

Meningitis in infancy in England and Wales: follow up at age 5 years

Helen Bedford, John de Louvois, Susan Halket, Catherine Peckham, Rosalinde Hurley, David Harvey

Abstract

Objective To describe important sequelae occurring among a cohort of children aged 5 years who had had meningitis during the first year of life and who had been identified by a prospective national study of meningitis in infancy in England and Wales between 1985 and 1987.

Design Follow up questionnaires asking about the children's health and development were sent to general practitioners and parents of the children and to parents of matched controls. The organism that caused the infection and age at infection were also recorded.

Setting England and Wales.

Participants General practitioners and parents of children who had had meningitis before the age of 1 year and of matched controls.

Main outcome measures The prevalence of health and developmental problems and overall disability among children who had had meningitis compared with controls.

Results Altogether, 1584 of 1717 (92.2%) children who had had meningitis and 1391 of 1485 (93.6%) controls were successfully followed up. Among children who survived to age 5 years 247 of 1584 (15.6%) had a disability; there was a 10-fold increase in the risk of severe or moderate disability at 5 years of age among children who had had meningitis (relative risk 10.3, 95% confidence interval 6.7 to 16.0, $P < 0.001$). There was considerable variation in the rates of severe or moderate disability in children infected with different organisms.

Conclusion The long term consequences of having meningitis during the first year of life are significant: 32 of 1717 (1.8%) children died within five years. Not only did almost a fifth of children with meningitis have a permanent, severe or moderately severe disability, but subtle deficits were also more prevalent.

Introduction

Children are most likely to get meningitis during their first year. Although it is widely acknowledged that the consequences of meningitis in infancy may be severe, there are few reliable data from large prospective studies that focus on the outcome of infection in infancy. None of these have been based on a national population.

In a meta-analysis of 19 prospective studies of the outcome of bacterial meningitis in 1602 children¹ and a review of follow up reports of neonatal meningitis² there were wide variations in the rates of adverse sequelae associated with infection by different organisms and also variations within groups of organisms. Few studies have investigated the full range of sequelae associated with meningitis³⁻⁵; most have focused on specific outcomes, notably cognitive function and hearing loss.⁵⁻⁹

A prospective study of the incidence of meningitis in infancy in England and Wales was carried out between 1985 and 1987.¹⁰ In that study 1880 children with meningitis were identified; we present the results of a follow up investigation at 5 years of age of the children who survived the initial illness.

Participants and methods

This follow up study is based on data from the 1717 children who survived an acute attack of meningitis between 1985 and 1987. Controls were matched by sex and age to the index child. For both cases and controls general practitioners were asked to complete a questionnaire detailing any health or developmental problems in the areas of neuromotor development, learning, vision, hearing, speech and language, or behaviour, and to indicate whether the child had a seizure disorder. Parents of children in both groups also completed a questionnaire about their child's health, development, and schooling. Information from general practitioners and parents was combined to provide a complete picture of each child's health.

Children were allocated to one of four categories of disability based on a model developed by McIntyre et al.³ Children were classed as having a severe disability if they were unable to attend a mainstream school. This category included children with multiple problems such as severe neuromotor impairment, significant intellectual impairment, severe seizure disorders, and severe visual or auditory impairment.

Children were classed as having a moderate disability if their disability impaired their functioning but was not associated with severe intellectual or developmental impairment. Children in this category attended mainstream schools with or without additional support. This category included children with mild neuromotor disabilities, intellectual impairment, moderate sensorineural hearing loss, mild or moderate

Editorial by
Grimwood

Centre for
Paediatric
Epidemiology and
Biostatistics,
Institute of Child
Health, London
WC1N 1EH

Helen Bedford
senior research fellow
Catherine Peckham
*professor of paediatric
epidemiology*

Public Health
Laboratory Service,
Environmental
Surveillance Unit,
London NW9 5EQ
John de Louvois
director

The Karim Centre
for Meningitis
Research, Imperial
College School of
Medicine,
Department of
Paediatrics and
Neonatal Medicine,
Queen Charlotte's
and Chelsea
Hospital, London
W6 0XG

Susan Halket
senior scientist
Rosalinde Hurley
*professor of
microbiology*
David Harvey
*professor of
paediatrics and
neonatal medicine*

Correspondence to:
H Bedford
h.bedford@ich.ucl.
ac.uk

BMJ 2001;323:533-6

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The full version of
this paper appears
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visual impairment, epilepsy that was controlled with treatment, and hydrocephalus without complications.

Children were classed as having mild disorders if they had a condition that is prevalent among children of the same age but is not typically associated with meningitis. This category included children with middle ear disease, squint, febrile convulsions, and behavioural problems.

