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Meningococcal infections in Scotland 1972–82

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SUMMARY

Strains of *Neisseria meningitidis* isolated from patients with meningitis or septicaemia without meningitis in Scotland during the years 1972–82 have been reviewed together with details of the age, sex, disease and outcome of the patients from whom they were isolated. A total of 1185 strains were isolated, of which 927 were examined at the Meningococcal Reference Laboratory (Scotland): 19·3 % were of serogroup A, 63 % of group B, 9·6 % of group C, 6 % of W135 and 1·6 % of other groups. Non-groupable strains were rare. Disease was most common in the first years of life but there was a difference in the age distribution of disease due to the different serogroups, the proportion of disease due to group B being smaller in adults than that due to other serogroups. The overall mortality in meningitis was 7·5 % and in septicaemia was 20·6 %, although there were differences between the rates for the various serogroups. The serogroup distribution differed in disease as opposed to meningococci isolated from carriers although group B strains were predominant in both series. Overall, approximately 15 % of strains were resistant to sulphadiazine, the proportion of resistant group A strains being higher than that of other serogroups.

INTRODUCTION

Until the introduction of polysaccharide vaccines for the prevention of infection due to groups A and C *Neisseria meningitidis* no specific measures were available for the prevention of meningococcal infection other than the use, in limited circumstances, of chemoprophylaxis. Even so, the lack of a vaccine which would protect against group B meningococcal infection means that the majority of infections in Britain at the present time cannot be prevented. Nevertheless, should a situation arise that such vaccines as are available (and these now include vaccines against serogroups W135 and Y) are to be employed effectively it would be essential to know the pattern of disease in a community and also to look for trends which may indicate that an endemic situation is developing into an epidemic situation and would therefore require rapid action. In addition, it is important to know the outcome of infection in order to appraise the management of disease in comparison with results obtained in other centres and countries. Such surveys may give rise to revealing results (Bohr *et al.* 1983*a*) and lead to a reappraisal of

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management to the benefit of the patient. Hence, ongoing surveillance is an important part of the overall approach to meningococcal infections and has been developed in Scotland over the past 15 years. Laboratory isolations of meningococci were first notified to the Communicable Diseases (Scotland) (CDS) Unit in February 1967 but 1968 was the first full year of such notifications. Since that time, increasing proportions of the meningococci isolated have been forwarded to the Meningococcus Reference Laboratory (Scotland) for determination of serogroup, serotype and sulphadiazine sensitivity. Since 1972 details of age, sex, nature of disease and outcome have been sought for all patients from whom meningococci were forwarded in order to determine the mortality and morbidity associated with infection and to see whether the pattern of infection and age group distribution varied between different serogroups. With the finding that some serotypes of group B meningococci are more often associated with systemic disease than others (Frasch & Chapman 1973) some strains have been serotyped during the latter part of the period under review.

MATERIALS AND METHODS

Strains of N. meningitidis. Meningococci of serogroups A, B, C and D were obtained from the National Collection of Type Cultures, London. Strains of serogroups X, Y, Z and Z^1 were obtained from Dr K. Slaterus of Amsterdam and serogroups W135 and 29E from the late Dr M. S. Artenstein of the Walter Reed Army Institute of Research, Washington, D.C. Group B meningococci of serotypes 1, 2, 4, 5, 6, 7, 8, 9, 10, 11, 12 were obtained from Dr C. E. Frasch of the Bureau of Biologics, Food and Drug Administration, Bethesda, of serotype 15 from Dr E. Holten of the University of Oslo and serotypes 2b, 2c, 13 and 14 from Dr D. M. Jones of Manchester.

Strains were kept either lyophilized and stored at 4 °C or suspended in Mueller Hinton broth and stored at −70 °C.

