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Serogroup C meningococcal disease outbreak associated with discotheque attendance during carnival

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SUMMARY

In the week following a carnival during 19–24 February 1998, an outbreak of meningococcal disease occurred in a rural German county. The available isolates belonged to phenotype C:2a:P1.2,5 and were clonally related by pulsed-field gel electrophoresis. A case-control study was done to identify risk factors for the outbreak and to define possible vaccination target groups. Five persons aged 13–16 years who fell ill during 24–27 February were included in the study. Four of 5 cases and 10 of 32 controls visited local discotheques (OR = 8·8; $P = 0{\cdot}06$). Cases also visited discotheques more frequently than controls (χ^2 for trend, $P = 0{\cdot}0002$). Multiple discotheques during the carnival may have been predominant locations of transmission in this outbreak. Because this risk factor was limited in time, a mass community vaccination campaign was not initiated.

INTRODUCTION

Serogroup C meningococcal disease (SCMD) outbreaks are an emerging health problem [1, 2]. Outbreaks have been described in different settings, including universities, schools, correctional facilities, nightclubs, bars and a discotheque [3–10]. Factors which have been associated with serogroup C meningococcal infection are close contact with a case, preceding viral-like respiratory infections, crowded housing, alcohol consumption and active or passive smoking [4, 11–14]. We report a community outbreak of SCMD related to discotheque attendance during carnival and its implications for possible control strategies.

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METHODS

The outbreak

Between 10 December 1997 and 2 March 1998, six persons with meningococcal disease were reported to the health department of Rottal-Inn County, Germany. Five were reported between 25 February and 2 March 1998. One patient was 62 years old, five were aged 13–16 years. One, a 16-year-old boy, died. Close contacts of patients were given antimicrobial chemoprophylaxis. The county principal administrator closed all schools and day care centres during

2–6 March pending further assessment of the outbreak's cause.

Rottal-Inn is a rural German county with a population of 116496 inhabitants, including 9505 adolescents aged 12–18 years (Regional Statistical Office, Munich, 1997). During 1996 no case of meningococcal disease was reported to the Rottal-Inn health department. In 1997 only the case of serogroup C meningococcal disease mentioned above was reported. During the carnival season, 19–24 February 1998, many local residents attended carnival events and discotheques. A special bus transported discotheque patrons between heavily crowded discotheques. During the carnival week, all schools were closed from 21–24 February 1998. No other events where large numbers of persons met took place in the county in the 10 days before the outbreak.

Case finding and case definition

Persons living in Rottal-Inn and neighbouring counties were considered as cases if between 1 December and 30 March 1998 they had had (1) a positive blood or cerebrospinal fluid culture for *Neisseria meningitidis*, or (2) serogroup C polysaccharide antigen in the cerebrospinal fluid, or (3) clinical meningitis and antibiotic treatment started before blood or cerebrospinal cultures were taken. To establish the actual number of cases, hospitals and health departments in Rottal-Inn and neighbouring counties were contacted and questioned about suspected or confirmed cases of meningococcal disease. Identified cases or their close relatives were visited and interviewed about personal contacts and social activities.

Attack rates for the Rottal-Inn County population during carnival were calculated using census figures from 1997. Cases living in neighbouring counties were not included in the calculation of attack rates.

Case-control study

A case-control study was performed on 3 March 1998 to identify risk factors for the outbreak and to help suggest measures to limit the further spread of the outbreak such as defining target groups for vaccination programmes. Thirty-six controls aged 12–18 years were chosen randomly from the town registers of Rottal-Inn County. Information about places and events visited during 19–24 February was gathered using a standardized questionnaire. Cases or their relatives were interviewed face-to-face and controls were interviewed by telephone.

Microbiological methods

Local hospitals and laboratories sent strains isolated from eight patients (patients 1–6, 8, 9) to the German National Reference Center for Meningococci for further processing. One *N. meningitidis* isolate was cultured from a throat swab, 5 isolates were obtained from blood and 3 from cerebrospinal fluid cultures.

Serogroup confirmation of meningococcal isolates was performed by slide agglutination using monoclonal (serogroup B) and polyclonal (serogroups A, C, X, Y; Z, W135, 29E) antisera. Serotypes and serosubtypes of *N. meningitidis* strains were determined in whole-cell enzyme linked immunosorbent assay (ELISA) [15] using the currently available panel of monoclonal typing reagents (serotype-specific monoclonal antibodies 1, 2a, 2b, 4, 14, 15, 21, 22; serosubtype-specific monoclonal antibodies P1.1–P1.7, P1.9, P1.10, P1.12–P1.16).

