AN OUTBREAK OF MENINGOCOCCAL MENINGITIS IN GAUTENG, SPRING 1996

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Objective. To describe a *Neisseria meningitidis* outbreak in Gauteng during the period 1 July to 31 December 1996.

Design. A descriptive study.

Setting. Patients with meningococcal meningitis in Gauteng who had been diagnosed by laboratory means, or notified during the period 1 July to 31 December 1996.

Main outcome measures. Data including age, sex, date of admission to hospital, *N. meningitidis* serogroup and outcome were collected from Gauteng notification lists, South African Institute of Medical Research (SAIMR) records, a linelist compiled by the Gauteng Health Department, and hospital records.

Results. A total of 201 patients was studied; of this number 87 (43%) had been notified. Seventy per cent of cases were below 30 years of age and 78% were male. More than half (54%) of the cases were from the West Rand. The case fatality rate for 70 cases of known outcome was 14%. Serotyping of 85 isolates showed that a majority (76%) were serogroup A, with 57% being serogroup A clone I-1. Serogroup A clone III-1 accounted for 14% of the typed isolates. All isolates were sensitive to penicillin with minimum inhibitory concentrations of $< 0.05\ \mu g/ml$.

Conclusion. In 1996 Gauteng experienced an epidemic of serogroup A meningococcal meningitis. The serotype that caused the majority of cases had been recorded in South Africa before, but serogroup A clone III-1, responsible for epidemics spreading across two continents, was recorded in South Africa for the first time. Notification of cases by health workers was inadequate in this epidemic.

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Meningitis due to *Neisseria menigitidis* occurs worldwide and is a serious disease. There are eight common serogroups, A, B, C, L, X, Y, W-135 and Z.[1] Meningitis is the common clinical presentation of meningococcal disease; other manifestations include septicaemia, pneumonia, arthritis and benign bacteraemia. Meningococcal disease is sporadic or endemic in developed countries, with serogroups B and C accounting for most disease.[1-6] Most major epidemics of meningococcal infection in developing countries are caused by serogroup A.[1,3] Within the savannah region of sub-Saharan Africa the geographical region extending from Upper Volta to Ethiopia is known as the meningitis belt, as large epidemics of serogroup A disease occur there every 5 - 10 years.[3,7]

On the basis of serotyping performed by the South African Institute of Medical Research (SAIMR), serogroup A predominated in Gauteng up to 1973, but more recently serogroups B and C have emerged as important causes of meningitis (SAIMR Annual Reports).

Strains of serogroup A differ in their ability to cause epidemics. Clones identified by multilocus enzyme electrophoresis (MLEE) or by DNA restriction fragment analysis have caused widespread outbreaks of disease.[2]

Two MLEE serogroup A clones, confirmed by Dr Dominique Caugant of the World Health Organisation (WHO) Meningococcal Reference Centre in Oslo, Norway, have been identified in South Africa. The first, clone I-1, was already documented in South Africa in 1968.[8] In the 1980s it caused several cases in this country, as well as fairly large outbreaks in the former Eastern Transvaal and Mozambique. In 1995, before the present epidemic, a few isolates of this clone were already shown to be present in Gauteng (McGee *et al.* — unpublished data).

The second clone, clone III-1, has been associated with large-scale epidemics that started in Nepal in 1983 - 1984, spread to India and Pakistan in 1985 and caused a further epidemic during the Mecca pilgrimage in 1987.[2] By 1990 the clone had reached Uganda, and in the following year it was documented in Tanzania.[2] The existence of clone III-1 has not previously been documented in South Africa.

The incidence rate for meningococcal disease in developed countries is 1 - 3/100 000 persons,[4-6] whereas in endemic areas in developing countries it can range from 10 to 25/100 000.[9] In 1991 the incidence rate for the seven regions of South Africa, which excluded independent homelands, was 2.6/100 000, with a rate in the Western Cape of 8.7/100 000.[10] The Western Cape notifies more than half the cases recorded in South Africa.[11,12]

The number of meningococcal infections notified in South Africa for 1994 and 1995 was 343 and 348 respectively, while for the same years in Gauteng the figures were 24 and 36.[11,12] In the 1996 notification figures for South Africa and Gauteng were

398 and 118 respectively (Department of Health — personal communication).