Preparation of antisera. Antisera for serogrouping were produced by repeated intravenous inoculation of whole meningococci into rabbits as described by Fallon (1976). Antisera for serotyping by precipitation in agar (Frasch & Chapman, 1972*a*) were prepared in rabbits using the immunisation schedule of Frasch & Chapman (1972*b*) or by subscapular injection of the serotype protein extract and Freund's complete adjuvant (Frasch personal communication) and some using the immunization schedule of Gold & Wyle (1970). Sera for typing by co-agglutination were either those raised for precipitation or those raised by a course of intravenous injections of live meningococci given three times a week for 2 weeks (D. M. Jones personal communication).

Serogrouping. Strains were grouped by slide agglutination as described by Devine & Hagerman (1970). In some instances strains were grouped using the precipitation in serum agar technique (Sivonen, Renkonen & Robbins 1977). Strains which gave a smooth suspension in 0·06 M-NaCl but failed to agglutinate with antisera to the serogroups noted above were designated as non-groupable. Those strains which auto-agglutinated in 0·06 M-NaCl saline were designated as saline-agglutinable strains but for the present analysis were counted together with the smooth non-groupable strains.

Serotyping. This was performed for most strains by double diffusion in agar gel as described by Frasch & Chapman (1972*a*). Latterly, strains were serotyped by co-agglutination as described by Danielsson & Olcén (1979).

Sulphadiazine sensitivity testing. This was performed using the agar dilution technique described by Feldman as detailed by Fallon (1978) with the exception that, because of the heavier growth obtained by incubating the final inoculum on a shaker at 37 °C, the final inoculum applied to the plates was first diluted 1 in 50. Disc sensitivity testing was found to be unreliable with a 100 μg disk, but a 25 μg disk differentiated between sensitive and resistant strains.

Penicillin sensitivity testing. This was performed by an agar dilution technique incorporating benzyl penicillin in Mueller Hinton agar and using the same inoculum as for sulphadiazine sensitivity testing. The final concentrations of penicillin ranged, in a doubling dilution series, from 0·25–0·0078 mg/l.

Epidemiology. For the years 1972 to 1976 a retrospective questionnaire was sent to the laboratories forwarding strains of meningococci for examination requesting details of age and sex of the patient, site from which the meningococci were isolated (and, in the case of strains isolated from sites other than brain or cerebrospinal fluid, whether the patient had signs of meningitis) and the outcome of infection. After 1976 a request for details of the case was sent together with the report on meningococcal group, sulphonamide and penicillin sensitivity to the forwarding laboratory.

RESULTS AND DISCUSSION

Table 1 shows the cases of meningococcal disease and fatal cases notified from clinical sources together with the laboratory isolations of meningococci for the years 1972–82. The Table also shows the number of strains of *N. meningitidis* forwarded to the Reference Laboratory and it can be seen that apart from 1972 a high proportion of strains was available for serogrouping and antibiotic sensitivity testing. More cases of infection were notified than of laboratory isolations of meningococci. Some discrepancy is to be expected, for instance, due to cases diagnosed at autopsy where bacteriological confirmation may not have been possible but the reasons for the wide discrepancies, sometimes greater than twofold, are unknown. Apart from 1974–6 the eleven years from 1972 to 1982 have seen a decline in meningococcal infections in Scotland. Hence, if notifications are related to population the overall rate of disease per 100000 of the population ranged from approximately 6·2 in 1975 to 2·1/100000 in 1982. However, based on laboratory isolations the figures range from a peak of 4/100000 in 1974 to 1·2/100000 in 1982. The increased prevalence of infection in 1974–6 was due to an increase in group B strains and paralleled a similar increase in England and Wales. Infections followed a seasonal pattern over the period, 35·5% of laboratory isolations being reported in the first three months of the year, 28% in the second three months, 17% in the third and 19·5% in the last three months of the year.

