination in the Czech Republic, however, neither Hib incidence in the age groups above 5 years, nor frequency of 'non-b' haemophilus disease increased.

Conclusions

The results of enhanced surveillance indicate a rapid decrease in Hib invasive disease incidence in the target age group following the introduction of routine Hib vaccination in infants in the Czech Republic in July 2001. The most noticeable decrease in Hib-related disease has been seen for meningitis. Hib vaccine failure has been very rare. Neither Hib incidence in the age groups above 5 years, nor frequency of 'non-b' haemophilus invasive disease increased after routine Hib vaccination was introduced.

References

1. Krizova P, Lebedova VV, Benes C. [The effect of routine vaccination in the Czech Republic on the incidence of invasive diseases caused by Haemophilus influenzae b]. Klin Mikrobiol Infekc Lek 2004; 10(3):118-123. [in Czech]
2. Hargreaves RM, Slack MP, Howard AJ, Anderson E, Ramsay ME. Changing patterns of invasive Haemophilus influenzae disease in England and Wales after introduction of the Hib vaccination programme. BMJ 1996; 312(7024): 160-1. (http://bmj.bmjjournals.com/cgi/content/full/312/7024/160)
3. McVernon J, Trotter CL, Slack MP, Ramsay ME. Trends in Haemophilus influenzae type b infections in adults in England and Wales: surveillance study. BMJ 2004; 329(7467):655-8. (http://bmj.bmjjournals.com/cgi/content/full/329/7467/655)

Death from rabies in a UK traveller returning from India

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A fatal case of imported human rabies has been reported in England. The patient was bitten by a dog while on holiday in Goa, India. The diagnosis of rabies was confirmed by the United Kingdom National Reference Laboratory for Rabies in Weybridge, Surrey [1].

In February of this year, a German woman died of rabies after spending four weeks in India in late 2004 [2], and in May 2004, a man in Bavaria, Germany died from a rabies infection that he acquired during his five month stay in India [3]. India reports at least 30 000 human deaths from rabies per year [4].

There are risks associated with travel to rabies endemic countries [5]. Travellers should avoid all unnecessary contact with animals. If bitten or scratched by a warm blooded animal they should wash the wound with plenty of soap and water and seek medical attention immediately, even if previously vaccinated. If they do not seek medical treatment while abroad, they should seek it when they return to their home country, even if it is some time after the event. Promptly administered post-exposure prophylaxis is extremely effective in preventing rabies. For people who have not received any rabies vaccine prior to a potential exposure, post-exposure prophylaxis consists of a dose of vaccine as soon as possible after the bite followed by four further doses 3, 7,14 and 30 days later. If the person has been previously vaccinated, fewer doses of vaccine are required. Human rabies immunoglobulin may also be given if the exposure is considered to be high risk.

Travel agents need to stress the importance of obtaining travel health advice well before holidays or trips overseas to ensure that the risks of all travel associated illness, not just rabies, have been explained.

In the United Kingdom, while rabies vaccine is not routinely advised for all travellers, pre-exposure immunisation is recommended for those living in or travelling for more than one month to rabies enzootic areas, unless there is reliable access to prompt, safe medical services; those travelling for less than one month in rabies enzootic areas but who may be exposed to rabies because of their travel activities; and those who have limited access to post-exposure medical services.

References

1. HPA. Case of imported rabies in the UK. Commun Dis Rep CDR Weekly 2005; 15(30): news. (http://www.hpa.org.uk/cdr/index.html)
2. Robert Koch-Institut. Informationen zu den Tollwutübertragungen durch Spenderorgane. Epidemiologisches Bulletin 2005; (8): 69 (http://www.rki.de/cln_006/nn_335538/DE/Content/Infekt/EpidBull/Archiv/2005/08__05,templateId=raw,property=publicationFile.pdf/08_05)
3. Summer R, Ross S, Kiehl W. Imported case of rabies in Germany from India. Eurosurveillance Weekly 2004; 8(46): 11/11/2004 (http://www.eurosurveillance.org/ew/2004/041111.asp#4)
4. World Health Organization. Immunization, Vaccines and Biologicals. Rabies vaccine. [Updated April 2003, cited 28 July 2005] (http://www.who.int/vaccines/en/rabies.shtml)
5. Fooks AR, Johnson N, Brookes SM, Parsons G, McElhinney LM. Risk factors associated with travel to rabies endemic countries. J Appl Microbiol 2003; 94 Suppl 1; 31-6.

