 International Journal of Epidemiology 2001;**30**:1440–1446

INFECTIOUS DISEASES

Survival and sequelae of meningococcal meningitis in Ghana

Abraham Hodgson,[a] Thomas Smith,[b] Sebastien Gagneux,[b] Isaac Akumah,[a] Martin Adjuik,[a] Gerd Pluschke,[b] Fred Binka[a] and Blaise Genton[b]

Background Meningococcal meningitis epidemics are frequent in the Sahel zone of Africa but there is little information on the frequency of long-term sequelae. We analysed excess mortality in the two years following the 1997 epidemic in northern Ghana and carried out a case-control study to assess sequelae in the survivors.

Methods Two-year survival of 696 meningitis cases recorded at the War Memorial Hospital, Navrongo, was analysed using data from a demographic surveillance system. A structured questionnaire on disability and on psychiatric, neuropsychological and behavioural problems was administered to 505 of the survivors and 505 age- sex- and location-matched controls as well as to their respective relatives. Cases and controls underwent full neurological and neuropsychological examination and were evaluated for hearing impairment by audiometry.

Results Survival rates after the first month following the attack were similar in cases and controls. Hearing impairment was the major sequela, and was reported in 6 per cent of cases and 2 per cent of controls (odds ratio [OR] = 3.10; 95% CI : 1.48–7.09). Audiometry detected severe and profound hearing loss in the worse affected ear (⩾70 db) in 8/496 (1.6%) survivors but in only one control. Survivors of meningitis were more likely to suffer from feelings of tiredness (OR = 1.47; 95% CI : 1.03–2.11) and were more often reported by relatives to have insomnia (OR = 2.31; 95% CI : 1.17–4.82) and daily alcohol consumption.

Interpretation Meningococcal meningitis annually causes approximately 10 000 cases of deafness in sub-Saharan Africa; there is a need for early detection of affected survivors and promotion of simple hearing devices. There is a sizeable burden of depressive disorders secondary to meningitis which should be identified and looked after appropriately.

Keywords Sequelae, mortality, survival, meningitis, *Neisseria meningitidis,* deafness, epidemic, Ghana

Accepted 3 May 2001

Bacterial meningitis remains an important cause of morbidity and mortality, with the main aetological agents outside the neonatal period being *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Neisseria meningitidis*. *N. meningitidis* meningitis is of major importance in the meningitis belt of sub-Saharan Africa where it occurs in epidemics every 8–12 years. For example, in the 1996 epidemic in Burkina Faso, there were 42 129 cases with a case fatality rate (CFR) of 10 per cent; in 1997 in Ghana, there were 18 551 cases, of whom 8 per cent died.[1] The World Health Organization (WHO) estimates that globally, there are 500 000 cases of meningococcal meningitis each year with a CFR of 10 per cent. Of the cases, 250 000, and 27 000 of the deaths occur in the African region.[1]

Studies on survivors of bacterial meningitis have shown a wide range of neurological and audiological[2–11] as well as intellectual and behavioural sequelae.[7,9,10] *S. pneumoniae* has the highest rates of sequelae[4,12–15] as well as the highest case fatality.[11–13]

Many of the studies done specifically on meningococcal meningitis have been in developed countries.[16–18] In Africa, there have been very few studies on the sequelae of meningococcal disease and fewer still on the survivors of epidemics,[8,19] thus it is difficult to determine the magnitude of the social burden caused by these epidemics. Despite high background

[a] Navrongo Health Research Centre, Ghana.

[b] Swiss Tropical Institute, Basel, Switzerland.

Correspondence: Dr Blaise Genton, Swiss Tropical Institute, Socinstrasse 57, Postfach 4002 Basel, Switzerland. E-mail: Blaise.genton@hospvd.ch

levels of disability in affected communities, there has been only one sequelae study that included controls.[8] In uncontrolled studies it is not possible to attribute the disability observed to the meningitis *per se*.

There was a meningitis epidemic in the Kassena-Nankana district of Northern Ghana in 1997 in which 1396 cases with 65 deaths were recorded at the district hospital and three health centres.[20] As is typical of epidemics in the belt, where major epidemics usually last for two or three dry seasons dying out during the intervening rainy seasons,[21,22] there was a resurgence of the epidemic the next dry season; bacteriological analysis of samples from this resurgence indicated that the causal organism was *N. meningitidis* serogroup A subgroup III;[23] the predominant organism of meningococcal epidemics in Africa during the 1990s. We now report a case-control study of excess mortality, and neurological, psychiatric and neuropsychological impairment amongst survivors of the 1997 epidemic. The goal was to assess the social burden caused by the disease in Africa and to make recommendations for rehabilitation of survivors and prevention of further disability.