Serogroups

Table 2 shows the results of serogroup determination. Group B predominated followed by groups A, C and W135 in that order. Group C strains were not only less prevalent than group A but in 1975 and 1976 were fewer in number than groups

Table 1. *Meningococcal disease Scotland*, 1972–1982

	Confirmed notifications and laboratory isolations											
	1972	1973	1974	1975	1976	1977	1978	1979	1980	1981	1982	Total
Notifications	113*	121*	170*	324	242	158	181	185	172	136	110	1,912
Notified deaths	22	21	23	29	16	9	12	8	10	5	10	165
Strains from meningitis	87	87	171	125	114	86	70	71	69	56	49	985
Strains from septicaemia	14	20	38	33	14	11	10	13	18	18	11	200
Total isolations of *N. meningitidis*	101	107	209	158	128	97	80	84	87	74	60	1185
Strains forwarded to Reference Laboratory	44	69	149	131	118	81	76	70	76	60	53	927
Proportion of total strains forwarded (%)	44	64	71	83	92	84	95	83	87	81	88	78

* Figures prior to 1975 are confirmed notifications of cerebrospinal fever (sources; Scottish Health Statistics 1972–81, Scottish Health Service Advance Tables June 1983, and Registrar General's Annual Reports, Registrar General Scotland).

Table 2. *Serogroups of* N. meningitidis *isolated from patients in Scotland* 1972–1982

rogroup	A	B	C	X	Y	Z	W135	Not groupable	Tot
1972	3	32	8	0	0	0	0	1	4
1973	8	43	13	0	1	0	3	1	6
1974	25	113	5	0	1	0	4	1	14
1975	33	73	8	0	0	0	17	0	13
1976	27	72	6	1	0	0	11	1	11
1977	27	43	5	0	1	0	5	0	8
1978	15	43	11	0	2	0	5	0	7
1979	15	42	8	0	2	0	3	0	7
1980	9	53	9	0	3	0	2	0	7
1981	8	34	13	0	1	0	4	0	6
1982	9	36	3	0	2	1	2	0	5
Total	179	584	89	1	13	1	56	4	92
portion of tal (%)	(19·3)	(63)	(9·6)	(0·1)	(1·4)	(0·1)	(6)	(0·4)	(10

A, B and W135. Of the other serogroups, group Y was the commonest in disease but no fatalities occurred, nor was any case of meningococcal pneumonia seen, a disease, although rare, reported to be associated with group Y meningococci (Irwin, Woelk & Coudon, 1975; Yee, Katz & Neu, 1975). One thousand, one hundred and fifty-six strains of meningococci isolated from carriers were also forwarded to the Reference Laboratory, many from a study of meningococcal carriage in patients attending a department of sexually transmitted diseases (Young *et al.* 1983). Although the majority of strains came from the respiratory tract, many were isolated from genital sources. The serogroup distribution differed from that in disease. Hence, only 2·9% of meningococci isolated from carriers were of group A and, although group B strains predominated (40% of all strains), non-groupable strains were common (32%) as opposed to 0·4% in cases. Meningococci of group Z[1] (29E) (Fallon, 1976) were seen only in carriers. The increase in group B strains seen both in England and Wales as well as in Scotland in 1974–6 might lead one to expect that the general serogroup distributions in the UK would be similar. However, the serogroup distribution differed in that group C strains formed a much smaller proportion of those isolated in Scotland compared with England and Wales except in 1973 when they were 19% of the total, the same as England and Wales, 1978 when they were 14% of the total compared with 15% in England and Wales (Jones & Eldridge, 1981) and in 1981 when 21·6% of strains isolated in Scotland were of group C. Overall, group C strains were much less prevalent than in the same period in Norway, Denmark and Sweden and Holland but closer to the prevalence noted in France (Report, 1981). At the beginning of the period most group C strains were isolated by laboratories in the East of Scotland and it is interesting that the higher prevalence of group C strains in 1981 was principally due to strains isolated in the East of Scotland. At the beginning of the period, group A strains were isolated by laboratories in the West of Scotland but not from the North-East; later, however, group A strains appeared in the North-East raising the possibility of the effect of population movement from the West to the North-East

Table 3. *Meningococcal meningitis Scotland* 1972–1982: *Distribution of patients by age and serogroup isolated*