MRSA infections increasing in the Nordic countries

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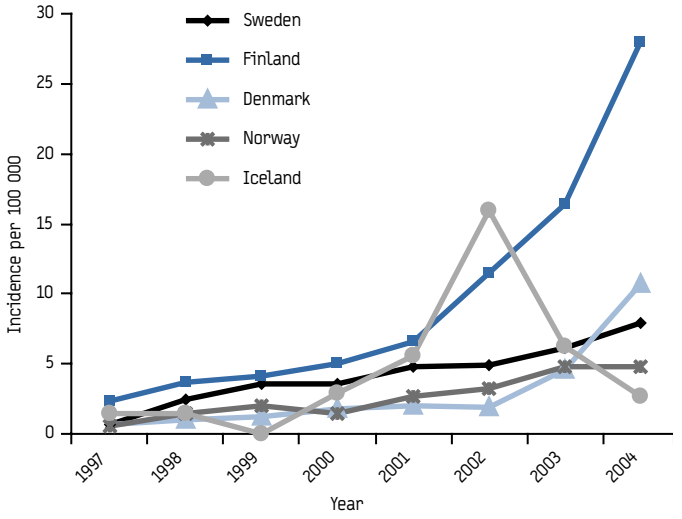
Although the incidence of methicillin-resistant *Staphylococcus aureus* (MRSA) infection is low in the Nordic countries (Denmark, Finland, Iceland, Norway and Sweden) compared with many other European countries, a significant increase has been observed in the last 3-5 years in all of these countries (Figure) [1].

FIGURE

Incidence of MRSA reported to the national surveillance institutes in the Nordic countries from 1997-2004. Denmark, Finland, Iceland and Sweden reported infections and colonisations; Norway only reported infections



In response to this threat to the regional healthcare systems, the Scandinavian Society for Antimicrobial Chemotherapy Working Party on MRSA (http://www.srga.org/SSAC/index.html) has published a report on the epidemiology, similarities and dissimilarities among the individual countries as well as suggestions for future initiatives [1].

The observed increase has occurred despite there having been no changes in the strict infection control policies enforced in the Nordic countries. These measures have successfully kept the incidence of MRSA infections at low levels (<1%) since the mid-1970s.

Until recently, MRSA was mainly a hospital problem, and patients with MRSA had almost all recently been in hospital outside the Nordic countries. Such patients were screened for MRSA when admitted to hospital after returning to their home countries and if positive, treated in isolation.

Major changes in MRSA epidemiology have been observed during the past five years in the Nordic countries:

1. Most MRSA patients do not have a connection to foreign healthcare facilities.
2. Onset of MRSA infections is no longer confined to hospitals.
3. A significant proportion of infections have community onset and there have been several cases where no risk factors for contracting MRSA can be identified.
4. The increase of MRSA in the community in otherwise healthy people has led to increased introduction of MRSA to hospitals, which has resulted in an increasing number of intra-hospital transmissions or outbreaks.
5. Outbreaks of MRSA have been reported from nursing homes in several regions.

Skin and soft tissue infections predominate in patients with community-acquired MRSA.

We have observed that the MRSA increase has been geographically uneven. It seems to be more limited in areas where strict MRSA infection control policies have been upheld, and in areas where there is vigorous eradication of MRSA carriage in community-acquired cases. This indicates that containment may be possible.

The observed increases in community- and hospital-acquired MRSA, demonstrate the need to adapt previously successful MRSA eradication strategies. However, it is important to consider potential disadvantages of additional infection control precautions. For example, it is known that contact isolation of patients can result in inadequate observation and treatment. For the successful control of MRSA, it is imperative that MRSA positive and negative patients are offered the same access to medical care. It is possible to care for MRSA positive patients without causing dissemination of MRSA, but, this often means more staff, as treatment of patients in contact isolation is labour intensive. In addition, to ensure compliance, the staff need continuous education in infection control precautions and repeated information on why MRSA control is so important.

The major challenge now is dealing with the increase in non-healthcare-associated MRSA. There is a general lack of knowledge of which precautionary measures are effective. Containment should be pursued, not only to avoid an increase in the incidence of MRSA, but also to maintain a full armament of therapeutic alternatives for the treatment of staphylococcal infections. The Scandinavian Society for Antimicrobial Chemotherapy believe that the Nordic tradition of conservative antimicrobial consumption, coupled with preferential prescribing of narrow-spectrum antibiotics, have been at least partly responsible for the successful combating of antimicrobial resistance development in the Nordic countries in general. Although we still do not have all the necessary knowledge, it is obvious that the healthcare authorities in the Nordic countries now need to take the threat of MRSA very seriously. If policy makers act now rather than later, lives and money can be saved.

Reference

1. Robert Skov, Hans Jørn Kolmos, Reijo Peltonen, Jaana Vuopio-Varkila, Hjordis Hardardottir, Olafur Gudlaugsson, Stig Harthug, Yngvar Tveten, Barbro Olsson-Liljequist, Christina Åhrén. The First Report of the SSAC Nordic Working Party on MRSA, Year 2004. Scandinavian Society for Antimicrobial Chemotherapy (SSAC); June 2005 (http://www.srga.org/SSAC/doc/2005/SSAC_MRSAreport_2004.pdf)

FIRST ISOLATION OF VACCINE-DERIVED POLIOVIRUS IN SLOVAKIA

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In April 2003, a vaccine-derived poliovirus Sabin 2 (VDPV) was isolated from sewage water in Vrakuna, a Bratislava city district in western Slovakia. The mutated strain was 87% genetically identical to the vaccine strain and differed from the wild poliovirus strain by 1.6%, and it was assumed that the strain isolated in sewage had already gained wild poliovirus neurovirulence and infectivity. Investigators hypothesised that this divergence could have been caused by immunodeficient people excreting vaccinal poliovirus Sabin 2. There were concerns that this modified virus could cause paralytic disease in people.

