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An outbreak of meningococcal disease in Stonehouse: planning and execution of a large-scale survey

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SUMMARY

In November 1986 a large-scale survey was undertaken in the Gloucestershire town of Stonehouse during an outbreak of meningococcal disease due to group B type 15 subtype P1.16 sulphonamide-resistant strains. There were 15 cases in Stonehouse residents during the 4 years from April 1983, an annual attack rate of 56·5 per 100000. Four secondary cases occurred despite rifampicin prophylaxis. The objectives of this community survey were to investigate patterns of meningococcal carriage, transmission and immunity and to determine the proportion of non-secretors of blood group antigens in the Stonehouse population and amongst meningococcal carriers. A total of 6237 subjects participated including 75% of the 6635 Stonehouse residents. Over 97% of the participants provided all three of the requested specimens – nasopharyngeal swabs, saliva and blood samples.

The co-operation between the many organizations involved in the detailed

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preliminary planning was instrumental in the success of the survey; in particular the value of effective collaboration between Departments of Community Medicine and Microbiology and of the Public Health Laboratory Service network of laboratories in undertaking investigations of this size and type was clearly demonstrated.

INTRODUCTION

Since 1974 meningococcal disease due to group B type 15 p1.16 sulphonamide-resistant (B15.16R) strains has been encountered increasingly in several European countries including Britain (Poolman *et al.* 1986). It has been characterized by prolonged outbreaks with high attack rates in teenagers and young adults and a low carriage rate in community contacts (Cartwright, Stuart & Noah, 1986). These unusual features of meningococcal disease suggest that B15.16R strains have a greater virulence, longer duration of carriage and lower transmissibility than most other strains of meningococci and that they may not have circulated in the affected communities for 20 years or more.

The factors influencing susceptibility of the non-immune individual to meningococcal disease are not fully understood though recent studies have shown that a genetically determined inability to secrete ABO blood group antigens in saliva and other body fluids (non-secretion) is one such predisposing factor (Blackwell *et al.* 1986).

In south-west England both Gloucester and Plymouth Health Districts have experienced prolonged outbreaks of meningococcal disease due to B15.16R strains since 1981 (Cartwright, Stuart & Noah, 1986; Dawson, Rickard & Wilkinson, 1986). In Gloucester Health District (population 308500) 94 cases occurred between 1 October 1981 and 31 March 1987, an average annual attack rate of 5·5 per 100 000. Of these cases 15 occurred in the parish of Stonehouse (population 6635), a town in Stroud Local Authority District. Eleven of the 15 cases lived on one estate, which housed 26% of the town's population.

This report describes the outbreak in Stonehouse and the planning and execution of a large scale study which had the following principal objectives:

1. To measure the prevalence of nasopharyngeal carriage of, and immunity to, B15.16R and other strains of meningococci in the Stonehouse population by age, sex, school and area of residence during an outbreak of meningococcal disease caused by B15.16R strains.

2. To examine the hypothesis that B15.16R meningococci have a relatively low transmissibility and long duration of carriage.

3. To determine the proportion of non-secretors in the Stonehouse population and amongst meningococcal carriers.

The bacteriological findings are described in the companion article (Cartwright *et al.* 1987). The serological and secretor results will be described in further papers.

METHODS

Planning

Planning meetings were held during the summer and autumn of 1986. Six of the authors (J.S., K.C., D.J., N.N., R.W., C.B.) constituted the core planning team.

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The local planning team was made up of one nursing, one administrative and one finance officer, a general practitioner, a computer programmer, two head medical laboratory scientific officers (MLSOs), a county education officer, a community physician and three Public Health Laboratory (PHL) directors. The laboratory planning team consisted of the Directors and Head MLSOs of Gloucester, Manchester, Bristol and Hereford PHLs.