Methodology

Study area

The Kassena-Nankana district (KND) is within the guinea Savannah area of northern Ghana bordering Burkina Faso. It covers an area of 1675 sq km with a population of about 140 000. The entire population of the district are included in a demographic surveillance system, the Navrongo Demographic Surveillance System (NDSS), in which births, deaths, in and out migrations and other demographic parameters are recorded in a database and updated every 90 days.[24] Informed consent was obtained from chiefs and elders in the area before the study began.

Survival study

A list of all clinically/laboratory diagnosed meningitis cases at the district hospital during the 1997 epidemic was compiled from the hospital records. In accordance with WHO guidelines, a case was defined by sudden onset of fever and stiff neck, or fever and stiff neck and altered mental status. Cases were traced during mid-1999 to ascertain or confirm their identification numbers in the NDSS database and their vital status. All the patients identified were included in the analysis of survival, and for each of them two controls, matched for age (±10%) and sex, were also selected from the NDSS dataset of the population existing at the time of the epidemic. A geographical information system was used to locate the nearest eligible controls to the home of the case.

The NDSS was used to determine dates of death or migrations of both patients and controls.

Kaplan-Meier estimates of the survival curve were constructed separately for the patients and controls for the period up to the end of June 1999. Migrating out of the district during that period was treated as a censoring event.

Disability study

A simple random sample of the survivors of the epidemic who could be traced was included in the disability investigation. For each of these cases, a list of possible controls aged within 10 per cent of the age of the case and of the same sex as the case was generated from the NDSS dataset. They were ordered by their proximity to the compound of the case using a geographical information system. They were traced according to their order on the list; the chosen control being the person living nearest to the home of the case, who had not suffered meningitis and who was alive in mid-1999.

After informed consent had been obtained from both case and control and their relatives, an appointment was made with them and both were transported to the hospital on the appointed day with their relatives for investigation.

A trained research assistant who was blind to the case/control status administered a standard questionnaire to cases, controls and their relatives. The questionnaire was adapted from a previous one used in a national survey on disability,[25] translated from English into the two local languages (and back translated) then pre-tested among survivors of the 1998 outbreak, and modified accordingly. It comprised separate sections for the subjects and for their relatives. In the subject section, there was an open-ended question to those aged ⩾6 years about the general condition of their health over the past 2 years. Subjects and/or their relatives then answered a series of closed questions to determine if the respondents had any major disability (Table 1) and whether they were able to exercise daily living skills (feeding, cleansing, use of latrines, dressing, understanding simple instructions, expression of needs, speaking and movement in the home and community).

Subjects over 6 years old were then interviewed for symptoms of depression, anxiety, addiction and psychosis (Table 2). Depressive and anxiety symptoms were graded either as (1) occurring never or very rarely, (2) occurring sometimes, (3) occurring everyday. Possible addiction was assessed by

Table 1 Disability

	Case n (%)	Controls n (%)	χ^2	OR[a] (95% CI)	*P*-value
Difficulty in moving any part of body	22 (4.4)	24 (4.8)	0.03	0.89 (0.42–1.85)	0.86
Difficulty in seeing	42 (8.3)	42 (8.3)	0.02	1.00 (0.56–1.79)	0.89
Difficulty in hearing normal speech	31 (6.1)	10 (2.0)	9.8	3.10 (1.48–7.09)	0.002
Loss of feeling in hands or feet	1 (0.2)	0 (0.0)	0.0	–	1.00
Difficulty in speaking like person of same age	7 (1.4)	3 (0.6)	0.9	2.33 (0.53–14.0)	0.34
Episodes of fits in the last year	2 (0.4)	2 (0.4)	0.3	1.00 (0.07–13.8)	0.62
Any of the above disabilities	86 (17.0)	67 (13.3)	3.6	1.53 (0.99–2.39)	0.059

[a] Odds ratio.

Responses were obtained for all 505 cases and 505 controls.