After active environmental surveillance was launched in October 2003, two more genetically mutated polioviruses from the vaccine strain Sabin 2 were isolated from sewage water samples in Skalica, a town 150 km west of Bratislava. These isolates also showed high divergence from the vaccine strain, and in both localities the strains had almost identical differences to the vaccine strain.

VDPV occurs as a result of excretion by immunodeficient patients, but also by healthy vaccinated people. Tests on 556 sewage water samples from eight different sewage system branch collectors were carried out, and 72 mutated strains of Sabin 2 derived from the oral polio vaccine were found. Isolated viruses were highly divergent: the level of genetic difference of the most recent ones from the wild poliovirus was 0.05%. Two of these isolates were less than 85% (84.9% and 84.4%) similar to the vaccine strain, which is the threshold theoretically beyond which a mutated strain gains the neurovirulent and infective characteristics of a wild poliovirus [1].

Investigation of the VDPV source

Additional samples from sewage water and stool samples from immunodeficient people in the Skalica area were tested to locate the VDPV excretors. The investigation focused on this local area because it had a relatively small sewage system serving fewer residents.

Test on samples from immunodeficient children were all negative. Testing of samples from immunodeficient people with B lymphocyte disorders, and from people who had moved to the area since 2001 is ongoing. All results have so far been negative.

Polio surveillance in Slovakia

Polio has been under surveillance in Slovakia for more than 50 years. In the past, polio epidemics occurred in 5 year cycles, the last being in 1953 before the start of mass vaccination with the inactive Salk vaccine in 1957.The live attenuated (weakened) oral polio Sabin vaccine was introduced in 1960, the year of the last reported poliomyelitis cases in Slovakia.

Monitoring the circulation of polioviruses by examining sewage waters began in Slovakia in 1970. Samples of polioviruses and other enteroviruses are collected throughout the year in selected drainage inlets to municipal sewage plants throughout Slovakia. To reinforce surveillance of high-risk population groups, sewage waters from all refugee centres providing accommodation and basic services for refugees coming to Slovakia mostly from Asia (e.g., Pakistan, Afghanistan or Chechnya) are regularly taken for examination. Wild poliovirus was last isolated from sewage water in 1972, and vaccinal polioviruses have been sporadically detected since 1972.

Vaccination and polio immunity

Inactivated (dead) parenteral polio vaccine has been used nationally since 2005. Vaccination coverage in children has been very high for the past 20 years, reaching almost 98%. The effectiveness of the vaccination policy has been regularly monitored by seroprevalence studies, the most recent being in 1997. The results showed that immunity of the Slovak population to all polio types was high. The proportion of individuals with poliovirus type 1 antibodies was 94%; with poliovirus type 2 antibodies, 97%; and with poliovirus type 3 antibodies, 97%. In children aged between 0 and 15 years, the proportion ranged from 98% to 100%.

Surveillance of acute flaccid paralysis in Slovakia

Reporting, examination and analysis of acute flaccid paralysis (AFP) has been done in Slovakia since 1970. No cases of AFP compatible with poliomyelitis were reported in Slovakia in 2004 or in previous years. The last case of paralytic poliomyelitis was recorded in 1960. No cases of postvaccinal paralytic poliomyelitis were reported in 2004 or in previous years. The temporary circulation of vaccinal polioviruses in the population as a result of short-term vaccination campaigns and vaccination of immunodeficient people with inactive polio vaccine have probably contributed to this situation.

Conclusions

A special epidemiological situation has occurred in Slovakia, where a poliovirus contained in a live polio vaccine used in Slovakia since 1960 has changed its genetic characteristics and differs only minimally from the wild poliovirus.

VDPV can cause serious neurological disease, particularly in immunodeficient people, and in groups of susceptible unvaccinated or incompletely vaccinated people. This is why monitoring of polio vaccination coverage in children as well as vaccination of susceptible people in places with incidence of VDPV is carried out. In Skalica, the live vaccine was immediately replaced with an inactivated (dead) vaccine, and since 1 January 2005, inactivated vaccine has been used nationwide.

Repeated VDPV isolation within a relatively short time period presents a problem for experts, particularly in regard to the Certification of Poliomyelitis Elimination in Slovakia as a part of the polio-free WHO European Region and other planned global activities to eradicate poliomyelitis in the world [2,3].

Acknowledgements

World Health Organization, for their assistance in carrying out the investigations.

References

1. WHO. Poliomyelitis, Dominican Republic and Haiti. Wkly Epidemiol Rec 2000; 75(49):397-9. (http://www.who.int/docstore/wer/pdf/2000/wer7549.pdf)
2. WHO EURO, Copenhagen, 2005: National Documentation for Certification of Poliomyelitis Eradication for the European Certification Commission for the years 2004, Slovak Republic
3. World Health Organization. Europe achieves historic milestone as Region is declared polio-free. Press release Euro 12/02, 21 June 2002. (http://www.euro.who.int/epri/main/WHO/MediaCentre/PR/2002/20020620_1)

Increased hantavirus infections in Luxembourg, August 2005

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The larger than usual increase in hantavirus infections in France, Belgium and Germany in 2005 that was recently reported [1] is also being observed in Luxembourg, which is surrounded by these three countries.