Timing

The duration of the survey needed to be as short as practicable so that an estimate of point prevalence of meningococcal carriage and immunity could be obtained. It was also considered important to complete the survey before the end of 1986 in order to study the community during a period of high disease activity. The two weeks beginning 3 November 1986 were chosen; sampling sessions were planned on weekday evenings and Saturdays at Stonehouse Health Clinic and at Stonehouse schools during the week days.

Sample size

A low carriage rate of B15.16R organisms (1% or less) was anticipated. The uneven distribution of the cases made it important to compare the prevalence of immunity, carriage rates and secretor state in different areas of the town. With the exception of infants who were excluded for practical reasons, all residents of Stonehouse Parish were invited to participate. All children and staff at Stonehouse schools, whether or not Stonehouse residents, were included so that comparisons could be made between schools. The total sample size was estimated as 7700 from Gloucestershire Family Practitioner Committee (FPC) records and school lists.

Specimens

Postnasal swabs were needed to determine rates of nasopharyngeal carriage of meningococci, saliva samples to determine secretor status, and blood samples to validate the secretor results and to detect specific IgM and IgG antibodies against B15.16R and other meningococci by ELISA tests.

Staff and equipment

A 'dummy run' was held at the Health Clinic. Estimates were made of the time to complete sampling, the staff and equipment needed, and costs. Calculations were based on a 90% attendance rate with a maximum throughput of 90 people per hour in each evening session and 60 per hour in each school session. Medical, nursing, laboratory, administrative and clerical staff were recruited and equipment was ordered pending approval of funding.

Ethical issues

Approval for the study was obtained from the District Ethical Committee and medico-legal advice was sought on wording of consent forms.

Publicity

Plans of the survey giving details of the reasons for its undertaking, the dates, and further general information were made widely available through the local media.

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Representatives of the national press and television were invited to a press conference on the first morning of the survey. This increased local awareness and allowed the survey to proceed thereafter without disruption from the media. The Press Office of the South Western Region Health Authority handled enquiries during the survey.

Implementation

The Meningitis Trust, a locally based charity, arranged for the separate delivery of two explanatory letters, the second with four registration cards, to each household in Stonehouse Parish. The registration cards included details of surname, forename, date of birth, sex, address, postcode, general practitioner, school and class (where relevant) and signed consent.

The 1985 electoral register was used to divide the town into 10 localities with approximately equal adult populations. Householders were asked if possible to attend Stonehouse Health Clinic with their completed cards on one of the 10 designated weekday evenings between 4 p.m. and 9 p.m. Children of pre-school age or at school outside Stonehouse were also invited to these evening sessions. Residents who were unable to attend during a weekday evening were asked to come between 9 a.m. and 6 p.m. on one of the two Saturdays.

The head teachers of the Stonehouse schools issued a letter to parents and a registration card to each pupil prior to the start of the survey. Pupils were asked to take the letter and card home, complete the card, obtain signed parental consent (if aged less than 16) and return the completed card to form teachers. Days and times for sampling at schools were agreed with head teachers.

Three teams, each consisting of one clerical assistant, three nurses, one MLSO and one phlebotomist, collected the specimens at each evening session; there were two teams at the schools. In addition there was an administrator assisted by volunteers to control flow of subjects to the teams, a medical officer to deal with emergencies and to assist in taking blood samples, the two co-ordinators (K.C. and J.S.) to supervise and to assist in specimen collection, a volunteer from the Red Cross to administer first aid, a clerical officer to enter registration data on to a computer and a driver to transport specimens. Each team had the use of three rooms – the first for checking data registration and for saliva collection, the second for throat swabbing and plating and the third for blood sampling.

Room One: A clerical officer helped to complete registration cards where necessary and checked that data entry was complete and legible. Postcodes were cross-checked against addresses on a Post Office list. Six adhesive labels bearing an identical number were used to identify the registration card and all the specimens from one subject. No other specimen identification system was used.

Saliva specimens (2 ml) were collected by a nurse. Subjects expectorated into 20 ml sterile Universal containers; plastic disposable pipettes were used when necessary in young children. A flow of saliva was stimulated by smelling fresh cut lemons. Samples were frozen to −20 °C within 3 h of collection and subsequently transferred to Edinburgh in insulated containers.