Table 2 Self-reported psychiatric symptoms

	Case n (%)	Controls n (%)	χ^2	OR[a] (95% CI)	*P*-value
Depressive and anxiety symptoms					
Aches and pains	384 (81.9)	388 (82.4)	0.01	0.96 (0.63–1.46)	0.92
Tiredness or having little energy	188 (40.1)	163 (34.6)	4.60	1.47 (1.03–2.11)	0.03
Difficulty in sleeping	41 (8.7)	32 (6.8)	1.05	1.35 (0.79–2.33)	0.31
Tendency to cry	13 (2.8)	14 (3.0)	0.00	0.92 (0.37–2.27)	1.00
Suicidal tendencies	11 (2.3)	10 (2.1)	0.00	1.10 (0.42–2.89)	1.00
Tendency to worry a lot	70 (14.9)	75 (15.9)	0.21	0.88 (0.55–1.41)	0.65
Easily annoyed or irritable	65 (13.9)	63 (13.4)	0.01	1.05 (0.67–1.64)	0.91
Episodes of great fear or panic	51 (10.9)	36 (7.6)	3.21	1.59 (0.96–2.68)	0.07
Any one of the above symptoms	410 (87.4)	410 (87.0)	0.05	1.09 (0.67–1.77)	0.81
Psychotic symptoms					
Auditory hallucinations	3 (0.6)	3 (0.6)	0.17	1.00 (0.13–7.47)	0.68
Visual hallucinations	1 (0.2)	1 (0.2)	0.50	1.00 (0.01–78.50)	0.48
Persecutory delusions	5 (1.1)	3 (0.6)	0.13	1.67 (0.32–10.73)	0.72

[a] Odds ratio.

Responses were obtained for 469 cases and 471 controls.

asking about the subject's alcohol intake, and was graded as whether he/she (1) never took it or took it rarely, (2) took it sometimes, (3) took it daily. Psychotic symptoms were categorized as either present or absent. To assess neuro-psychological status, subjects above 6 years were also asked a series of questions to assess their orientation in time, place and sense of self. Memory was assessed by asking subjects to repeat the names of four items mentioned to them, to reverse the order of the names of four animals mentioned to them, to recall the names of these animals after an interval of about 15 minutes, and to remember what they had for breakfast the previous day. General knowledge was tested by asking the names of the chief of the locality, the head of state, and of the nearest big town. Those above 10 years were also asked to name the first head of state of Ghana, to explain a local proverb, and to carry out simple mathematical operations. These questions were adapted from questions generally used in medical practice to examine the mental status of patients.[26] Subjects who were deaf and dumb were not included in this section of the interview.

Relatives were interviewed in the absence of the subject to ascertain the presence of disabilities in subjects, to probe deeper into their psychiatric history, and to determine the severity of detected symptoms. This also afforded the opportunity to see how well the answers given by subjects correlated with those of the relatives. The relatives were asked whether they had noticed any changes in the general health status of the subject, and invited to grade any difficulties encountered by the subjects when compared to people of the same age. The relatives were also asked about presence of depression, anxiety, addiction, and psychotic symptoms in the subject (Table 3), and the playing

Table 3 Psychiatric symptoms reported by relatives

	Case n (%)	Controls n (%)	χ^2	OR[a] (95% CI)	*P*-value
Depressive and anxiety symptoms					
Shuts himself up alone	5 (1.0)	3 (0.6)	0.17	2.00 (0.29–22.11)	0.68
Difficulty in sleeping	35 (6.9)	18 (3.6)	5.95	2.31 (1.17–4.82)	0.01
Tendency to cry	13 (2.6)	8 (1.6)	0.84	1.71 (0.62–5.14)	0.36
Suicidal tendencies	6 (1.2)	3 (0.6)	0.44	2.00 (0.43–12.36)	0.50
Tend to worry	48 (9.5)	36 (7.1)	2.16	1.55 (0.88–2.77)	0.14
Easily annoyed or irritable	61 (12.1)	49 (9.7)	1.55	1.36 (0.85–2.21)	0.21
Any one of the above symptoms	95 (18.8)	80 (15.8)	1.94	1.35 (0.89–2.05)	0.16
Psychotic symptoms					
Strange behaviour	6 (1.2)	3 (0.6)	0.57	2.50 (0.41–26.25)	0.45
Auditory hallucinations	2 (0.4)	0 (0.0)	0.50	–	0.48
Visual hallucinations	3 (0.6)	2 (0.4)	0.00	1.50 (0.17–17.96)	1.00
Persecutory delusions	4 (0.8)	5 (1.0)	0.00	0.80 (0.16–3.72)	1.00
Hurt self	1 (0.2)	1 (0.2)	0.50	1.00 (0.01–78.50)	0.48
Refusal of food	2 (0.4)	3 (0.6)	0.00	0.67 (0.06–5.82)	1.00
Unprovoked fighting	4 (0.8)	5 (1.0)	0.00	0.80 (0.16–3.72)	1.00

[a] Odds ratio.