Since March 2005, 14 cases of *Puumala hantavirus* infection have been laboratory confirmed in Luxembourg, compared with 2 cases in 2003 and no cases in 2004. Two of these patients lived in towns on the borders with Belgium and France. The other 12 patients living in Luxembourg are clustered in the rural region of Mullerthal and surrounding areas in the east of the country, which suggests that the outbreak in Luxembourg is quite localised. The Mullerthal is an area characterised by beech forests and sandstone formations.

The mean age of patients is 41 years (range 21-70), similar to that observed in the neighbouring countries [1]. The male to female sex ratio is 1.9. Most cases so far confirmed occurred in June and it is not clear whether the incidence has already peaked.

Hantavirus is carried by bank voles and their population size is known to vary according to the availability of food. 2004 was a 'mast year' in Luxembourg for beech trees, a common broadleaf tree species. This means that there were unusually large seed crops, and is the most likely reason for an increase of the bank vole population this year. In the past, the peak of human hantavirus cases in the Ardennes region (which encompasses parts of northeastern France, Belgium, Luxembourg and Germany) have tended to occur in spring and summer, unlike the cases in northern Europe which tended to peak in autumn and early winter [2]. Given the direct epidemiological link between bank voles and hantavirus, it is quite likely that a higher incidence of human hantavirus infections are to be expected in other areas belonging to the western European broadleaf forests where beech mast years may also have occurred in 2004. Western European broadleaf forests are found in Austria, Belgium, the Czech Republic, France, Germany, Luxembourg and Switzerland [3].

In July 2005, all physicians and the general public in Luxembourg were informed by the Health Directorate's Health Inspection about the increased risks of hantavirus infections, and recommendations for avoiding infection were published [4-6].

References

1. Mailles A, Abu Sin M, Ducoffre G, Heyman P, Koch J, Zeller H. Larger than usual increase in cases of hantavirus infections in Belgium, France and Germany, June 2005. Eurosurveillance 2005; 10(7): 21 July. (http://www.eurosurveillance.org/ew/2005/050721.asp#4)
2. Vapalahti O, Mustonen J, Lundkvist A, Henttonen H, Plyusnin A, Vaheri A. Hantavirus infections in Europe. Lancet Infect Dis 2003; 3(10):653-61.
3. European Environment Agency. EEA data service: Digital Map of European Ecological Regions. (http://dataservice.eea.eu.int/atlas/viewdata/viewpub.asp?id=7) [accessed 25 August 2005]
4. Ministère de la Santé [Luxembourg]. Infections à hanta virus type puumala - Personnes à risque. Press release 22 July 2005. (http://www.ms.etat.lu/) [accessed 25 August 2005]
5. Ministère de la Santé [Luxembourg]. Infections à hanta virus type puumala - Information médecins. Press release 22 July 2005. (http://www.ms.etat.lu/) [accessed 25 August 2005]
6. Ministère de la Santé [Luxembourg]. Infections à hanta virus type puumala - Informations complémentaires. Press release 22 July 2005. (http://www.ms.etat.lu/) [accessed 25 August 2005]

Increase in viral meningitis cases reported in France, summer 2005

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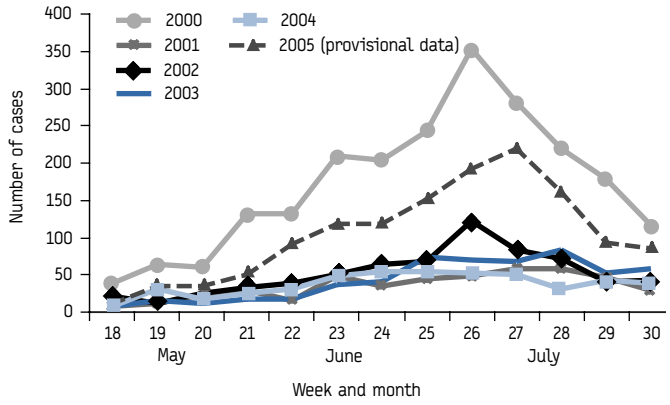
Since the end of May 2005, an increase in the number of viral meningitis cases has been observed, unevenly distributed throughout mainland France, with the following regions affected the most: Provence-Alpes-Côte d'Azur (southeast France), Ile de France (Paris and surrounding area), Rhône-Alpes (southeast France), Midi-Pyrénées (southwest France), et Haute-Normandie (northwest France) [1].

Information has been collected from virology laboratories participating in the enterovirus surveillance network, and although biased, they do not indicate an epidemic on the scale of the 2000 outbreak (Figure 1). However, the increase in case numbers is greater than that seen in 2001-2004. Numbers peaked in week 27, and a decrease has been seen since then.

Strains identified were mainly echovirus 30, coxsackievirus group B type 5, and to a lesser extent, echoviruses 13 and 6.

