Deaths from Meningococcal Infection in England and Wales in 1978

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Although deaths from tuberculosis in England and Wales fell from 3,806 in 1959 to 900 in 1978, and over the same period deaths from measles were reduced by four-fifths, mortality from meningococcal infection showed no reduction; it was 205 in 1973 compared with 170 in 1959, despite the fact that effective treatment has been available for over forty years and that, more recently, intensive care has been widely available and freely utilised (Fig. 1).

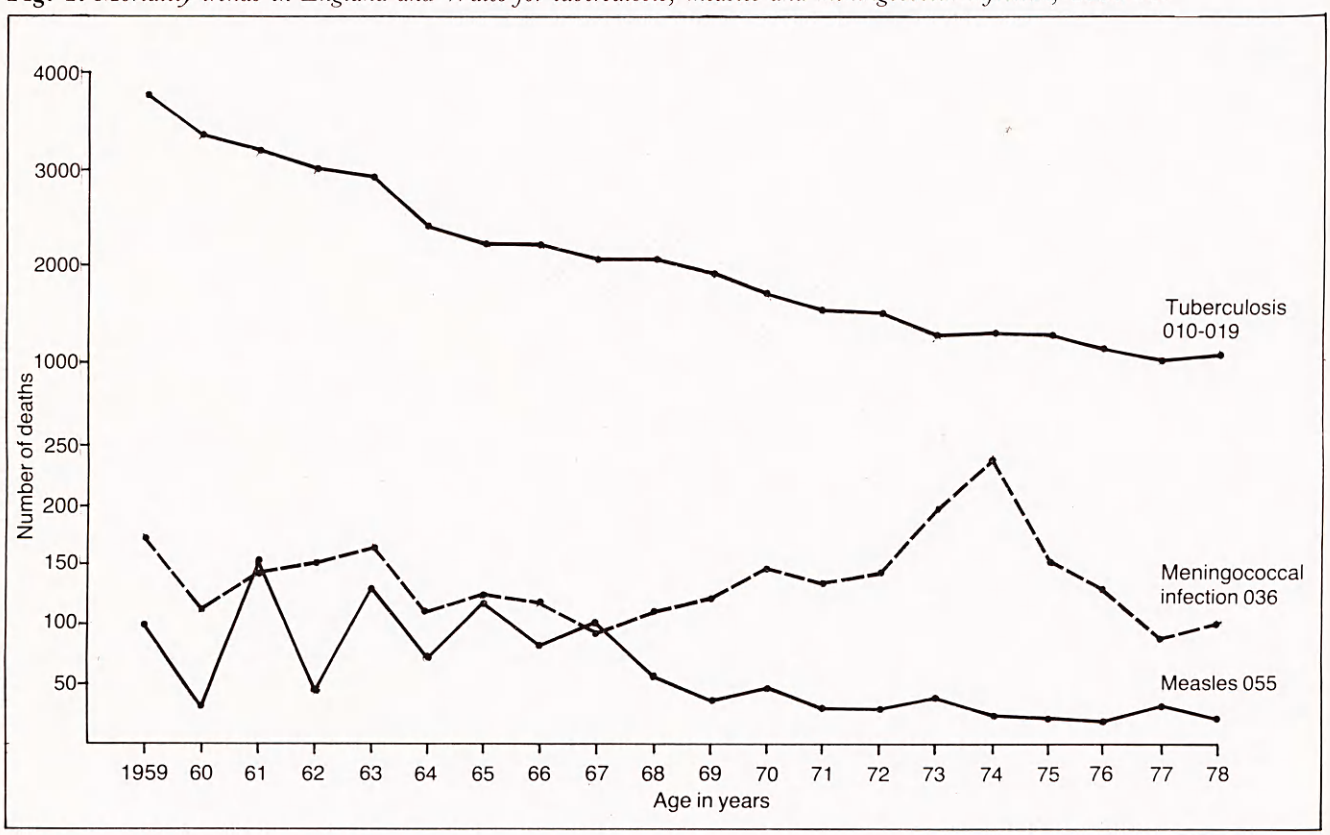
In 1978 there were 96 deaths in England and Wales attributed to meningococcal infection in the OPCS mortality statistics[1]. The question as to whether any of these deaths could have been prevented is the subject of this article.