Responses were obtained for all 505 cases and 505 controls.

habits of subjects less than 15 years old, the schooling of subjects aged 6–18 years, and the occupation of subjects more than 10 years old.

During questionnaire administration, sensitive issues were explored only after a good relationship had been established. Confidentiality of the data obtained was assured.

After completion of the interview each subject underwent a neurological examination by a physician who was blind to the case/control status, and who tested for cranial nerve palsies, motor defects, cerebellar disorders and hydrocephalus. A Snellen chart placed at 6 m from the subject was used to test for visual impairment. Pure tone audiometry using a portable screening audiometer (Micromate, Denmark) was done after otoscopic examination for subjects ⩾5 years. Children under 5 years were tested by behavioural observation audiometry. Thresholds were determined at 500, 1000 and 2000 Hz and hearing loss was classified as described by Dodge *et al.*[27]

Completed forms were checked for completeness and internal consistency. Data were coded and double entered into a computer using FoxPro. Matched analysis was done using standard Mantel-Haenszel methods.

Results

Tracing

In all, 1077 admissions were recorded during the epidemic. Of these, 100 proved to be re-admissions of the same individuals, leaving a total of 977 distinct patients. A total of 792 (81%) of the 977 patients could be traced (Table 4). Sixteen of the people found denied that they had suffered from meningitis, and so they could have been misidentified.

Survival study

Identification numbers within the NDSS could be determined for 696 patients. A total of 44 of them (6.3%) and 15/1392 (1.1%) of the controls included in the survival analysis, died before June 1999. The deaths among these patients were predominantly during the period of the epidemic (Figure 1), with only 11 deaths more than one month after the admission date, and eight deaths more than 2 months after admission. In the controls there were no deaths within 2 months of the admission of the matched case, but the death rate subsequently was very similar to that of the cases, with a total of 15 deaths over the whole period. Log rank tests indicated that the difference in survival over the whole period was highly significant ($\chi_1^2 = 47.5$, $P < 0.0001$) but there was no significant difference in survival once the first month after admission was excluded.

Table 4 Results of tracing

	n	% of patients
Found alive (history of meningitis)	557	57.0
Found alive (no history of meningitis)	16	1.6
Dead	69	7.1
Absent	150	15.4
Could not be traced	185	18.9
Re-admissions	100	
Total admissions followed-up	1077	

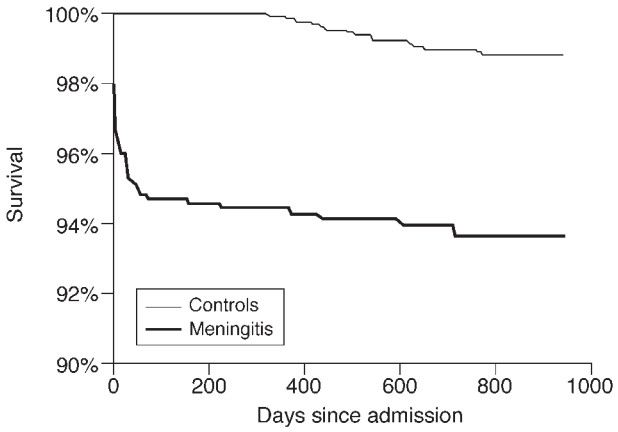

Figure 1 Kaplan-Meier survival curves

Disability study

Overall, 505 meningitis survivors were investigated for disabilities, along with their matched controls. The mean age for cases was 24.2 years (SD 15.4; range 2–73 years) and for controls 24.2 years, (SD 15.4, range 2–74 years). Thirteen (2.6%) of the cases were <5 years, 65 (12.9%) were 5–9 years, 174 (34.5%) were 10–19 years, 80 (15.8%) were 20–29 years, 85 (16.8%) were 30–39 years, 47 (9.3%) were 40–49 years, 29 (5.7%) were 50–59 years and 12 (2.4%) were ⩾60 years. The age distribution of the controls was not significantly different from that of the cases. In each group there were 225 males and 280 females.