Figure 1

Positive LCR test results for enterovirus, comparison of 2005 with years 2000-2004, weeks 18-30, France

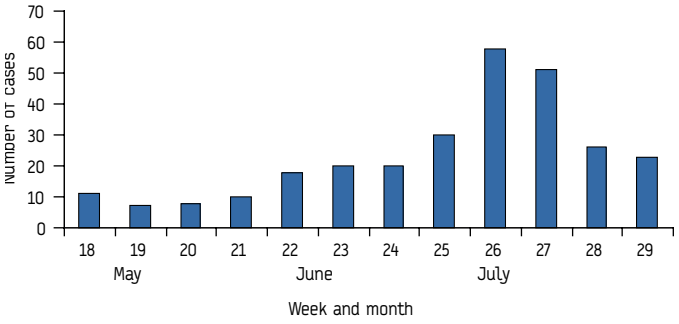


At the beginning of May (week 18), 11% of samples tested by ligase chain reaction (LCR) were positive for enterovirus, and this reached 60% in week 29 (18-24 July).

The activity registered by the virology laboratories reflects only a small part of the admissions to hospital emergency departments for viral meningitis, as not all patients are sampled for enterovirus testing. In Ile-de-France, admissions are monitored in 23 emergency departments. Figure 2 shows the weekly admissions from 1 May to 24 July 2005 (weekly 18 to 29) for viral meningitis: cases increased until week 26, then decreased.

Figure 2

Hospital admissions for viral meningitis, by week, in the 23 emergency service districts of Ile de France, 1 May-24 July 2005



A paper on the past 5 years of enterovirus surveillance in France will be published in the *Bulletin Epidémiologique Hebdomadaire* (http://www.invs.sante.fr/beh/default.htm) in October 2005, and a detailed report of the year 2005 is planned for publication in 2006.

Increases in incidence of echoviruses 13 and 30 in Europe were last mentioned in Eurousurveillance in 2002 [2].

This article has been translated and adapted from reference 1.

References

1. Institut de veille sanitaire. Epidémie de méningites virales en France. Le point au 1er août 2005. 1 August 2005. (http://www.invs.sante.fr/presse/2005/le_point_sur/meningites_010805/index.html)
2. Noah N, Reid F. Recent increases in incidence of echoviruses 13 and 30 around Europe. Eurosurveillance Weekly 2002; 6(7): 14/02/2002. (http://www.eurosurveillance.org/ew/2002/020214.asp#4)

Monitoring CA-MRSA infections in Slovenia

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In July and August 2004, an outbreak of furunculosis caused by methicillin-resistant *Staphylococcus aureus* (MRSA) occurred in members of a sports team in Slovenia. Fourteen of 27 exposed people developed symptoms (12 team members, a masseuse and a junior team member). MRSA (resistant to beta-lactam antibiotics and gentamicin only) was isolated from wound samples from 11 of the patients. This is the first identified outbreak of community-acquired MRSA (CA-MRSA) infection in Slovenia. The source of the infection was not found. The infection was probably spread by close contact between team members, such as sharing sports equipment and personal hygiene items, or during massages.

Two hundred and forty-six specimens were obtained from the patients' furuncles, skin and noses. Isolates obtained were resistant to penicillin, oxacillin, cefoxitin and gentamicin. Oxacillin resistance was confirmed by simultaneous detection of the *mecA* gene and *S. aureus* species-specific chromosomal DNA fragment (Sa442) with real-time PCR. Isolates were susceptible to, erythromycin, clindamycin, trimethoprim/sulfamethoxazole, vancomycin, rifampin, ciprofloxacin, teicoplanin, linezolid, mupirocin and fusidic acid. Pulse field gel electrophoresis (PFGE) typing was done on one isolate from each patient. The presence of *mecA* gene was confirmed. A comparison of PFGE patterns showed that 11 isolates were indistinguishable and one was different.

To prevent further transmission, the infected athletes were not allowed to attend team practices and matches, and the masseuse did not perform massages. The athletes were advised not to share sporting equipment or personal hygiene items, to keep wounds covered, maintain good personal hygiene and disinfect their hands. After these measures were implemented, further transmission ceased [1]. Infections were treated surgically, and with systemic clindamycin.

Community-acquired methicillin resistant *S. aureus* (CA-MRSA) infections have been reported worldwide since the 1990s, and in European countries since 2002 [2,3]. They are defined as MRSA infections in patients who do not have risk factors for MRSA such as recent hospital admission, operations, antibiotic administration, dialysis, drains or a nursing home stay.

CA-MRSA in Slovenia

Recent *S. aureus* isolates were re-examined to find out whether the CA-MRSA was present in Slovenia. At the Laboratory of Microbiology at the Kranj Institute of Public Health, which serves the Gorenjska region in western Slovenia (approximately 200 000 inhabitants), all 1203 *S. aureus* isolates obtained between 1 January 2000 and 29 February 2004 were tested for antibiotic susceptibility.