Mortality from meningococcal disease depends largely on the form of disease. For meningococcal septicaemia, the case fatality rate in the USA is 18.5 - 21%,[4,6] while case fatality rates as high as 70% have been recorded in some developing countries.[13] Mortality for meningitis is lower at 7 - 10% in developed countries.[1,4,6] In South Africa notifications for the period 1983 to 1992 showed a case fatality rate ranging from 9.9% to 16.1%, while for 1993 and 1994 these rates were 13% and 8%, respectively,[10,12,14]

In mid-August 1996 the Gauteng Health Department became aware of an outbreak when 22 cases of confirmed meningococcal meningitis occurred in mines on the West Rand and in Bekkersdal, a neighbouring community. The Gauteng Health Department set up a team to investigate the spread of the epidemic from the mines to other parts of Gauteng and to plan strategies for control.

OBJECTIVES

It was decided to describe the epidemic of meningococcal meningitis in Gauteng from 1 July to 31 December 1996 in terms of the following: (*i*) number of cases occurring per week; (*ii*) the source of identification of cases, including official notification; (*iii*) age and sex of patients; (*iv*) geographical distribution of patients; (*v*) case fatality; and (*vi*) laboratory typing of isolates.

METHODS

The total number of cases occurring within the defined 6-month period was obtained from three sources.

The first source was a linelisting drawn up by fieldworkers of the AIDS and Communicable Diseases Directorate of Gauteng Health Department during the epidemic. All local authorities and hospitals were required to report suspected cases of meningitis to the Directorate. This process took place from 1 July 1996 to 30 September 1996. From this linelisting the researchers only included those cases that had a final diagnosis of meningocccal meningitis in their hospital records. Not all these cases were bacteriologically proven, some were confirmed by antigen detection in CSF, using latex agglutination. This is referred to as the 'linelist' list in the text.

The second source of cases, referred to as the 'SAIMR' list, came from the SAIMR reference laboratory in De Korte Street, Johannesburg. *N. meningitidis* strains isolated at SAIMR laboratories serving the Gauteng academic hospitals, Leratong Hospital and Sizwe Hospital for Tropical Diseases were sent to the SAIMR reference laboratory for serotyping.[15] Strains from the mines were limited to two mines that submitted CSF specimens for culture to the reference laboratory. DNA fingerprinting using arbitrarily primed polymerase chain reaction (AP-PCR)[16] and ribotyping[17] were performed on these isolates. Penicillin susceptibility testing was carried out using standard broth microdilution methods as specified by the National Committee for Clinical Laboratory Standards.[18] This was a special request from the reference laboratory in view of the epidemic. The laboratory had specimens from the beginning of 1996, but only specimens collected from 1 July to 31 December were included in the study.

The third source of cases was the official notification records at the Information Directorate of Gauteng Health Department. These notifications were derived from local authority reports to the Directorate. To cater for delays in notification, notifications up to 10 March 1997 were reviewed to obtain all meningococcal meningitis cases with dates of notification or dates of onset of disease between and including 1 July 1996 and 31 December 1996. This is called the 'notification' list in the text.

The case definition of meningococcal meningitis in the linelist compiled by the Gauteng fieldworkers included those cases with a final hospital diagnosis of meningococcal meningitis. The case definition of the notified patients was based on the clinical assessment of the notifying medical doctor. The SAIMR cases were, by definition, all bacteriologically confirmed.

The date of admission to hospital was used as an approximation of the date of onset of disease.

Data including age and sex of patients, date of admission to hospital or date of specimen collection, address, outcome and laboratory typing were collected, entered and analysed on Epi-Info version 6.04.

RESULTS

Patient numbers

A total of 201 patients were recorded using the three lists described. Only 2 of the 201 cases appeared on all lists. Eighty-seven cases were in the Gauteng notification list, 70 on the Gauteng linelist and 85 on the laboratory list. The number of cases common to all three lists is illustrated in Fig. 1.