Disability

Fifty-four per cent of cases and 47 per cent of controls reported a change in the general condition of their health over the past 2 years (Mantel Haenszel odds ratio [OR] = 1.46; 95% CI : 1.09–1.96) indicating that meningococcal meningitis was indeed associated with subsequent perception of ill health. Of the cases, 86/505 (17%), and 67/505 (13%) of the controls or their relatives mentioned at least one disability (OR = 1.53; 95% CI : 0.99–2.39) (Table 1). The only significant difference in the individual disabilities between cases and controls was in perceived hearing impairment which was found in 6 per cent of cases and 2 per cent of controls (OR = 3.10; 95% CI : 1.48–7.09). There were no statistically significant differences between cases and controls for other disabilities (Table 1). The only subject, a case, who was taking anticonvulsants, reported a fit within the past year despite the medication.

Performance of daily living skills

There was no significant difference between cases and controls in their ability to perform daily living skills, but the meningitis survivors tended to have more difficulties than controls. Ten per cent of cases versus 8 per cent of controls mentioned one or more limitations of function. Three cases were reported as not being able to keep themselves clean at all; one case was reported as not being able to understand simple instructions at all and two cases could not speak at all. Apart from a prevalence of 9 per cent in cases and 7 per cent in controls in inability to clean

self, no other disabilities occurred in more than 3 per cent of either group.

Psychiatric and neuropsychological status

Prevalence of depressive, anxiety and psychotic symptoms are presented in Table 2. Five cases and two controls reported daily aches and pains; three cases reported daily tiredness. Survivors of meningitis were more likely to suffer from feelings of tiredness or having little energy (OR = 1.47; 95% CI : 1.03–2.11). There was no other significant difference. A score was constructed by assigning 0 if the subject reported no or very occasional depressive or anxiety symptoms, 1 if he/she reported them to occur sometimes and 2 if he/she reported them to occur every day. The mean of this score was 1.77 for cases and 1.66 for controls. This difference was not statistically significant. Only four cases and three controls mentioned a daily intake of alcohol. There were no significant differences between cases and controls in their ability to answer the questions in the neuropsychological questionnaire.

Relative interview

In 152/505 (30%) instances relatives of cases had noticed a change in the health status of their relation, as compared to 112/505 (22%) of the families of the controls (OR = 1.70; 95% CI : 1.21–2.4). The finding is similar to rates reported by the patients themselves.

Cases seemed to be more involved in social activities than controls. Some 0.4 per cent of cases versus 2 per cent of controls were not participating in family activities and 4 per cent versus 7 per cent in community activities (OR = 0.38; 95% CI : 0.15–0.90). There was no significant difference between responses of relatives of cases and controls to the question about whether subjects had any difficulty. However in 8/16 cases the difficulties faced by the case were rated as severe by the relatives, as compared to 0/12 of the controls.

The prevalence of anxiety, depressive and psychotic symptoms reported by the relatives is shown in Table 3. The relatives claimed that cases tended to have more sleep difficulties than controls. With this exception the differences were not statistically significant, but in general, a greater proportion of cases than controls tended to have depressive and anxiety symptoms. Eight relatives of cases mentioned a daily alcohol intake versus one relative of a control ($P = 0.02$). One case shut himself up alone every day, one case had difficulty sleeping every day, one case tended to worry every day and two cases and one control were easily annoyed every day.

For each subject, assigning a score of 0 if he/she never had a depressive or anxiety symptom or had it very rarely, 1 if he/she had it sometimes and 2 if he/she had it every day, the mean score for cases was 0.34, and for controls 0.23 ($P = 0.14$).

There was no significant difference between cases and controls in employment, playing habits, or school attendance. Two per cent of 170 paediatric cases and 1 per cent of the corresponding controls did not play like children of the same age; 28 per cent of the 213 cases of school age and 27 per cent of their controls were not attending school. However, among those attending school, 12 per cent of cases had problems versus 6 per cent of controls (OR = 2.40; 95% CI : 0.79–8.70). Seventeen per cent of cases and 16 per cent of controls had repeated the previous year in school. Among adults, 264/280 (94%) cases as compared to 258/282 (92%) controls had inadequate income for their needs.

Clinical examination

All 505 cases and 505 controls were examined. Only one subject, a 6 year old case, was ill-looking. He had a history of convulsions and an extensive ulcer on the forehead due to repeated falls during attacks. There were no cases of hydrocephalus. One case had tremor which was associated with alcohol consumption.