We reanalysed 79 MRSA isolates (one per patient). Nine MRSA strains with atypical susceptibility to antibiotics were defined in detail. Macrorestriction chromosome analysis with PFGE and tests for enterotoxin production were performed [4]. These 9 specimens, seven from patients and two from their relatives, came from outpatient clinics in the Gorenjska region. The predominant referral diagnosis was wound infection (6 patients). Six patients did not have risk factors for MRSA infection. All suspected CA-MRSA isolates were susceptible to more than five antibiotics in contrast to hospital-acquired MRSA (HA-MRSA), which were susceptible to 3 or 5 antibiotics. Eight of nine CA-MRSA isolates produced enterotoxins C or D or no enterotoxin, in contrast to our epidemic HA-MRSA, which produced enterotoxin A only [5]. Isolates suspected to be community acquired had different PFGE patterns compared with HA-MRSA isolates. Molecular testing revealed that the isolates belonged to the same clone, but that only two isolates displayed the characteristics associated with classical CA-MRSA (*mecA* gene, *SCCmec* type IV, Agr group III, Panton-Valentin leukocidin positive).

We concluded that the prevalence of MRSA was 6.6% of all *S. aureus* isolates collected during this period and that the prevalence of CA-MRSA was 0.17%. However, this is probably an underestimate, as we do not know how often physicians request laboratory investigations.

Recommendations for control of CA-MRSA in Slovenia

Currently, patients with community-acquired skin infections who are not at risk of MRSA infection are treated empirically with penicillin. Improper initial empirical treatment is known to be an important risk factor for unfavourable outcomes of hospital-acquired staphylococcal bacteraemia, which may also be relevant to community-acquired staphylococcal infections [6]. To prevent the clinical complications associated with CA-MRSA infection, physicians should consider changing the empirical management in areas with a high prevalence of CA-MRSA. These changes should include the following:

1. extended microbiological investigation (susceptibility to antibiotics, mecA gene, SCCmec typing, genotyping with PFGE, PVL-testing);
2. evaluation of empirical treatment of suspicious staphylococcal infections with beta-lactam antibiotics;
3. epidemiological follow-up including reporting.

Physicians should collect a sample from skin infections of patients with suspicious epidemiological histories, recurrent skin infections or poor responses to empirically prescribed antibiotics. Data collected by laboratory follow-up of resistance are the most appropriate basis for determining empirical treatment of infections.

In Slovenia, CA-MRSA belongs to the Group 2 infectious diseases, which are notifiable [7]. In June 2005, a working group of epidemiologists and microbiologists started to prepare criteria for diagnosing CA-MRSA and guidelines for reporting and follow-up of CA-MRSA. With systematic follow-up, we aim to establish how often CA-MRSA infections occur and whether it poses a threat to public health. The collected data will form a basis for directed measures aimed at reducing morbidity and mortality due to CA-MRSA infections. Reduced and more deliberate use of antibiotics is vital for reducing the prevalence of resistant bacteria in hospitals and community.

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References

1. Hocevar Grom A, Veninsek Perpar I. Spremenjena epidemiologija MRSA v Sloveniji [Changed epidemiology of MRSA in Slovenia]. In: Berger T, editor. 2. interdisciplinarni simpozij DDD, zdravje in okolje. Preventiva pred širjenjem zoonoz in drugih nalezljivih bolezni v okolju z mednarodno udeležbo. Zbornik referatov. Ljubljana: Slovenska veterinarska zveza, Sekcija za DDD in higieno okolja, ZZV Ljubljana, Slovensko društvo za bolnišnicno higieno, Veterinarska fakulteta, Medicinska fakulteta; 2004. p. 62–67.
2. Struelens MJ. How Europe is facing up to antibiotic resistance. Euro Surveill 2004; 9(1): 4. (http://www.eurosurveillance.org/em/v09n01/0901-221.asp)
3. Witte W, Braulke C, Cuny C, Heuck D, Kresken M. Changing pattern of antibiotic resistance in methicillin-resistant Staphylococcus aureus from German hospitals. Infect Control Hosp Epidemiol 2001; 22: 683–686.
4. Grmek-Kosnik I, Dermota U, Jutersek B. Proti meticilinu odporna bakterija Staphylococcus aureus domacega okolja (CA-MRSA) [Community-acquired methicillin-resistant Staphylococcus aureus]. Zdrav Vestn 2005; 74: 159–65.
5. Grmek-Kosnik I, Frei R, Dolenc M, Virnik B, Seljak M, Trampuz A. Isolates of Methicillin resistant S. aureus (MRSA) from stool of patients with acute gastroenterocolitis (AGEC) often produce enterotoxins. In: Schito GC, Piccinino F. 12th European Congress of Clinical Microbiology and Infectious Diseases Milan: Book of abstract. Milano: Clin Microbiol Infect 2002: 87.
6. Lodise TP, McKinnon PS, Swiderski L, Rybak MJ. Outcomes analysis of delayed antibiotic treatment for hospital-acquired Staphylococcus aureus bacteremia. Clin Infect Dis 2003; 36: 1418–1423.
7. Decree on communicable disease notification, Ministry of Health Republic of Slovenia, Ljubljana, Official Gazette of the Republic of Slovenia No. 112/2004. Ljubljana, 15 October 2004.