Children were classed as having no disability if there was no evidence of developmental problems

Results

Altogether, 1717 children survived an acute attack of meningitis. Information was available from general practitioners or parents, or both, for 1584 (92.2%) of children who survived an acute attack of meningitis and for 1391 of 1485 (93.6%) controls.

Deaths

Of the 1717 children who survived the initial attack 32 later died. Two children who had otherwise been healthy died, one of septicaemic shock at age 4 years and the other of acute bronchiolitis at the age of 22 months. Sixteen children had had conditions consistent with the sequelae of meningitis. Fourteen had had conditions associated with extreme prematurity, congenital abnormalities (four had Down's syndrome), or non-related conditions such as lymphoblastic leukaemia. The cause of death was unknown for one child. An additional five children (one with Down's syndrome) were reported to have died at the time of the acute attack of meningitis.

Health and development at five years

The proportion of children with health and developmental problems is summarised in table 1. The risk of problems was increased among children who had had meningitis, particularly the risk of having learning and neuromotor disabilities.

Learning and neuromotor disabilities

In 16 children learning difficulties were described as very severe; all of these children had had meningitis (1% of children in the meningitis group). Information on schooling was available for 90 children who had learning difficulties, and 70 were reported to have had special educational provision; 82 of the children with learning difficulties had had meningitis. Ten of the children who had had meningitis and who had learning difficulties also had congenital conditions associated with mental impairment: five had Down's syndrome, two had congenital mental impairment, two had dysmorphic

Table 1 Number (percentage) of children reported to have health or developmental problems

	Group		Relative risk (95% CI)	P value
	Meningitis (n=1584)	Control (n=1391)		
Learning difficulties	118 (7.5)	15 (1.1)	7.0 (4.1 to 11.8)	<0.001
Neuromotor disabilities	128 (8.1)	13 (0.9)	8.6 (4.9 to 15.2)	<0.001
Seizure disorders	116 (7.3)	37 (2.7)	2.7 (1.9 to 3.9)	<0.001
Hearing problems	408 (25.8)	190 (13.7)	1.9 (1.6 to 2.2)	<0.001
Ocular or visual disorders	217 (13.7)	55 (3.9)	3.4 (2.6 to 4.6)	<0.001
Speech or language problems, or both	247 (15.6)	64 (4.5)	3.5 (2.8 to 4.6)	<0.001
Behavioural problems	188 (11.9)	46 (3.3)	3.6 (2.6 to 4.9)	<0.001

Table 2 Number (percentage) of children with severe neuromotor disabilities at 5 years of age

Neuromotor disability	Group	
	Meningitis (n=1584)	Control (n=1391)
Cerebral palsy:	79 (4.9)	2 (0.1)
Spastic hemiplegia	28 (1.7)	1 (0.1)
Spastic quadriplegia	10 (0.6)	0
Spastic diplegia	8 (0.5)	0
Spastic paraplegia	1 (0.1)	0
Monoplegia	1 (0.1)	0
Double hemiparesis	1 (0.1)	0
Ataxia	6 (0.4)	0
Degree and type unspecified	24 (1.5)	1 (0.1)
Other severe motor problems:	5 (3)	0
Severe (unspecified)	1 (0.1)	0
No voluntary movements	1 (0.1)	0
Primitive reflexes only	1 (0.1)	0
Multiple congenital malformations	1 (0.1)	0
Bilateral amputations through knee	1 (0.1)	0
Total	84 (5.3)	2 (0.1)

features, and one had agenesis of the corpus callosum. Eighty four (5.3%) children who had had meningitis had severe neuromotor disabilities compared with two (0.1%) controls ($\chi^2 = 69.3$, $P < 0.001$) (table 2). Cerebral palsy was the most common condition reported.

Seizure disorders

Regular anticonvulsant medication was taken by 53 (45.7%) of the 116 children who had seizure disorders and had had meningitis; a further 24 had discontinued treatment. In contrast, only 5 (13.5%) of the children with seizure disorders in the control group regularly took anticonvulsant medication.

Hearing impairment

The overall relative risk of sensorineural hearing loss was 22.8 (95% confidence interval 7.22 to 72.1), with 90 (5.6%) of the children who had had meningitis being affected; 29 (1.8%) had a severe or profound bilateral loss. Three children in the control group (0.2%) had mixed sensorineural-conductive loss. Middle ear problems were more prevalent among children who had had meningitis (272 children; 17.1%) than among controls (100 children; 7.2%) ($\chi^2 = 67.22$, $P < 0.001$). However, 108 of 1399 (7.7%) parents of children who had had meningitis and 144 of 1180 (12.2%) parents of controls reported that their children's hearing had not been tested.

Visual and ocular problems

Six children were blind; they had all had meningitis. The most common condition reported was squint (116 children in the meningitis group (7.3%) v 31 controls (2.2%)). Parents reported that their children's vision had not been tested for 382 of 1414 (27%) children who had had meningitis and 276 of 1200 (23%) controls.