Goldacre's excellent work a decade ago in the North West Metropolitan Region indicated that death certification of meningococcal infection was likely to carry a high degree of accuracy[2] though statutory notification missed about half of those infected[3]. His work also reflected the apparent inability to abolish a significant mortality despite effective treatment[4] and the part played by diagnostic and therapeutic delay[5,6]. The DHSS Multicentre Postneonatal Study also stressed the importance of delay in diagnosis and treatment[7,8].

Methods

The OPCS kindly supplied copies of death certificates for those coded 036 (meningococcal infection) and 320.9 (meningitis with no specific organism specified as cause) during the year 1978. If death had occurred in hospital, the consultant in charge was approached, usually through the Medical Records Officer, with an explanation of the

Fig. 1. *Mortality trends in England and Wales for tuberculosis, measles and meningococcal infection, 1959-78.*



aim of the study, and permission to see the hospital notes was requested. If death had occurred at home, the family doctor and the coroner were asked for as much information as possible about the circumstances of death and the pathological findings.

Ascertainment

The OPCS was able to send copies of 92 of the 96 death certificates coded 036 and all of the 147 coded 320.9.

Information about 4 of the 92 coded 036 was refused, one by the coroner and 3 by the hospital because the notes could not be traced. In 2 others, death seemed unlikely to have been due to meningococcal infection and in another 2 it was shown conclusively to have been caused by other organisms (*Staph. pyogenes* and *Dip. pneumonia*). Two deaths from bilateral adrenal haemorrhage (which is always coded 036) were also discarded because in one it was associated with hepatic cirrhosis due to syphilis and in the other there was no evidence to support a diagnosis of meningococcal infection. This left 82 cases, 62 being confirmed bacteriologically, and 20 appearing on clinical grounds to be attributable to meningococcal infection.

Of the death certificates coded 320.9 information was provided in 140 of the patients. Two of these deaths were confirmed bacteriologically as due to meningococcal infection and a further two appeared to be so caused.

Thus, there was a total of 86 cases, 64 bacteriologically confirmed and 22 where the organism was not isolated but the diagnosis was not in doubt. Table 1 summarises

Table 1. Reasons for accepting the diagnosis of death from meningococcal infection without bacteriological confirmation.

(a) Purpuric rash. CSF sugar less than 4 mmol/litre. Gram-negative diplococci seen	1
(b) Purpuric rash. Bilateral adrenal haemorrhage	2
(c) Purpuric rash. CSF sugar less than 4 mmol/litre	4
(d) Purpuric rash	13
(e) Bilateral adrenal haemorrhage	1
(f) Gram-negative diplococci seen	1
Total	22

the grounds for accepting the diagnosis in the 22 cases not proven bacteriologically.

Results

There were 45 males and 41 females with ages ranging from three weeks to 76 years. Fig. 2a shows the age distribution of the whole series and Fig. 2b that of those under one year. There was no gross distortion of the expected distribution of social class.

Eight patients died at home and six were dead on arrival at hospital; all were children and eight were less than eighteen months old.

The diagnosis of meningococcal infection was not made before autopsy in 18, of whom 9 were under eighteen months and 3 over sixty years. These ages indicate the difficulty of diagnosis in the very young and in the older age groups. In 13 of the 18 cases first diagnosed at autopsy positive cultures of *N. meningitidis* were obtained from postmortem material; however, a purpuric rash was present in 13, meningitis in 9 and bilateral adrenal haemorrhage in 12 cases. Among these 18 were the 8 who died at home and 5 of the 6 who were dead on arrival at hospital.