The frequencies of cranial nerve abnormalities ranged from 0 per cent for nerves V, VII, XI, or XII to 13 per cent for nerve I. There was no significant difference between cases and controls, except for an excess of hearing problems in cases: severe and profound loss in the worst affected ear (⩾70 db) in 8/496 (1.6%) of cases versus 1/495 (0.2%) of controls (OR = 8.0; 95% CI : 1.07–355). Of those in whom hearing loss was detected, 8/32 (25%) of cases and 1/21 (4.8%) of controls had a severe or profound loss (Table 5).

There was a tendency for cases to have more hyperreflexia than controls; the difference was significant in the upper limbs (78/505 [15%] versus 55/505 [11%]; OR = 1.56; 95% CI : 1.04–2.37). All 1010 subjects had normal plantar reflexes.

All cases and controls had normal bulk and tone for all four limbs, as well as normal power in the upper limbs except for one case who had grade 4 power in the left upper limb, and another who had grade 3 power in the right upper limb. Only one case and two controls had power <5 in one of the lower limbs.

Discussion

The survival analysis showed that 94 per cent of the meningococcal meningitis cases that reported to the hospital survived the epidemic. After the acute phase, the death rate was very similar to that of the controls. These findings contrast sharply with the known outcome of meningitis caused by *Streptococcus pneumoniae* or *Haemophilus influenzae* which lead to much higher immediate case fatality rates and significantly higher long-term mortality.[11] Besides the potential difference in virulence of the micro-organism, it is likely that the age at which the meningitis occurs plays a role. Meningoccal meningitis occurs in older individuals, especially during epidemics, and they are likely to have a better ability to fight the disease, and hence its complications. Since the mortality attributable to meningoccal meningitis is mainly related to the acute episode, there is a need to focus the efforts on this phase in order to reduce the number of deaths, and probably also the incidence of sequelae. The

Table 5 Hearing assessment

Hearing class	Cases n (%)	Controls n (%)	Total
Normal hearing (<30 dB)	464 (93.5)	474 (95.8)	938
Mild loss (30–55 dB)	17 (3.4)	18 (3.6)	35
Moderate loss (55–70 dB)	7 (1.4)	2 (0.4)	9
Severe/profound loss (⩾70 dB)	8 (1.6)	1 (0.2)	9
Total	496	495	991

The frequencies quoted are for the worse affected ear.

19 subjects could not do the audiometry because they were generally too young to understand the procedure. They could all however hear normal speech.

community should be well aware of the forthcoming epidemic and of the importance of seeking medical care early in the course of the disease.

The survivors of meningitis were more likely to suffer ill-health than controls. The most dramatic impairment was in hearing loss where 1.6 per cent of cases and 0.2 per cent of controls had severe or profound hearing loss which confirms previous reports.[8,19] The excess risk of self-reported hearing impairment among the cases was 4 per cent, which implies that in Africa, where there are about 250 000 cases of meningococcal meningitis each year,[1] the disease leaves approximately 10 000 people in the region with impaired hearing. Besides treating acute episodes early, there is a need to improve the detection of cases with hearing impairment and to promote the distribution of simple hearing devices in communities where meningitis epidemics occur.

There was a general tendency for cases or their relatives to report disabilities or reduced performance of daily living skills more often than controls. All subjects with severe limitation of function (not being able to perform the skill at all) were meningitis cases, and although these form only one per cent of meningitis cases this is of importance since these people will need full support for their entire life. The use of more advanced tests for mental retardation and behavioural problems, which are difficult to apply in this setting, may have picked up more differences between the two groups.

There has been no attempt in the past to assess the incidence of psychiatric disorders attributable to an episode of meningococcal meningitis. We found that meningitis survivors reported more often feeling tired or having little energy than controls. Relatives mentioned also more sleeping difficulties and increased alcohol consumption for cases. The latter item was significantly different only from the relatives' perspective, which is expected for health problems associated with community stigma. There may have been some bias in reports of ill health following the meningitis episode since meningitis cases and their relatives were sensitized to the possibility of illness following the meningitis episode. However, in general, the fact that the relatives independently gave similar answers to those of the subjects provides some internal validation for the responses. Our findings suggest that an episode of meningitis can favour the occurrence of depressive symptoms and hence alcohol addiction. Since our psychiatric assessment was rather rudimentary, we may well have underestimated the true incidence of depressive illness secondary to meningitis. This problem can pose a substantial burden for the family and society in general. The challenge is to be able to identify the meningitis survivors who are affected, and to offer them decent specialized care.