PREPARATIONS FOR IMPLEMENTING HUMAN PAPILLOMAVIRUS VACCINATION SHOULD BEGIN

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The World Health Organization held a meeting in Geneva on 14-15 April 2005 on the latest developments in human papillomavirus (HPV) vaccination [1]. The leading theme that emerged was how to implement within national programmes the concept of vaccinating adolescents both against a common sexually transmitted infection (STI) and against a chronic disease. HPV is the most common (often asymptomatic) STI in young people. The worst outcome occurs when infection with high risk (hr) HPVs progresses over about 20 years to anogenital cancer in 1/100 of infected individuals. This is the most important known cause of mortality from cancer among women worldwide (there are 239 000 deaths annually from cervical cancer alone). Fortunately, the incidence of other HPV-associated anogenital cancers is not very high, and most HPV-associated cancers can probably be prevented by HPV vaccination. The first generation of virus-like particle (VLP) vaccines against the most common hrHPVs (types 16 and 18) will probably be licensed in 2006 or 2007.

The fact that infection with hrHPVs (types 16,18,31,33,35,39, 45,51,52,56,58,59,66) is the major and necessary cause of cervical cancer and many anogenital cancers was underlined at the meeting in a presentation by Professor Harald zur Hausen (Deutsches Krebsforschungszentrum, Heidelberg), who also discussed the carcinogenic action of hrHPVs. The increase in sexual risk-taking behaviour since the 1970s has increased the prevalence of hrHPVs in women <25 years of age to 30% [2].

The ongoing work of assessing HPV type-distribution in young and old women and in cervical neoplasia cases on five continents was introduced by Dr Nubia Munoz and Dr Silvia Franceschi (International Agency for Research on Cancer, Lyon). The proportion of cervical cancer preventable by HPV16/18 vaccine was 80% in developed countries and 60%-65% in the developing countries. Developing countries might benefit from inclusion of some of the other hrHPV types (31,33,45,52,58) in the vaccines.

Tetravalent (HPV6/11/16/18, Merck & Co. Inc.) and bivalent (HPV16/18, GlaxoSmithKline Biologicals) vaccines are administrated in three doses during a conventional six month schedule. In phase II trials, both vaccines have induced 100-fold higher antibody levels than natural infections, and ≥90% vaccine efficacy (VE) against persistent HPV16 and HPV18 infections as outlined by Dr Elaine Esber (Merck) and Dr Gary Dubin (GlaxoSmithKline). Ongoing phase III trials will determine vaccine efficacy against HPV16/18 positive cervical intraepithelial neoplasia grade 2+ (CIN2+) and probably enable licensure of both the vaccines in 2006/7.

Dr Matti Lehtinen (Finland) described the enrolment of 7000 girls aged 16 and 17 years, in a population study of 20% of all the 15 to 25 year old women who have received the tetravalent or the bivalent HPV vaccine in the phase III trials. To assess direct, indirect and total long term effects of the intervention, 18 000 non-vaccinated women aged 18 and 19 years were also enrolled. Passive follow up of all 25 000 young women by the Finnish Cancer Registry will assess vaccine efficacy of the different HPV vaccines against cervical carcinoma in situ by 2015.

The effectiveness of hrHPV vaccination against cervical cancer in the developed and developing countries was considered by Dr Sue Goldie (Harvard University) and Dr Ewan Myers (Duke University). The duration of protection of HPV vaccination in adolescence is especially important if women acquire new infections later in life. In the worst case scenario, waning of immunity in 5 years would result in low or no reduction of cervical cancer incidence. On the other hand, assuming 10 to 30 year protection from HPV vaccines, a combination of HPV16/18 vaccination at the age of 12 years and a single lifetime hrHPV screening would most cost effectively decrease the incidence of cervical cancer by almost half, compared with no intervention or different (hrHPV screening or cervical smear screening) interventions.

In summary, even affluent societies do not offer many health services that adolescents recognise to be related to their health and wellbeing. Soon to be licensed HPV vaccines probably pave the way for a variety of interventions against common STIs in the young. In this context, promotion of condom use, and screening for Chlamydia trachomatis and hrHPVs in young adults can be highly synergistic with the herd immunity induced by HPV vaccination of the new birth cohorts entering sexually active life. It is clear that the appropriate ages for these interventions vary by continent, country and even within countries.

New work must be done to find out how not only the various stakeholders at the societal level but also adolescents and their parents can best become committed to the promotion of the sexual wellbeing of the young. Finland is starting a series of community randomised trials (preventive HPV vaccination, condom promotion and C. trachomatis screening) among 13 to 15 year olds, 15 to 17 year olds and 17 to 19 year olds in 2007, with the aim of tackling the silent STI epidemics of the young, most notably hrHPV.

The author is the Finnish principal investigator of both Merck and GSK phase III HPV vaccination trials.