Diagnosis was made in life in the remaining 68 patients; 52 of these had the characteristic purpuric rash and 32 had signs of meningitis.

Lumbar puncture was performed in 71 of the 86 patients and a positive culture of *N. meningitidis* obtained from 51. In one, organisms were grown from a ventricular tap. However, in only 16 patients did the cerebrospinal fluid provide a diagnosis previously not made. In 38 patients the diagnosis was obvious on clinical grounds and in most, but not all, of these 38 treatment had already been started before the results of the lumbar puncture were known.

Blood culture was done in 59 of the 86 patients and was positive in 27. In 12 patients it was the only source from which the organism was isolated but in no instance was blood culture the diagnostic instrument.

Grouping of Organisms

Cultures obtained from the cerebrospinal fluid and blood during life and in 3 instances from the nose, spleen and meninges at postmortem, were grouped in a total of 34 patients; 27 were group B, 5 group A and 2 were group C.

Coning

Six patients with meningitis died from coning[9]. One died in a convulsion without a lumbar puncture being performed. In two the lumbar puncture provided the diagnosis but in the other three the diagnosis had already been made and treatment started before the lumbar puncture was done.

Interval Between Onset of Symptoms, Diagnosis, Treatment and Death

In 15 of the 86 patients no evidence of delay in diagnosis or treatment could be found at any stage of the illness; the infection was so overwhelming that nothing could have been done to prevent a fatal outcome. The rapidity with which the infection may kill is exemplified by parents who awoke in the morning to find their child dead or moribund beside them. One baby died on the day she was christened and a 9-year-old was admitted to hospital moribund six hours after attending a wedding.

Once a diagnosis was made, appropriate treatment was started promptly in the majority of patients, but there were exceptions. However, the overall impression was that, in many, diagnostic uncertainty made a serious contribution to the fatal outcome.

The interval between the onset of symptoms and death has been examined at four main stages. First, between the onset of illness and the parents or adult patient recognising the severity of symptoms and calling for professional help; second, between the call for help and the arrival of