Speech and language problems

Fifty five children had severe communication problems or an absence of speech; all had had meningitis. A further 149 (9.4%) children in the meningitis group and 53 in the control group (3.8%) had speech or language delay, or both. In both groups children with speech and language problems also had hearing impairment,

Table 3 Number (percentage) of children by severity of disability at 5 years of age

	Group	
	Meningitis (n=1584)	Control (n=1391)
Severe disability	92 (5.8)	1 (0.07)
Moderate disability	155 (9.8)	20 (1.4)
Mild disorder	461 (29.1)	275 (19.8)
No disability	876 (55.3)	1095 (78.7)

intellectual impairment, or both, (217/247 (87.8%) children with meningitis *v* 39/64 (60.9%) controls).

Behavioural problems

Behavioural problems were more frequently described by parents than by general practitioners. The most common problems among children who had had meningitis were severe temper tantrums (44 children; 2.8%), hyperactivity (17; 1.1%), and having poor concentration or being slow at school (42; 2.6%). Among the 32 children classed as having poor concentration or being slow at school there was no other apparent health problem. The behavioural problems reported for children in the control group were similar but less common.

Categories of disability

Table 3 classifies the children by severity of disability. Children who had had meningitis had a 10-fold increase in the risk of having severe or moderate disabilities (relative risk 10.33, 95% confidence interval 6.6 to 16.0, $P < 0.001$). Altogether, 617 of 1584 (38.9%) affected children had multiple conditions. They also had an increased risk of mild disorders, such as middle ear disease, squint, and behavioural problems (relative risk 1.47, 95% confidence interval 1.29 to 1.68, $P < 0.001$).

Age at infection and organism of infection

Children who were infected as neonates had more health and developmental problems than those who had meningitis when they were older than one month ($\chi^2 = 4.5$, $P = 0.03$). In each area of health and development evaluated, prevalence rates for problems were significantly higher for children who had had neonatal meningitis; this was particularly marked for neuro-motor disabilities, seizure disorders, and learning difficulties (data not shown). Although children with neonatal meningitis had an overall increase in the risk of having hearing problems, there was no significant difference in the prevalence of sensorineural hearing loss between the age groups. Children with neonatal meningitis were significantly more likely to have moderate disabilities ($\chi^2 = 72.2$, $P < 0.001$), but the rate of severe disability was not significantly different between the groups. The rates of severe or moderate disability differed widely between children infected with different organisms (table 4). Although some of the differences may relate to the age at which the child contracted meningitis, infection with certain organisms was consistently associated with a poorer long term prognosis.

Effects of gestational age and birth weight

Since prematurity and low birth weight are likely to have independent effects on outcome, the relative risk of severe or moderate disability when birth weight and gestational age were controlled for were calculated. In these analyses children with pre-existing conditions,

such as Down's syndrome or cerebral palsy, were excluded. A sevenfold increase in the risk of severe or moderate disability remained after birth weight and gestational age were controlled for.

Discussion

This study shows that meningitis in infancy has serious consequences. Two per cent of children who survived the acute attack died before the age of 5 years. Among the survivors there was a 10-fold increase in the risk of severe or moderate disability compared with the control group. Neonatal meningitis was associated with a higher frequency of disability—especially neuro-motor disabilities and seizure disorders—than meningitis after one month of age; however, there was no difference in the prevalence of sensorineural hearing loss between the groups. Infection with *Streptococcus pneumoniae* was associated with a higher rate of disability than infection with *Haemophilus influenzae* and *Neisseria meningitidis*. This is consistent with the rates reported by Baraff et al and other prospective investigations, although their rates were not specific to infants.^{1,3,4} In this national cohort, severe disability was significantly more common in infants with meningitis associated with Group B streptococcus than with *Escherichia coli*. The highest rates of severe disability occurred among children whose meningitis was associated with Gram positive and Gram negative organisms classed as "other" (table 4). Our finding that 56% of infants with meningitis associated with Gram negative bacteria had severe or moderate disability is comparable with the 69% reported from a 20 year (1969-89) study in the United States.¹¹

Although meningitis is more common during the first year of life than at any other age, it remains relatively uncommon. Because of the difficulty in finding adequate numbers of children in specific age groups for studies, reports of outcomes have relied on retrospective investigations, often done over many years, or on data from children referred to specialist centres, which by definition attract the more serious cases. As a result, there are few reliable estimates of the risk of long term disability associated with meningitis, particularly during the first year of life and during the neonatal period.² The findings in this paper, based on follow up at five years of age of children enrolled in a national prospective study of meningitis in infancy,