	Age (years)									
Serogroup	0–4	5–9	10–14	15–19	20–29	30–39	40–49	50–59	60+	Total
A	43	21	14	17	17	8	15	10	13	158
B	357	42	16	18	10	6	4	5	9	467
C	27	11	8	9	4	3	3	1	5	71
X	—	—	—	—	—	—	—	—	1	1
Y	1	1	1	1	2	1	—	—	2	9
Z	—	—	—	—	—	—	—	1	—	1
W135	26	1	3	1	4	2	1	1	4	43
Not groupable	1	1	1	—	—	1	—	—	—	4
Total	455	77	43	46	37	21	23	18	34	754
Proportion of total strains	60·3	10·2	5·7	6·1	4·9	2·8	3·1	2·4	4·5	

in association with North Sea oil production as a means of influencing the serogroup distribution within Scotland. Other serogroups, with the exception of W135 in 1975 and 1976, when they were 13% and 9% of all strains isolated, were of little significance. The isolation of a group Z strain from one adult with meningitis is notable as such findings are very rare. Details of the case will be published elsewhere.

Serotypes

So far, only a limited number of strains of serogroups B, C, W135 and Y have been examined for serotype antigen. Only a proportion of the rabbits immunized by the technique of Frasch & Chapman (1972*b*) or of Gold & Wyle (1970) gave sera which were satisfactory. Those prepared using Freund adjuvant were better. The sera obtained were mainly of value for typing by precipitation in agar gel. Those produced by the short course of injections of whole live organisms were all satisfactory for typing by co-agglutination. Types of the 2 complex (2a, 2b, 2c, 2.7, 2.10) predominated amongst group B strains, with type 15 appearing in recent years. Types of the 2 complex were predominant also in the small number of group C strains so far examined.

Meningococcal meningitis

Details of disease, age and sex were available for 858 (93%) of the 927 patients from whom cultures were forwarded to the Reference Laboratory. The distribution of cases of meningococcal meningitis by age and serogroup is shown in Table 3. The majority of cases occurred in children aged three months to four years. Few cases occurred under three months of age. Ten percent of cases were aged 3–5 months, 14% 6–11 months, 14% 12–24 months and 19% 2–4 years. Hence, the age distribution was as to be expected in children, the cases in the first year of life exceeding those in succeeding years. Group B strains predominated in the young, 77% of strains coming from patients under five years old, and were relatively

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Table 4. *Meningococcal septicaemia Scotland* 1972–1982 *distribution of patients by age and serogroup*

	Age (years)									
Serogroup	0–4	5–9	10–14	15–19	20–29	30–39	40–49	50–59	60+	Total
A	7	3	4	1	1	—	—	—	—	16
B	57	3	—	1	—	—	1	2	2	66
C	3	—	2	1	—	—	—	2	1	9
Y	—	—	—	—	—	—	—	1	—	1
W135	3	—	—	1	2	—	—	—	6	12
Total	70	6	6	4	3	0	1	5	9	104
Percentage of total	67·3	5·8	5·8	3·8	2·9	0	1	4·8	8·6	100

uncommon in later life. In contrast, there was a more even distribution of groups A, C, Y and W135 between the different age groups and less than 50% of strains of groups A, C and Y were isolated from children under the age of five years. Even so, 65·5% of meningitis due to groups A and C occurred in patients aged under 20.

The suggestion has been made (Peltola, Kataja & Mäkelä 1982) that the age distribution of meningococcal meningitis shifts during an epidemic, the proportion of infections over the age of four increasing significantly. This shift could possibly happen in Scotland if groups other than B predominated as they are proportionately more prevalent in patients over the age of five than is the case with group B strains. A comparison of the age distribution of meningococcal meningitis for the years 1972–7 compared with the distribution for the whole period 1972–82 has not shown any notable age shift. This does not contradict the suggestion of Peltola, Kataja & Mäkelä (1982) since no epidemic has occurred in Scotland in the period under review.