Room Two: A nurse swept the posterior pharyngeal wall behind the uvula with a fluffy charcoal swab. Pernasal swabs were used if necessary in small children. Plates were inoculated directly by an MLSO and taken by van in alternate 3 h batches to Gloucester and Bristol PHLs.

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Room Three: Blood samples were collected by a phlebotomist and doctor, assisted by a nurse, using the 'Vacutainer' system into EDTA tubes (0·5–1·0 ml) for red cell grouping and into sterile plain screwtop tubes (9–10 ml) for serology. Both sets of specimens were taken to Gloucester PHL for overnight storage at 4 °C and clotted specimens were then transferred to Hereford PHL for serum separation.

Data processing

Data recorded on the cards were transferred to two microcomputers (Apricot Xi) using a proprietary software package (ASPECT, Microft Corp.) and programs written by PHLS Computer Services. All records were subsequently recalled and checked.

Following verification the database was distributed on floppy diskettes to the Meningococcal Reference Laboratory, Manchester and the Department of Bacteriology, Edinburgh University for entry on to Apricot XEN microcomputers using the same software. Test results were added to a linked database and redistributed to the collaborators by the same means.

RESULTS

The outbreak of meningococcal disease due to B15.16R strains in Gloucestershire began in 1981; the first case in the parish of Stonehouse occurred in May 1983 and a further 11 cases were recorded here prior to the survey (Table 1). Three more cases occurred during the 4 months following the survey. The average attack rate in Stonehouse during the 4 years from 1 April 1983 was 56·5 per 100000 per annum. Two children died.

Despite the routine prescription of a 2-day course of rifampicin to household contacts at the time of illness of the index case, a high secondary attack rate was observed (Table 1). Three pairs of cases occurred in siblings, the father in one of these families also subsequently developing meningococcal disease. The average time between index and secondary cases was 124 days.

Stonehouse is situated three miles west of Stroud and nine miles south of Gloucester. The parish is largely residential, with mixed council and private housing and there is an industrial estate to the west of the town. For the purposes of analysis the town was divided into five areas using main roads, the railway line, and natural boundaries between the main housing estates (Fig. 1). Eleven of the cases lived in Park Estate at the time of their illness, three in Verney Fields, and one in Rosedale.

The town has state secondary, junior and infant schools, the latter two on the same central site. There are in addition two private junior schools, one private senior school and a small special school (Fig. 1). All of these schools except the state infant and primary school take most of their pupils from outside the town. Of the 11 cases of meningococcal disease in Stonehouse school-children eight attended the state infant and junior school, one was at the secondary school, one at the special school and one at a school outside Stonehouse (Table 1).

The population of Stonehouse according to FPC records in October 1986 was 6635 and estimates from the County Planning Department agreed within 2%. The population aged under 16 years comprised 27·4% of the total compared with an

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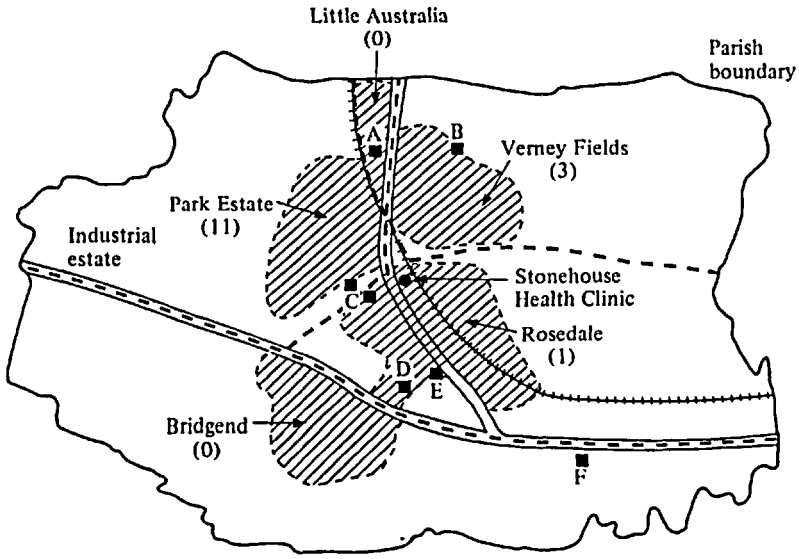