Interestingly, the social integration of the survivors did not appear to have suffered, and indeed there may have been an increase in social activity, possibly because of reduced social pressure to engage in physical work. There was no relationship between having had meningitis in the past and employment or adequacy of income. This may be due to the general poverty in the area where almost everyone is engaged in subsistence farming. However, with increasing urbanization, social integration of survivors may become more of a problem.

We found no evidence of neuropsychological sequelae. It may well be that the assessment was not sensitive enough to detect small differences in memory, orientation, abstraction etc., although the questionnaire was based on validated instruments used in other developing countries.

The percentages of cases and controls attending school were similar, but in the cultural setting of Northern Ghana, the decision to send a child to school depends less on intellectual performance than on fee-paying ability and the demands of domestic and farming activities. However, cases tended to report more learning problems at school than controls.

Meningococcal meningitis has a lower case fatality rate than meningitis caused by other bacteria *like Streptococcus pneumoniae*.[13] The incidence of long-term sequelae, which in this study were mainly hearing impairment and depressive disorders, is also lower than that following *Streptococcus pneumoniae*, *Haemophilus influenzae*[11,13] or *Escherichia coli* meningitis. However, most of the previous studies did not include controls from the general population in their assessment, so the mortality rate and the incidence of sequelae may have been largely overestimated in the past, especially in unprivileged populations where other diseases such as cerebral malaria and otitis media lead to the same type of health problems. Even if the fraction of sequelae attributable to meningococcal meningitis is lower than expected, it still poses a sizeable burden of disease in communities where repeated epidemics occur involving up to 5 per cent of the population. The sequelae need to be recognized and looked after appropriately.

KEY MESSAGES

- There is little information on the long-term survival and frequency of sequelae from meningococcal meningitis because of the difficulties in adequately tracing cases and precisely evaluating the meningitis-specific disabilities in populations where several diseases can be responsible for the observed pathologies.
- Excess deaths occurred during the first 30 days after the onset of meningitis; survival rates after the first month were similar in cases and controls.
- Hearing impairment was the major sequela, and was reported in 6 per cent of cases and 2 per cent of controls. Survivors of meningitis were more likely to suffer from symptoms of depression and were more often reported by relatives to drink alcohol daily.
- Meningococcal meningitis is one of the important cause of deafness in sub-Saharan Africa ; there is a need for early detection of affected survivors and promotion of simple hearing devices. There is a sizeable burden of depressive disorders secondary to meningitis which should be identified and cared for appropriately.

Acknowledgements

We would like firstly to acknowledge the willing participation of the subjects and their relatives. Technical assistance was provided by Pierre Ngom, Elizabeth Awine, Dickson Abanimi, Boniface Atosona and Genevieve Avogo. Nathan Mensah was responsible for data management, Mitchell Weiss assisted with questionnaire design, Kwaku Enos assured the co-operation of the health services while Marcel Tanner and Alex Nazzar ensured excellent institutional support. The study was financed by the Meningitis Research Foundation, and had ethical approval from the Ghana Ministry of Health.

References

[1] Tikhomirov E, Santamaria M, Esteves K. Meningococcal disease: public health burden and control. *World Health Statist Q* 1997;**50:** 170–77.

[2] Pomeroy SL, Holmes SJ, Dodge PR, Feigin RD. Seizures and other neurologic sequelae of bacterial meningitis in children. *N Engl J Med* 1990;**323:**1651–57.

[3] Ford H, Wright J. Bacterial meningitis in Swaziland: an 18 month prospective study of its impact. *J Epidemiol Community Health* 1994; **48:**276–80.

[4] Carroll KJ, Carroll C. A prospective investigation of the long-term auditory-neurological sequelae associated with bacterial meningitis: a study from Vanuatu. *J Trop Med Hyg* 1994;**97:**145–50.

[5] Choo KE, Ariffin WA, Ahmad T, Lim WL, Gururaj AK. Pyogenic meningitis in hospitalized children in Kelantan, Malaysia. *Ann Trop Paediatr* 1990;**10:**89–98.

[6] Zaki M, Daoud AS, ElSaleh Q, West PW. Childhood bacterial meningitis in Kuwait. *J Trop Med Hyg* 1990;**93:**7–11.