Meningococcal septicaemia

The distribution of cases of septicaemia by age and serogroup is shown in Table 4. Septicaemia without meningitis was much less frequent than meningitis. However, as with meningitis the majority of patients were under the age of five. There were proportionately more cases of meningitis due to group A meningococci than of septicaemia, but the converse was true with W135 strains. No case of septicaemia was caused by a non-groupable strain. Most cases of septicaemia were due to group B meningococci and were in virtually the same proportion as seen in meningitis. There was a difference in the proportion of cases aged 50 or over with meningitis (6·9% of all cases of meningitis) as opposed to septicaemia (13·4% of all cases) although the numbers were small. This does, however, raise the question as to the basis of this difference – particularly if borne out in other studies on meningococcal infections.

As shown in Table 5 meningitis was more common in males than in females, the overall ratio being 1·3:1, but differing from this in some age groups. There was no overall difference between the sexes in septicaemia although, as with meningitis. there was a predominance of females in the over 60–year age group probably reflecting the larger female population at risk.

Outcome of disease

The outcome of disease in relation to the infecting serogroup is shown in Table 6. Fewer patients (694 as opposed to 858) are reviewed in this table as information about the outcome of disease was incomplete for patients who were ill in the years 1972–6. The overall mortality in meningitis was 7·5 % but was higher in infections due to groups A and C than in those due to groups B and W135. Infections with other groups were too few for analysis. The mortality in septicaemia was 20·6 %, reflecting the severity of the illness compared with meningitis. No details were available about the combination of septicaemia with meningitis in the fatal cases of meningitis, nor of the severity of illness on admission to hospital, but uncomplicated meningitis usually has a favourable prognosis. Davey *et al.* (1982) noted that all but one of their fatal cases were ill for no more than one day before death and Goldacre (1976) noted that only 5 % of 23 fatal cases admitted to hospital survived more than 24 h. Hence, the paradoxical situation arises that in a country where good medical care ensures rapid and early admission to hospital, the mortality rate may seem higher because patients will tend to be admitted before what is an inevitable outcome, whereas where cases die before admission, laboratory confirmation of the cause of death may be lacking, thus reducing mortality statistics based on laboratory confirmation. Cases where there is a delay in admission may have a lower mortality because their disease is not severe enough to kill rapidly and is amenable to treatment. Naturally, early admission to hospital should always be the aim but with therapy commenced as soon as even a provisional diagnosis has been reached in order to try and prevent death or disability. It may be possible to lower the mortality of severe meningococcal infections if aggressive therapy as suggested by Bjorvatn *et al.* (1984) is adopted.

Table 6. *Outcome of meningococcal infections Scotland* 1972–1982 *in relation to serogroup*

		Outcome			
Disease	Serogroup	Well	Disabled (%)	Fatal (%)	Total
Meningitis	A	112	6 (4·4)	17 (12·6)	135
	B	335	6 (1·7)	17 (4·7)	358
	C	51	3 (4·9)	7 (11·5)	61
	W135	38	1 (2·3)	4 (9·3)	43
	Total	536	16 (2·7)	45 (7·5)	597
Septicaemia	A	12	0	2 (14·3)	14
	B	45	0	13 (22·4)	58
	C	9	0	4 (30·8)	13
	W135	11	0	1 (8·3)	12
	Total	77	0	20 (20·6)	97

Table 5. *Meningococcal infections Scotland* 1972–1982*: relationship between disease, age and sex of patient*

		Age													
		Months				Years									
Disease	Sex	0–2	3–5	6–11	12–23	2–4	5–9	10–14	15–19	20–29	30–39	40–49	50–59	60+	Total
Meningitis	Male	10	49	66	52	87	45	19	26	29	14	12	9	8	426
	Female	12	28	42	53	56	32	24	20	8	7	11	9	26	328
Septicaemia	Male	2	3	8	18	9	3	2	1	1	0	0	2	2	51
	Female	0	3	9	7	11	3	4	3	2	0	1	3	7	53
															858

Table 7. *Outcome of meningococcal infections in relation to age Scotland* 1972–1982

		Age													
		Months				Years									
Disease	Outcome	0–2	3–5	6–11	12–23	2–4	5–9	10–14	15–19	20–29	30–39	40–49	50–59	60+	Total
Meningitis	Fatal	1	2	5	8	5	3	2	3	2	0	3	3	9	46*
	Disabled	—	—	2	1	6	1	2	0	1	1	0	2	3	19
Septicaemia	Fatal	—	—	4	7	2	1	2	—	—	—	1	2	1	20
	Disabled	—	—	—	—	—	—	—	—	—	—	—	—	—	0

* Includes one death due to *N. meningitidis* serogroup X.