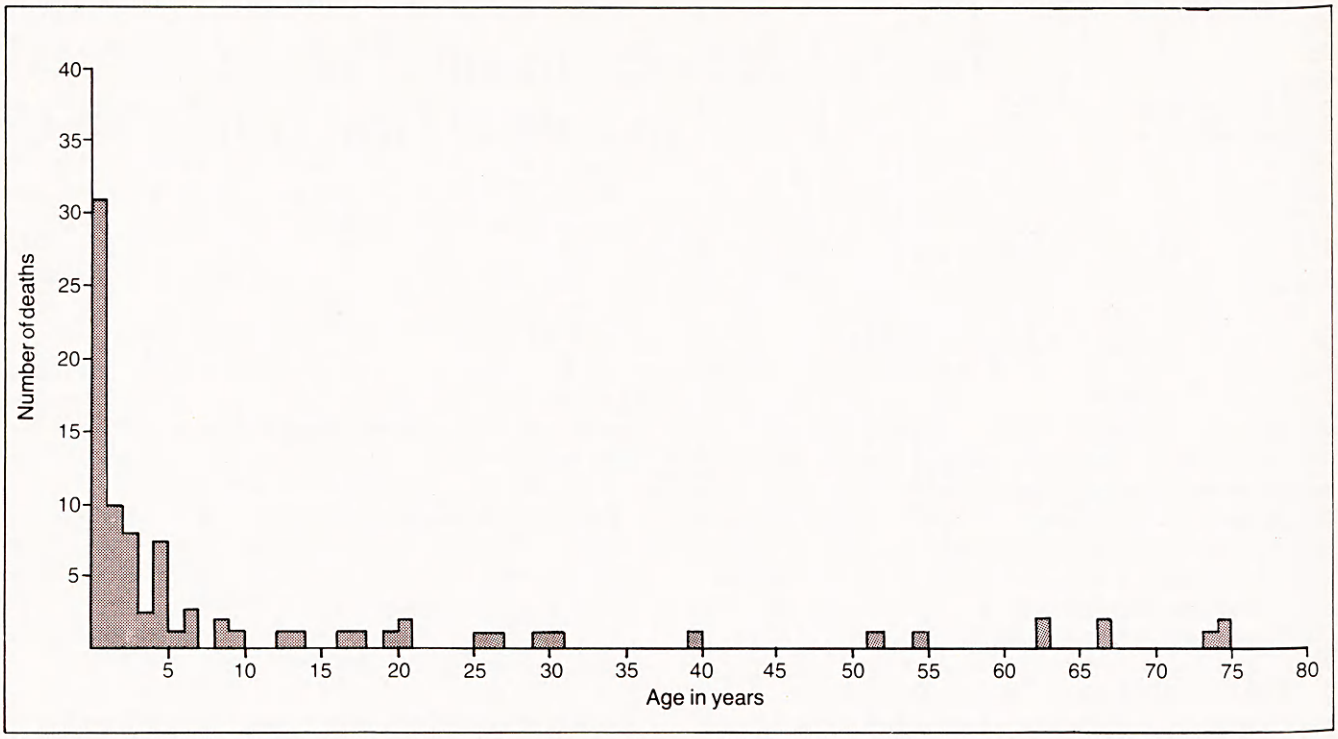
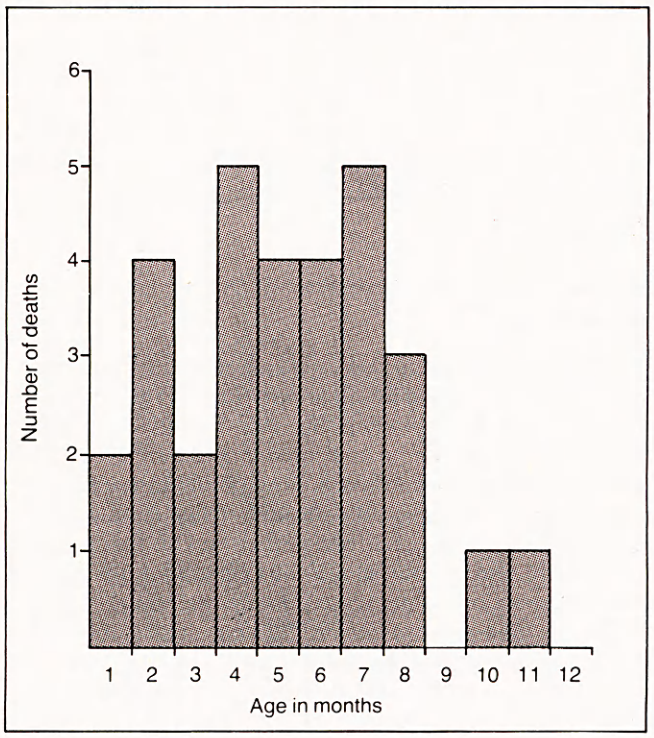


Fig. 2a. *Age distribution of the 86 patients dying from meningococcal infection in England and Wales in 1978.*

Fig. 2b. *Age distribution of the patients dying under the age of one year from meningococcal infection in England and Wales in 1978.*



the general practitioner; third, in the general practitioner recognising the gravity of the situation, and fourth, in diagnosing previously undiagnosed patients after arrival at hospital. An attempt was made to assess the stage and extent of any possibly avoidable delay, but it was deemed inappropriate to contact those concerned for retrospective consideration of such factors.

The most frequent and lengthy intervals occurred in the first stage. In 21 cases the parents failed to recognise that their child was seriously ill. Some couples were very young and some mothers were either unmarried or unsupported by husbands who were abroad. These contrasted strongly with others who, alarmed by the illness, showed tenacity in demanding help and, in some instances, took their child directly to the casualty department. In 6 young adults and 2 older patients there was serious delay in seeking medical care. One of the former received no medical attention because he was suspected of being drunk, and one husband was reluctant to call his doctor 'on his Saturday' while his wife, aged 62, sank into unconsciousness at home.