References

1. WHO. WHO consultation on human papiloomavirus vaccines. Wkly Epidemiol Rec 2005; 80(35): 299-301. (http://www.who.int/wer/2005/wer8035.pdf)
2. Laukkanen P, Koskela P, Pukkala E, Dillner J, Laara E, Knekt P, Lehtinen M. Time trends in incidence and prevalence of human papillomavirus type 6, 11 and 16 infections in Finland. J Gen Virol. 2003 Aug;84(Pt 8):2105-9. (http://vir.sgmjournals.org/cgi/content/full/84/8/2105)

Erratum

Euro Surveill 2005;10(4-6):89

In the article 'Infectious diseases surveillance activities in the north of Portugal, during the EURO 2004 football tournament', in Figure 4, there should be no notification on the 10th day. The correct figure can be found and printed at http://www.eurosurveillance.org/em/v10n04/1004-224.asp

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Weekly, print and online versions available. In Danish and English.
http://www.ssi.dk

England and Wales
Communicable Disease Report Weekly (CDR)
Health Protection Agency
61 Colindale Avenue
London NW9 5EQ
Weekly, online only. In English.
http://www.hpa.org.uk/cdr

Finland
Kansanterveys
Department of Infectious Disease Epidemiology
National Public Health Institute
Mannerheimintie 166
00300 Helsinki
Monthly, print and online versions available. In Finnish.
http://www.ktl.fi/portal/suomi/julkaisut/kansanterveyslehti/

France
Bulletin epidémiologique hebdomadaire
Institut de veille sanitaire
12, rue du Val d'Osne
94415 Saint-Maurice Cedex
Weekly, print and online versions available. In French.
http://www.invs.sante.fr/beh/default.htm

Germany
Epidemiologisches Bulletin
Robert Koch-Institut
Presse, Oeffentlichkeitsarbeit, Bibliotheken
Nordufer 20
D-13353 Berlin
Weekly, print and online versions available. In German.
http://www.rki.de/DE/Content/Infekt/EpidBull/epid__bull__node.html

Hungary
Epinfo (Epidemiológiai Információs Hetilap)
National Center For Epidemiology
Gyali ut 2-6
1097 Budapest
Weekly, online version available. In Hungarian.
http://www.antsz.hu/oek/epinfo/szoveg/Heti2004/hetiindit04.htm

Ireland
EPI-INSIGHT
Health Protection Surveillance Centre (HPSC)
25-27 Middle Gardiner Street
Dublin 1
Monthly, print and online versions available. In English.
http://www.ndsc.ie/EPI-Insight/

Italy
Notiziario dell'Istituto Superiore di Sanità
Istituto Superiore di Sanità
Reparto di Malattie Infettive
Viale Regina Elena 299
I-00161 Roma
Monthly, online only. In Italian and English.
http://www.iss.it/publ/serie.php?id=4

Bolletino Epidemiologico Nazionale (BEN)
Istituto Superiore di Sanità
Reparto di Malattie Infettive
Viale Regina Elena 299
I-00161 Roma
Monthly, online only. In Italian and English.
http://www.epicentro.iss.it/ben/

Latvia
Epidemiologijas Bileteni
State Public Health Agency
7 Klijanu Street
1012 Riga
Online. In Latvian.
http://www.sva.lv/epidemiologija/bileteni/

Netherlands
Infectieziekten Bulletin
Rijksinstituut voor Volksgezondheid en Milieu
PO Box 1
NL-3720 Bilthoven
Monthly, print and online versions available. In Dutch, some summaries in English.
http://www.rivm.nl/infectieziektenbulletin/

Northern Ireland
Communicable Disease Monthly Report
Communicable Disease Surveillance Centre (Northern Ireland)
McBrien Building, Belfast City Hospital,
Lisburn Road
Belfast BT9 7AB
Monthly, print and online versions available. In English.
http://www.cdscni.org.uk/publications/

Norway
MSIS-rapport
Folkehelseinstituttet
Postboks 4404 Nydalen
N-0403 Oslo
Weekly, print and online versions available. In Norwegian.
http://www.folkehelsa.no/nyhetsbrev/msis/

Poland
Reports on cases of infectious disease and poisonings in Poland
Instytut Naukowo-Badawczy (National Institute of Hygiene)
ul. Chocimska 24
00-791 Warsawa
Fortnightly. In Polish and English.

Portugal
Saúde em Números
Direcção-Geral da Saúde
Alameda D. Afonso Henriques 45
1049-005 Lisboa
Sporadic, print only. In Portuguese.
Ministry website: http://www.dgsaude.pt/

Romania
Info Epidemiologia
Bulletin of the National Center for Surveillance and Control of Communicable Diseases, Institute of Public Health of Bucharest
1-3 Dr Leonte Street (Strada Dr.Leonte 1-3)
Sector 5 Bucharest Romania
Sporadic, print only.

Scotland
Health Protection Scotland Weekly Report
Health Protection Scotland
Clifton House, Clifton Place
Glasgow, G3 7LN
Scotland
Weekly, print and online versions available. In English.
http://www.show.scot.nhs.uk/scieh/wrhome.html

Slovenia
CNB Novice
Institut za varovanje zdravja Republike Slovenije
Center za nalezljive bolezni
Trubarjeva 2
Ljubljana
Monthly, online only. In Slovene.
http://www.ivz.si/ivz/aktualno/

Spain
Boletín Epidemiológico Semanal
Centro Nacional de Epidemiología - Instituto de Salud Carlos III
C/ Sinesio Delgado 6 - 28029 Madrid
Bi-weekly, print and online versions available. In Spanish.
http://193.146.50.130/htdocs/bes/bes.htm

Sweden
EPI-aktuellt
Smittskyddsinstitutet
171 82 Solna
Weekly, online only. In Swedish.
http://193.146.50.130/htdocs/bes/bes.htm

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