Fig. 1. Map of Stonehouse. Key to schools: A, Special; B, state secondary; C, state infant and junior; D, private junior (*a*); E, private senior; F, private junior (*b*). Numbers of cases of meningococcal disease are shown in parentheses. -----, Boundaries between areas.

Table 1. *Meningococcal disease in Stonehouse residents: case details*

Case number	Disease onset (month/year)	Age at onset	Sex	Area of residence	School	Organism isolated
1	5/83	46	M	PE	—	B15:P1.16R
2	3/84	10	M	PE	State junior	B15:P1.16R
3	9/84	12	F	PE	State secondary	B2bR
4	12/85	11	F	PE	Outside Stonehouse	CSF film positive
5	12/85*	6	M	PE	State infant	B15:P1.16R
6	1/86*	11	F	PE	Special	B15R
7	3/86**	5	M	PE	State infant	B15:P1.16R
8	6/86**	9	F	PE	State junior	B15:P1.16R
9	7/86*	32	M	PE	—	B15:P1.16R
10	7/86***	4	M	VF	—	Clinical diagnosis
11	7/86 (Died)	7	M	PE	State infant	Clinical diagnosis
12	7/86	6	M	VF	State infant	Clinical diagnosis
	Survey November 1986					
13	12/86 (Died)	7	M	PE	State junior	B15:P1.16R
14	12/86***	2	M	VF	—	B15:P1.16R
15	3/87	9	F	R	State junior	B15:P1.16R

*, **, *** indicate cases in same households.
PE, Park Estate; VF, Verney Fields; R, Rosedale.

estimated 20·7% in Stroud District; the proportions in Park Estate and Verney Fields were close to the mean for Stonehouse (Table 2). The proportion of people aged 65 and over was 17·6% in Stonehouse compared with an estimated 16·0% in Stroud District; of the five Stonehouse areas Park Estate had the highest figure at 20·6%.

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Table 2. *Population and age distribution in Stonehouse*

Population	Park Estate	Verney Fields	Little Australia	Rosedale	Bridgend	Total
Total	1729	1836	869	1423	778	6635
< 16 years (%)	26·3	27·9	31·8	26·8	24·9	27·4
> 64 years (%)	20·6	20·1	8·8	15·9	18·1	17·6

Sources: Glos. F.P.C.; Stroud District Council.

Table 3. *Housing, population density and occupation in Stonehouse*

	Park Estate	Verney Fields	Little Australia	Rosedale	Bridgend	Total
No. of houses	641	760	370	541	289	2610
Council-owned (%)	56·5	57·2	0	5·2	17·5	33·6
Mean no. people per house	2·7	2·4	2·4	2·6	2·6	2·5
Mean no. people per acre	26·6	24·6	28·8	14·6	12·1	20·0
Household heads with manual occupation (%)	77·5	74·1	51·7	46·5	65·0	63·7

Sources: Glos. F.P.C.; Stroud District Council; 1981 Census.

Boundaries of enumeration districts did not coincide with the boundaries of the designated areas. An analysis of the 1981 Office of Population Census and Surveys Small Area Statistics showed that in those enumeration districts most closely corresponding to Park Estate and Verney Fields there was a higher incidence of employed household heads in Social Classes IIIM, IV and V compared with the rest of Stonehouse (Table 3). Another socio-economic indicator, the proportion of council-owned housing, was 33·6% in Stonehouse at the time of the survey compared with 17·8% in Stroud District. Park Estate and Verney Fields contained 91% of council-owned housing in Stonehouse. There was little variation in the average number of people per house though Park Estate had the highest figure; estimates of population density within the residential parts of each area averaged 20 people per acre, the highest density being in Little Australia (Table 3).