In 11 patients there was a substantial interval in the second stage, that is between the call for help and the arrival of the general practitioner. The parents of one child, who phoned their general practitioner twice, were told at 6.30 a.m. by the doctor's wife that 'steam would help'. By 11 a.m. the child was dead. In 22 there was apparent delay in the third stage, that is between the general practitioner's visit and admission to hospital. In most instances this clearly resulted from failure to make or suspect the diagnosis. For 2 children a domiciliary consultation was arranged, but no treatment was prescribed meanwhile, and one became moribund while the consultant opinion was awaited. In others, oral antibiotics were prescribed and before the doctor's next visit the purpuric rash had developed. In another 6 no treatment was given before death and in none of the patients were intravenous antibiotics administered before arrival at hospital.

In 13 there was delay in starting treatment in stage four, that is after admission to hospital. In 2 children the diagnosis of meningococcal meningitis was made at one hospital and they were transferred to another without any treatment being given at the first. In others with signs of meningococcal infection, laboratory confirmation was awaited before treatment was started and in one the development of purpura during the night was noted by the nursing staff but it was not regarded as a significant development.

The interval between the onset of symptoms, the call for help, the start of intravenous therapy, and death, is summarised in Tables 2(a), (b), (c) and (d).

Table 2. Interval between onset of symptoms, diagnosis, treatment and death in those of the 86 patients where this information was available.

(a) *Hours between first symptoms and call for help*	
None	7
1- 2	5
3- 5	4
6-12	25
13-24	10
25-48	13
More than 48	9
Found dead (duration of symptoms uncertain)	4
(b) *Hours between call for help and i.v. treatment*	
None	12
1- 2	6
3- 5	8
6-12	15
13-24	11
25-48	1
More than 48	3
Dead on arrival (duration of symptoms 10-72 hours)	6
(c) *Hours between onset of symptoms and i.v. treatment*	
None	4
1- 2	1
3- 5	1
6-12	21
13-24	26
25-48	12
More than 48	13
(d) *Time between onset of symptoms and death*	
Less than 12 hours	9
12-23 hours	15
24-48 hours	22
3 days	5
4 ,,	9
5 ,,	5
6 ,,	4
7 ,,	3
8 ,,	0
9 ,,	1
10 or more days	3

There were 5 patients over 65 who all presented especial diagnostic difficulty; only 2 of them had purpura and in one it was not apparent until shortly before death; in only one of the 5 was neck stiffness elicited. Two died with a diagnosis of cerebrovascular accident and in the other three a lumbar puncture was done but not until the day after admission; the laboratory findings were not reported with any sense of urgency.

The question as to whether reduced hospital cover or diminished accessibility of general practitioners at weekends might be a related factor was considered (Fig. 3). A smaller number were admitted on Wednesdays and Saturdays than on other days.