Table 4 Number (percentage) of children by disability and infectious organism

Organism	Severe disability	Moderate disability	Mild disorder	No disability	Total
<i>Haemophilus influenzae</i>	14 (3.4)	30 (7.3)	134 (32.5)	235 (57.0)	413 (26.0)
<i>Neisseria meningitidis</i>	12 (2.9)	26 (6.5)	120 (29.8)	244 (60.7)	402 (25.4)
<i>Streptococcus pneumoniae</i>	14 (9.7)	20 (13.9)	37 (25.8)	72 (50.3)	143 (9.0)
<i>Escherichia coli</i>	4 (5.7)	13 (18.6)	18 (25.7)	35 (50.0)	70 (4.4)
Group B streptococcus	13 (13.3)	17 (17.3)	18 (18.4)	50 (51.0)	98 (6.2)
Echovirus	0	2 (6.4)	11 (35.5)	18 (58.0)	31 (1.9)
Other virus	4 (21.1)	0	4 (21.1)	11 (57.9)	19 (1.2)
Other Gram positive bacteria	6 (20.6)	8 (27.6)	5 (17.2)	10 (34.5)	29 (1.8)
Other Gram negative bacteria	8 (25.0)	10 (31.3)	7 (21.9)	7 (21.9)	32 (2.0)
<i>Listeria monocytogenes</i>	0	4 (25.0)	3 (18.8)	9 (56.3)	16 (1.0)
Other micro-organisms	2 (28.6)	4 (57.1)	1 (14.3)	0	7 (0.4)
No organism grown	15 (4.7)	21 (6.6)	100 (31.3)	184 (57.5)	320 (20.2)
Not known	0	0	3 (75)	1 (25)	4 (0.2)
Total	92	155	461	876	1584

What is already known on this topic

Meningitis in infancy is associated with important long term consequences

There is considerable variation in outcome depending on which organism caused the infection

What this study adds

This follow up study of 1717 children who had meningitis in infancy found that they had a 10-fold increase in risk of severe or moderate disabilities at age 5 years compared with children in the control group

The outcome of having meningitis was associated with the age at infection, and children who had meningitis in the neonatal period were more likely to have health and development problems than those older than 1 month

Subtle deficits, such as middle ear disease and visual and behavioural problems, were more prevalent among children who had had meningitis in infancy

provide a complete picture of the range of problems experienced by children from England and Wales who have had meningitis in infancy.¹⁰

We thank the parents and general practitioners who completed the questionnaires and the paediatricians for assisting in the fol-

low up of the children. We thank David Dunn for statistical advice and Janet Masters for assistance in coding and entering the data.

Funding: Action Research and the Fayed Charitable Foundation.

Competing interests: None declared.

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(Accepted 8 March 2001)

Prevalence of permanent childhood hearing impairment in the United Kingdom and implications for universal neonatal hearing screening: questionnaire based ascertainment study

Heather M Fortnum, A Quentin Summerfield, David H Marshall, Adrian C Davis, John M Bamford

Editorial by Russ

MRC Institute of Hearing Research, University Park, Nottingham NG7 2RD

Heather M Fortnum
epidemiologist

A Quentin Summerfield
deputy director

David H Marshall
statistician

Adrian C Davis
epidemiologist

continued over

BMJ 2001;323:536-40

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Abstract

Objective To estimate the prevalence of confirmed permanent childhood hearing impairment and its profile across age and degree of impairment in the United Kingdom.

Design Retrospective total ascertainment through sources in the health and education sectors by postal questionnaire.

Setting Hospital based otology and audiology departments, community health clinics, education services for hearing impaired children.

Participants Children born from 1980 to 1995, resident in United Kingdom in 1998, with permanent childhood hearing impairment (hearing level in the better ear > 40 dB averaged over 0.5, 1, 2, and 4 kHz).

Main outcome measures Numbers of cases with date of birth and severity of impairment converted to prevalences for each annual birth cohort (cases/1000 live births) and adjusted for underascertainment.

Results 26 000 notifications ascertained 17 160 individual children. Prevalence rose from 0.91 (95% confidence interval 0.85 to 0.98) for 3 year olds to 1.65 (1.62 to 1.68) for children aged 9-16 years.

Adjustment for underascertainment increased estimates to 1.07 (1.03 to 1.12) and 2.05 (2.02 to 2.08). Comparison with previous studies showed that prevalence increases with age, rather than declining with year of birth.

Conclusions Prevalence of confirmed permanent childhood hearing impairment increases until the age of 9 years to a level higher than previously estimated. Relative to current yields of universal neonatal hearing screening in the United Kingdom, which are close to 1/1000 live births, 50-90% more children are diagnosed with permanent childhood hearing impairment by the age of 9 years. Paediatric audiology services must have the capacity to achieve early identification and confirmation of these additional cases.

Introduction

Permanent childhood hearing impairment can have a devastating impact on communication skills,¹ educational attainment,² and quality of life,^{3,4} with a high cost to society.⁵ Improved outcomes for children with congenital impairment are associated with confirma-