[7] Salih MA, Khaleefa OH, Bushara M *et al.* Long term sequelae of childhood acute bacterial meningitis in a developing country. A study from the Sudan. *Scand J Infect Dis* 1991;**23:**175–82.

[8] Smith AW, Bradley AK, Wall RA *et al.* Sequelae of epidemic meningococcal meningitis in Africa. *Trans R Soc Trop Med Hyg* 1988;**82:**312–20.

[9] D'Angio CT, Froehlke RG, Plank GA *et al.* Long-term outcome of *Haemophilus influenzae* meningitis in Navajo Indian children. *Arch Pediatr Adolesc Med* 1995;**149:**1001–08.

[10] Grimwood K, Anderson VA, Bond L *et al.* Adverse outcomes of bacterial meningitis in school-age survivors. *Pediatrics* 1995;**95:** 646–56.

[11] Goetghebuer T, West TE, Wermenbol V *et al.* Outcome of meningitis caused by *Streptococcus pneumoniae* and *Haemophilus influenzae* type b in children in The Gambia. *Trop Med Int Health* 2000;**5:**207–13.

[12] Daoud AS, al-Sheyyab M, Batchoun RG, Rawashdeh MO, Nussair MM, Pugh RN. Bacterial meningitis: still a cause of high mortality and severe neurological morbidity in childhood. *J Trop Pediatr* 1995;**41:** 308–10.

[13] Baraff LJ, Lee SI, Schriger DL. Outcomes of bacterial meningitis in children: a meta-analysis. *Pediatr Infect Dis J* 1993;**12:**389–94.

[14] Jadavji T, Biggar WD, Gold R, Prober CG. Sequelae of acute bacterial meningitis in children treated for seven days. *Pediatrics* 1986;**78:** 21–25.

[15] Shaltout AA, Auger LT, Awadallah NB *et al.* Morbidity and mortality of bacterial meningitis in Arab children. *J Trop Med Hyg* 1989;**92:** 402–06.

[16] Schildkamp RL, Lodder MC, Bijlmer HA, Dankert J, Scholten RJ. Clinical manifestations and course of meningococcal disease in 562 patients. *Scand J Infect Dis* 1996;**28:**47–51.

[17] Naess A, Halstensen A, Nyland H *et al.* Sequelae one year after meningococcal disease. *Acta Neurol Scand* 1994;**89:**139–42.

[18] Ellsworth J, Marks MI, Vose A. Meningococcal meningitis in children. *Can Med Assoc J* 1979;**120:**155–58.

[19] Salih MA, Ahmed HS, Osman KA *et al.* Clinical features and complications of epidemic group A meningococcal disease in Sudanese children. *Ann Trop Paediatr* 1990;**10:**231–38.

[20] Enos K. *Cerebrospinal Meningitis in Northern Ghana: The Experience of the War Memorial Hospital, Navrongo*. Ministry of Health, Ghana [Report], 1997.

[21] Greenwood BM, Bradley AK, Wall RA. Meningococcal disease and season in sub-Saharan Africa. *Lancet* 1985;**ii:**829–30.

[22] Greenwood B. Meningococcal meningitis in Africa. Manson Lecture. Royal Society of Tropical Medicine and Hygiene meeting at Manson House, London, 10 December 1998. *Trans R Soc Trop Med Hyg* 1999;**93:** 341–53.

[23] Gagneux S, Hodgson A, Ehrhard I *et al.* Microheterogeneity of serogroup A (subgroup III) *Neisseria meningitidis* during an outbreak in northern Ghana. *Trop Med Int Health* 2000;**5:**280–87.

[24] Binka FN, Kubaje A, Adjuik M *et al.* Impact of permethrin impregnated bednets on child mortality in Kassena-Nankana district, Ghana: a randomized controlled trial. *Trop Med Int Health* 1996;**1:** 147–54.

[25] Ngom P, Debpuur C, Bawah AA *et al. Survey on Disability in Upper East Region, Ghana*. Navrongo Health Research Centre documentation note No. 40. 1999 (unpublished).

[26] Berkow R, Fletcher AJ (eds). *The Merck Manual of Diagnosis and Therapy*. Rahway, NJ: Merck Research Laboratories, 1992.

[27] Dodge PR, Davis H, Feigin RD *et al.* Prospective evaluation of hearing impairment as a sequela of acute bacterial meningitis. *N Engl J Med* 1984;**311:**869–74.