For pulsed-field gel electrophoresis (PFGE), meningococcal cells embedded in agarose were lysed with lysozyme and proteinase K. Subsequently, the plugs containing chromosomal DNA were digested with the infrequent cutting restriction endonuclease *Nhe*I [16]. The resulting fragments were separated by PFGE. Strains were considered to be clonally related when the number of fragment differences of their PFGE patterns was three or fewer. This is consistent with a single genetic event [17].

Multilocus enzyme electrophoresis (MLEE) was performed at the WHO Collaborating Centre for Reference and Research on Meningococci in Oslo as described previously [18].

Statistical analysis

A univariate analysis was conducted. Odds ratios, exact 95% confidence limits, χ^2 for trend and Fisher's exact test were calculated using Epi Info, version 6.03 software.

RESULTS

Nine patients met the case definition (Fig. 1). These included a 16-year old Rottal-Inn boy who fell ill on 10 December 1997 (patient 1), the five initially

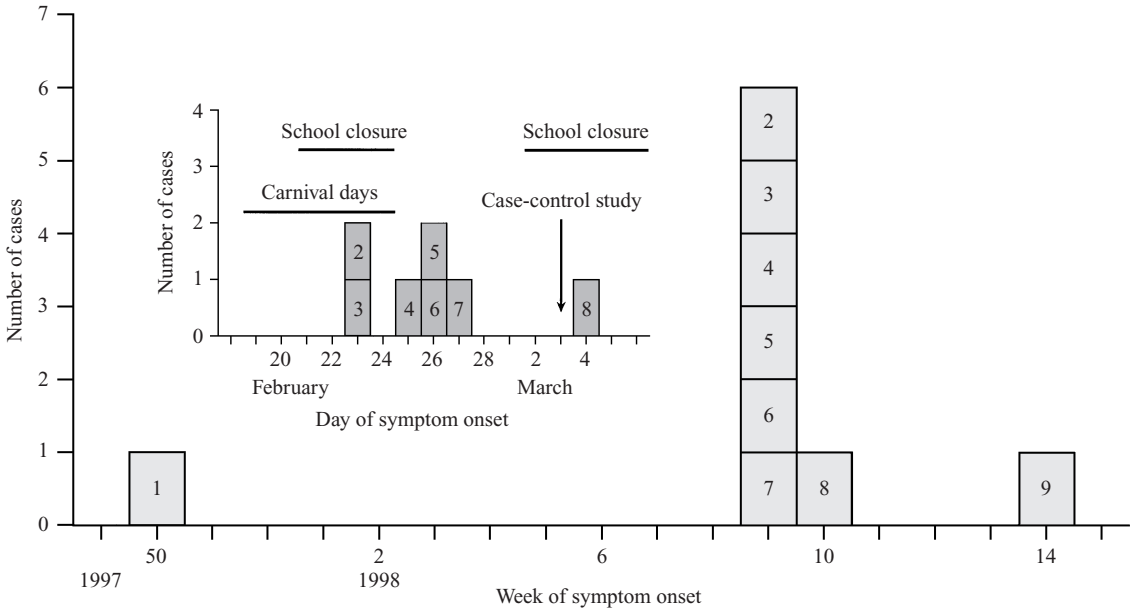

Fig. 1. Number of persons with serogroup C meningococcal disease in Rottal-Inn County, by date of symptom onset, December 1997–March 1998.

reported to the Rottal-Inn Health Department following carnival (patients 2–6), as well as a 15-year-old boy who lived in a neighbouring county but who regularly spent time in Rottal-Inn County and who fell ill on 27 February 1998 (patient 7). On 4 March 1998, a 2-year old girl living in Rottal-Inn County (patient 8) and on 30 March an 11-year old boy from a neighbouring county (patient 9) developed symptoms of SCMD. Patients 1–3, 5 and 6 had a positive blood culture, patients 6, 8 and 9 had a positive cerebrospinal fluid culture and patient 7 had serogroup C polysaccharide antigen in the cerebrospinal fluid. Patient 4 had clinical meningitis as well as petechiae and had been treated empirically with penicillin. From this patient *N. meningitidis* was isolated from a throat swab, white blood culture was negative and cerebrospinal fluid was not taken.

The nine isolates belonged to phenotype C:2a:P1.2,5. A clonal relationship between the isolates was shown by MLEE and PFGE. The isolates belonged to clone ET-15 of the ET-37 complex. In PFGE, isolates of patients 4 and 5 differed from the other six by one fragment.

The attack rate for the Rottal-Inn County population for the time from 1 December 1997 to 31 March 1998 was 6 cases per 100000 persons and 53 per 100000 persons for the 12–18-years age group.