During the fortnight of the survey 6237 persons attended for screening; 5006 were Stonehouse residents and the remaining 1231 were non-resident pupils and staff of Stonehouse schools. This represented a 75% attendance by the residents of Stonehouse and included 87% of the 1–19-year-olds (Table 4). The under 1-year-olds had not been invited but 16 (15%) were tested on request by their parents.

The lowest attendance from the five areas was 66% from Verney Fields (Table 5). All the schools had very high attendance figures including those pupils not living in Stonehouse. The overall percentage of school-children tested was 96% (Table 6). Technical failures in testing or refused consent were uncommon – 99·8% of the 6237 attenders provided a nasopharyngeal swab, a saliva sample was collected from 98·9% and a blood sample from 97·5% (Table 7). Even in the 1–4-year age group venepuncture was successful in 87%.

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Table 4. *Attendance of Stonehouse residents by age and sex*

Age in years	Males			Females		
	Population	Tested		Population	Tested	
		No.	(%)		No.	(%)
< 1	59	6	(10·2)	46	10	(21·7)
1–4	214	179	(83·6)	169	133	(78·7)
5–9	237	226	(95·4)	198	195	(98·5)
10–14	182	181	(99·5)	193	186	(96·4)
15–19	261	187	(71·6)	256	201	(78·5)
20–24	257	177	(68·9)	257	209	(81·3)
25–34	492	388	(78·9)	533	424	(79·5)
35–44	421	324	(77·0)	418	354	(84·7)
45–54	298	216	(72·5)	295	226	(76·6)
55–64	300	214	(71·3)	381	296	(77·7)
65+	475	268	(56·4)	693	406	(58·6)
Total	3196	2366	(74·0)	3439	2640	(76·8)

Table 5. *Attendance of Stonehouse residents by area*

	Population	Tested	
		No.	(%)
Park Estate	1729	1273	(73·6)
Verney Fields	1836	1216	(66·2)
Little Australia	869	750	(86·3)
Rosedale	1423	1226	(86·2)
Bridgend	778	541	(69·5)
Total	6635	5006	(75·4)

Table 6. *Attendance rate of children at school in Stonehouse*

School*	No. of children on school roll			Pupils tested	
	Total	Resident in Stonehouse			
		No.	(%)	No.	(%)
State infant/junior	443	428	(96·6)	441	(99·1)
Private junior (a)	49	4	(8·2)	49	(100·0)
Private junior (b)	194	19	(9·8)	180	(92·8)
State secondary	781	280	(35·9)	736	(94·2)
Private senior	337	14	(4·2)	331	(98·2)
Special	58	5	(8·6)	51	(87·9)
Total	1862	750	(40·3)	1788	(96·0)

* See Fig. 1.

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Table 7. *Sampling compliance in all attenders*

Age group in years	Total no. of attenders	Postnasal swab samples		Saliva samples		Blood samples	
		No.	(%)	No.	(%)	No.	(%)
1–4	324	324	(100·0)	296	(91·4)	282	(87·0)
5–9	537	535	(99·3)	531	(98·9)	515	(95·9)
10 & over	5376	5375	(100·0)	5340	(99·3)	5285	(98·3)
Total	6237	6234	(99·9)	6167	(98·9)	6082	(97·5)

Throughput sometimes reached the planned maximum of 90 subjects per hour but waiting rarely exceeded 15 min at any time. The school testing also kept to schedule.

One brief grand mal seizure was recorded in a boy with no history of fits; there were no other serious adverse events.

DISCUSSION

Interesting features of the Stonehouse outbreak include the localization of the disease within the town, the high attack rate in 5- to 9-year-old children and the high secondary attack rates.