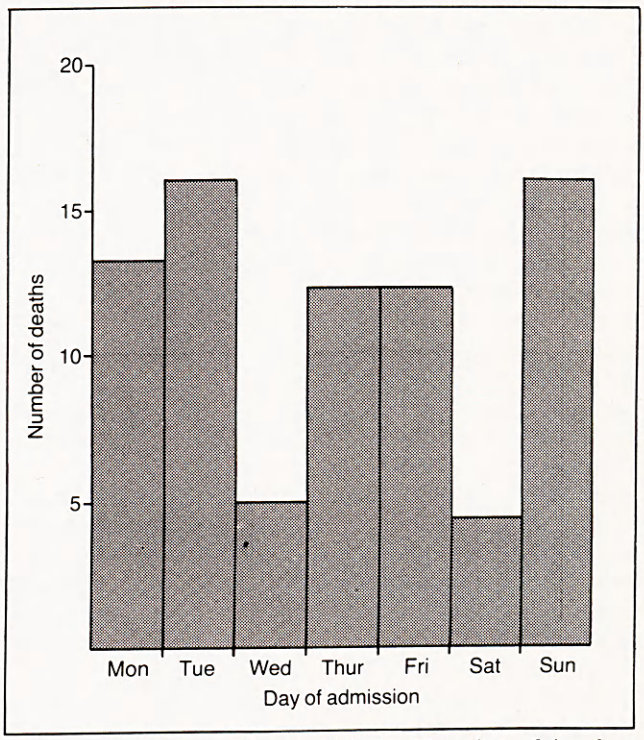


Fig. 3. *Day of the week on which the 86 patients dying from meningococcal infection in England and Wales in 1978 were admitted to hospital.*

Discussion

There was no control series of patients who survived, but the study of these 86 deaths suggests that the cardinal needs are prompt diagnosis and immediate and effective treatment. Even so, it appears that in some patients the infection is so overwhelming that life cannot be saved. That treatment is curative in a high proportion of patients is shown by an epidemic in Bolton between 1971 and 1974 which has been the subject of a separate study by the Medical Services Study Group[10,11]; 68 of the 82 patients survived.

The most promising measure to reduce mortality appears to be that of familiarising doctors with the clinical features of the disease and the disastrous consequences of diagnostic failure and therapeutic delay. Rare though meningococcal infection must be in the practice of any individual general practitioner, it is the cause of 2 per cent of all deaths between one and four years and it killed 65 children under ten in England and Wales in 1978. The 5 elderly patients described in this survey reflect the greater delay and difficulty in diagnosis among older people and indicate that the incidence may be higher in this group than the 6 per cent we have found.

Parents, especially those of low intelligence and poor educational achievement, cannot be expected to recognise the gravity of their child's illness or to appreciate how quickly it may progress. Adults who saw much meningococcal infection and meningitis in members of the Services during the Second World War will recall how swiftly those afflicted were deprived of coherent thought and action and could become violent in behaviour. General practitioners and hospital doctors cannot be blamed for diagnostic failure in respect of a relatively uncommon disease which they have not previously encountered, but a febrile patient with a purpuric rash or meningeal signs demands immediate intravenous antibiotic therapy. In 7 patients, an erythematous rash was observed before frank purpura developed, and this or febrile convulsions are not infrequent early features of the disease.

Transfer of a diagnosed or suspected meningococcal patient from home to hospital or from one hospital to another must not preclude the immediate institution of appropriate treatment, and whenever symptoms or physical signs suggest the possibility of meningococcal infection, to await bacterial confirmation of the diagnosis before instituting treatment is to court almost certain disaster. If the toll of deaths from this life-threatening infection is to be diminished, the only avenue is reduction of the intervals between the onset of symptoms, diagnosis and treatment. Table 2(d) shows that in 9 patients there were less than twelve hours between the first symptoms and death, and in more than half the cases death ensued within the first 48 hours.

A great deal of concern was expressed by the doctors involved regarding these deaths from meningococcal infection and the proceedings of three postmortem case conferences were made available to the Medical Services Study Group.

Though it is not the purpose of this article to examine the effectiveness of different treatment regimens, several of the consultants who kindly participated in this survey raised the question of the use of heparin in patients with evidence of disseminated intravascular coagulation. A controlled study would be difficult, if not impossible, and in such a desperate situation the use of heparin could scarcely be criticised.

Our experience of coning is limited to 6 patients. It can be caused by the disease itself but it can also be precipitated by lumbar puncture and, where the diagnosis is obvious on clinical grounds, immediate treatment is the clamant need. Some may feel that lumbar puncture is better omitted.

The fact that many who die from meningococcal infection do not have meningitis is well recognised[3,4,7,8], and was a feature of this series.

The majority of the organisms grouped were found to be *N. meningitidis* B and this precludes the benefits in this country of vaccine prophylaxis which is at present only effective against groups A and C.

Acknowledgements

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