The five persons aged 13–16 years who fell ill during 23–27 February were included in the case-control study (patients 3–7). Thirty-two of the 36 selected controls could be interviewed. None of the cases visited cinemas, theatres, youth centres, restaurants or rock concerts. Only one case had visited a private party. The patients included in the case-control study lived in five different communities and went to different schools. None knew each other, and none visited the same events or places other than discotheques during the 10 days preceding disease. Four of 5 cases and 19 of 30 controls reported visiting carnival events (OR 2·3; 95% CI 0·2–124·3). Cases and controls visited a similar number of carnival events (χ^2 for trend, $P = 0{\cdot}9$). Four of five cases and 10 of 32 controls visited Rottal-Inn discotheques (OR = 8·8; 95% CI = 0·7–452·5; $P = 0{\cdot}06$). Cases also visited these discotheques more frequently than controls (χ^2 for trend, $P = 0{\cdot}0002$) (Table 1). During carnival, the 4 cases went to 9 different discotheques a total of 12

Table 1. *Number of discotheque visits of cases and controls during carnival, Rottal-Inn County, 19–24 February 1998*

Number of discotheque visits	Cases ($n = 5$)	Controls ($n = 32$)
4	1	0
3	2	0
2	1	4
1	0	6
0	1	22

χ^2 for trend; P-value = 0·0002.

times. Only on one day did two patients attend the same discotheque. The 62-year-old patient not included in the case-control study (patient 2) had not left her house during carnival, but had a 20-year old household member who frequented discotheques during carnival. The mother of the 2-year-old child (patient 8) who developed symptoms of SCMD on 4 March 1998, had visited a discotheque on 27 February 1998.

DISCUSSION

An outbreak of SCMD occurred in Rottal-Inn and neighbouring counties following the carnival period. Discotheques were the likely locations of transmission for most patients. In no other places did large numbers of adolescents meet during the 10 days preceding the outbreak, the timing of the discotheque visits corresponded to the usual incubation period of 3–4 days for SCMD and the results of the case-control study showed a strong dose-response relationship between discotheque visits and SCMD. In addition, two case-patients who did not visit discotheques had household members who did. Transmission may have occurred in several different discotheques as only two case-patients went to the same discotheque on one day.

SCMD outbreaks related to a single tavern [8], discotheque [10], nightclub [6] and a university campus bar [9] have been described. These environments have been suggested to provide unique opportunities for nasopharyngeal acquisition of meningococci and, in a small number of susceptible hosts, subsequent invasive disease. Because only a small percentage of susceptible hosts develop invasive disease, the finding of seven persons with SCMD during or immediately after the carnival period suggests that a very large number of asymptomatic infections were acquired within a few days.

Recently described mathematical models of 'small-world' networks may provide insight into how this epidemic could have occurred [19]. These models indicate that two measures used to characterize connected networks influence the spread of infectious agents in a population: (1) the characteristic path length, or the average number of acquaintances to connect one person to another and (2) the cliquishness of the network, or the extent to which friends of one person are also friends of each other. Social networks are usually characterized by a high degree of cliquishness and long characteristic path lengths; however, the introduction of even a few random connections between cliques greatly decreases the characteristic path length. Because the mathematical models indicate that the time required for an infectious disease to spread throughout an entire population correlates to the characteristic path length, the introduction of a few random connections leads to a marked increase in the propagation speed of an infectious agent.

We hypothesize that the considerable number of random acquaintances that must have occurred at the crowded discotheques during carnival greatly increased the transmission speed of *N. meningitidis* in the Rottal-Inn community. In addition, the frequent travel between discotheques probably produced a condition where the many Rottal-Inn discotheques functioned as one virtual county-wide discotheque. In addition, the discotheques were favourable environments for transmission of *N. meningitidis* [6–10, 13, 14] and, thus, may have in effect increased its contagiousness.

Deciding when to initiate mass vaccination campaigns in the context of *N. meningitidis* outbreaks is one of the most difficult decisions in public health. A precise threshold for intervention has not been set. Consideration of the need for mass vaccination has been recommended when the age specific attack rate during a 3-month period is high [20] or when the attack rate in a 3-month period in a specific population exceeds 10 SCMD cases per 100 000 persons [21]. For community outbreaks, such as that which occurred in Rottal-Inn, a subset of the population at risk including all or almost all cases is usually defined for the calculations. The attack rate for 12–18-year-olds from 1 December 1997 to 31 March 1998 was 53 per 100 000. Nevertheless, we did not initiate a routine vaccination campaign. Based on the epidemiological evidence that indicated that crowded discotheques were the predominant locations of transmission, we believed that their decreased use after carnival greatly lowered the risk of acquiring *N. meningitidis* among the remaining susceptibles in the community. In fact, the two cases that occurred after the cluster immediately following carnival would not have been in a target vaccination group based on age criteria. Our results indicate that circumstances limited in time may be important for the development of a community-based SCMD outbreak. Our experience suggests that when these circumstances are no longer present, mass vaccination may not be required. Further outbreak investigations will be necessary to determine the utility of this approach for the management of SCMD outbreaks.

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