It is difficult to obtain an accurate age–sex structure of any defined population between each 10-year census. Electoral registers are updated annually but provide only a list of residents eligible to vote. Consequently it was considered that the computerized FPC registration list, despite inaccuracies due to logistic delays, would provide the most accurate estimate of the Stonehouse population without conducting a separate household census. Although Stonehouse had a 7% higher proportion of under-16-year-olds than the mean for the Stroud District, the proportions of under-16-year-olds (and of 5- to 9-year-olds) in Park Estate and Verney Fields were close to the mean for Stonehouse so that the higher disease rates in these areas could not be explained by a predominance of the more susceptible age groups. The mean number of people per house was marginally higher in Park Estate but the population density was higher in Little Australia. The main associations found in this analysis were that the two areas in which all but one of the cases lived had considerably higher proportions of council-owned housing and of correspondingly lower social class in household heads than the rest of the town. Previous research has also shown an association between lower socio-economic indicators and meningococcal disease (Farries *et al.* 1975).

Rifampicin prophylaxis for household contacts of a case of meningococcal disease is recommended in Britain and North America in order to reduce secondary attack rates (PHLS, 1986; Centers for Disease Control, 1981). Compliance is likely to be good in the family members of a child with meningococcal disease. The high secondary attack rate reported here is disappointing and raises doubts about the effectiveness of rifampicin in preventing secondary cases. The long delay between index and secondary cases could be explained by the time taken for the virulent strain to be reintroduced into the family and thence to reach another susceptible family member; rifampicin may do

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no more than defer the onset of disease in close contacts of cases. The long interval between primary and secondary cases adds further weight to the hypothesis that B15.16R organisms are less transmissible than other strains of pathogenic meningococci.

Although there have been extensive studies of meningococci in military populations, particularly in the USA (Goldschneider, Gotschlich & Artenstein, 1969), no study on this scale has been previously undertaken to investigate meningococcal carriage and immunity in a civilian population. The relationship between non-secretion and meningococcal carriage has not been examined previously.

There was a very high overall attendance and nearly all who came to a sampling session provided all three requested samples. Several factors may have contributed to the high attendance. First, meningococcal disease can be frightening in its severity. It often begins suddenly in previously healthy individuals and may cause death within a few hours. A case in a school causes intense anxiety in pupils, parents and teachers, whereas cases occurring in infants generally receive less publicity. As several cases had occurred recently in school-children living in Stonehouse, parents and school-children were all well aware of the problem. Second, enlisting the support of the local and national media ensured that interest was maintained at a high level. Third, individual explanatory letters to each household accompanied by registration cards ensured that all individuals were aware that their active participation was being sought. Fourth, the provision of an adequate number of sampling sessions ensured that processing of subjects was rapid and that delays were minimal. The co-operation of the school authorities in this respect was invaluable in providing facilities for sampling at the individual schools and in releasing children class by class to attend.

The high compliance in providing all three specimens was primarily a reflection of the willingness of nearly all the subjects to help. An additional factor was the use of a single signed consent for all three tests. Separate rooms for the sampling procedures assisted in reducing anxiety and in improving compliance in blood testing. Only a few individuals declined to provide the full set of specimens. The main reason for not achieving even higher compliance for blood collection was occasional technical failure, particularly in very young children. Nevertheless it is possible, with the co-operation of parents, to collect blood samples from the majority of children as young as 1 year of age.

The survey was completed within the planned 2-week period, and continuing disease activity was confirmed by the occurrence of the three further cases.

Early recruitment of nurses, phlebotomists, technical, clerical and medical staff and their subsequent briefing meant that all the teams were well informed about the methods and objectives of the survey. Sharing of data in the collaborating centres was made possible by the use of compatible computer hardware and by the early involvement of PHLS Computer Services in the design of programs. The division of the laboratory work between four Public Health Laboratories proved essential in managing the large workload additional to the routine services. The high attendance and high compliance for all three sampling procedures emphasized the importance of detailed preliminary planning. Effective collaboration between the Departments of Community Medicine and Microbiology and within the network of PHLS laboratories was vital to the success of this survey.

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