Disability was relatively infrequent, the overall rate being 2·7 % in meningitis. No case of septicaemia showed residual disability. It is of interest to compare these findings with others in Europe and the USA. Bohr *et al.* (1983*a*) found that the mortality of all meningococcal infections admitted directly to the Rigshospitalet in Copenhagen was 0·4 % of 495 patients as opposed to 7·2 % for those admitted to other units and then referred. Davey *et al.* (1982) found mortality rates of 3·5 % of cases admitted to the East Birmingham Hospital and of 4·1 % in those admitted to other Birmingham Area hospitals. Andersen (1978) found that in the period 1971–6 10 % of cases of meningitis in Norway were fatal and noted the unfavourable prognosis in patients with petechiae.

Septicaemia is well known to be associated with a higher mortality rate than meningitis (Peltola, 1983) and the rate for Scotland of 20·6 % is not surprising but is much lower than that reported from Norway by Bjorvatn *et al.* (1984). The overall fatality rate for all meningococcal disease of 9·5 % may be compared with the rates in Scandinavia, which ranged from 4·1 % to 13·7 % (Peltola *et al.* 1982) but is higher than that of 3·7 % noted in a preliminary survey of 500 patients in Holland (Bol *et al.* 1983). Rates for two series published in the USA were higher than 9·5 %, that of a cooperative study in 1975 (Meningococcal Disease Surveillance Group, 1976) being 19 % and that in New York City (Galaid *et al.* 1980) of 22·6 % for groups A, B and C. Table 7 shows the morbidity and mortality in those cases whose age was known. Only 20 (44 %) of the 45 fatal cases of meningitis were in children under the age of five years despite the fact that 60 % of cases were in that age group. Conversely, although only 10 % of cases were aged over 40 years 33 % of the fatalities occurred in that age group. Thirteen of the 20 fatal cases of septicaemia were aged under five years but the proportion of fatal cases mirrored the age distribution of all cases. Table 8 shows the age of fatal cases and the group of meningococcus isolated from them. As with all disease due to group B *N. meningitidis*, the majority of fatal cases due to group B were in those under five years of age in contrast to the other serogroups, where most cases were aged over five years. Altogether, 50 % of fatal disease occurred in those aged over five years, but if deaths from group B are excluded the figure rises to 77 %.

In Scotland there was a difference in mortality in meningitis due to the different serogroups, that due to groups A and C being similar (12·6 % and 11·5 % respectively, very similar to the figures for a study in Nigeria by Evans-Jones *et al.* 1977) but being slightly higher than that due to W135 (9·3 %) and much higher than group B (4·7 %). Differences in case fatality between the different serogroups have been noted by de Marie & Zanen (1983) in Holland but were not seen in New York City over the period 1973–8 (Galaid *et al.* 1980). The interesting observation was made by Evans-Jones *et al.* (1977) that the overall mortality was higher in group C infections compared with group A, but became the same if acute meningococcaemia, which was entirely due to group C meningococci, was excluded from the analysis. It is important to remember that mortality can be high in local outbreaks as in Bolton in 1971–4 (Moss, 1982), a finding which may be obscured by taking overall national figures. In Scotland the differences in mortality in septicaemia were slight except that only one (8·3 %) of all cases of septicaemia due to group W135 was fatal. The proportion of group A strains causing septicaemia was lower (14·5 %) than of

Table 8. *Fatal cases of meningococcal infection Scotland* 1972–82*: age of patient in relation to serogroup of infecting strain*

	Age													
	Months				Years									
Group	0–2	3–5	6–11	12–23	2–4	5–9	10–14	15–19	20–29	30–39	40–49	50–59	60+	Total
A	0	1	2	1	1	1	2	3	0	0	2	2	4	19
B	1	1	6	11	6	1	0	0	1	0	1	1	1	30
C	0	0	0	3	0	2	1	0	0	0	1	2	2	11
X	0	0	0	0	0	0	0	0	0	0	0	0	1	1
W135	0	0	1	0	0	0	1	0	1	0	0	0	2	5
Total	1	2	9	15	7	4	4	3	2	0	4	5	10	66

Table 9. *Sulphonamide sensitivity* (%) *of meningococci isolated from patients with septicaemia or meningitis Scotland* 1972–1982

	Year										
Sensitivity to sulphadiazine	1972	1973	1974	1975	1976	1977	1978	1979	1980	1981	1982
Sensitive (minimal inhibitory concentration (MIC) 1 mg/l)	38	34	29	31	37·5	24·5	28·5	21	45	45	56·5
Partially resistant (MIC 10 mg/l)	48	51·5	60	54·5	51	63·5	61·5	64	47·5	35·5	22·5
Resistant (MIC > 10 mg/l)	14	14·5	11	14·5	11·5	12	10	17	7·5	19·5	21

those causing meningitis (22·5%). The proportions of strains of group C and W135 causing septicaemia were higher than those causing meningitis. There is a difference in age distribution of the various serogroups. When age is related to the outcome there were fewer deaths due to meningococci of groups C and W135 in those under five years of age in relation to the proportion of cases in that age group.

Recognized residual disability was low in this series with only 16 (2·7%) cases being disabled, most mildly so and would accord with the findings of Moss in Bolton (1982). This contrasts sharply with the findings of Bohr *et al.* (1983*b*), who found a total of 34·6% of 308 cases of meningococcal meningitis to have sequelae. The assessment of disability in the Scottish cases was objective as opposed to the subjective assessment in the cases reviewed by Bohr and colleagues but it would be interesting to review the final outcome in cases more closely to see whether Bohr's findings can be confirmed.

Sulphonamide resistance

Prior to the emergence of sulphonamide-resistant meningococci sulphonamides could be used both for treatment and prophylaxis of infection. Sulphonamide-resistant meningococci were not detected in Scotland until 1970. Since that time they have been commonly seen as shown in Table 9. Full resistance to sulphonamides was fairly stable until 1979 since when the annual proportion of resistant strains has fluctuated between 7·5% and 21%. Fully sensitive strains were more prevalent in the last three years of the study.

Sulphonamide sensitivity of meningococci is only important in relation to cheap and easy treatment of infection and clearance of organisms from the nasopharynx of cases and carriers unless there is a relationship between sulphonamide resistance and virulence. Group A meningococci (which are principally isolated from cases of disease) have consistently shown a relatively high proportion of sulphonamide-resistant strains over the period 1974–82 similar to findings in England and Wales (D. M. Jones, personal communication). The lowest figure was 18% in 1975 but has been 40% or over since 1977, reaching a peak of 75% in 1981, unlike the USA, where, over the period 1975–80, 16% of group A strains were resistant compared with 67% of group C (Band *et al.* 1983). Group B strains are isolated frequently from both cases and carriers and here, apart from 1977 when 6·5% of strains from carriers were resistant to sulphonamides as opposed to 4·5% from cases, the proportion of resistant strains isolated from cases has been higher than the proportion from carriers. Over the nine years from 1974 to 1982 12·9% of group B meningococci from cases have been resistant as opposed to 5·5% from carriers. The significance of this observation is uncertain but it would be of interest to know if similar observations had been made elsewhere. The decrease in the proportion of 'partially resistant strains' in 1980–2 is at present unexplained but the results agree with the sensitivity results found by Dr H. A. Feldman with these strains.

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