Notifications

By 10 March 1997 only 87 (43%) of the 201 cases had been officially notified via local authorities to the Gauteng Health Department as having occurred or been notified between 1 July and 31 December 1996.

Out of the 70 cases compiled as a linelisting by the Directorate of AIDS and Communicable Diseases during the epidemic, 12 (17%) were subsequently notified through official channels to the Directorate of Information.

Nineteen (22%) of the 85 cases on the SAIMR list had been notified by 10 March 1997.

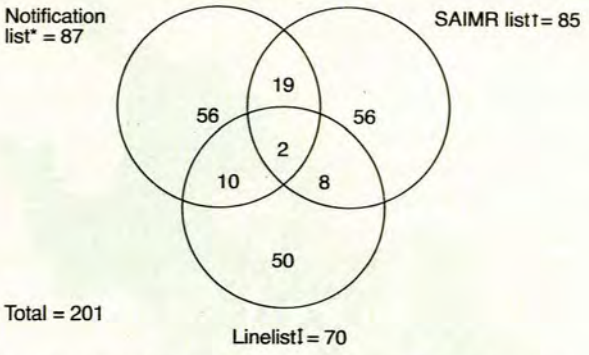

Fig. 1. Allocation of N. meningitidis *patients in Gauteng during the period July - December 1996, using three sources of information. *Patients officially notified by local authorities to the Health Information Directorate at Gauteng Health Department. †Isolates confirmed at the South African Institute of Medical Research Reference Laboratory, Johannesburg. ‡Patients with a hospital diagnosis of meningococcal meningitis, reported to the AIDS and Communicable Diseases Directorate at Gauteng Health Department.*

Distribution of patients according to date of admission

The admission dates of only 124 (62%) of the 201 cases could be ascertained. The epidemic curve is shown in Fig. 2. Most cases occurred during August (54% of total).

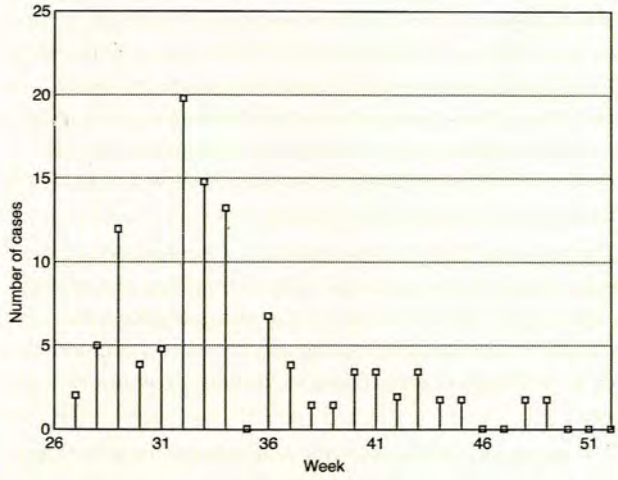

Fig. 2. Numbers of N. meningitidis *cases occurring per week in Gauteng during the period July - December 1996.*

Age

The ages of 161 of the 201 cases (80%) and 59 of the 85 SAIMR-confirmed cases (69%) were known. The age ranges for the total and SAIMR groups were the same, namely 11 months - 70 years, and the median ages were 22 and 16 years respectively. The age distribution shows that over 70% of cases were under 30 years of age (Table I).

Table I. Age distribution of *Neisseria meningitidis* cases

Age group (years)	Total		SAIMR-confirmed	
	N	%	*N*	%
0 - 9	48	30	17	33
10 - 19	25	15	14	26
20 - 29	47	30	15	28
30 - 39	26	16	6	11
> 40	15	9	1	2
Total	161	100	53	100

Sex

The sex of 182 of the total number of patients (90%) and 76 of the SAIMR patients (89%) was known. There was a preponderance of males in both groups — 78% of the total group and 70% of the laboratory group. The marked preponderance of males was to some extent influenced by the disease outbreak in mines, which employ mainly male workers.

Source of patients

Place of origin was known for 191 of the total of 201 patients, and for 79 of the 85 laboratory patients. Table II demonstrates that half the cases (103 of the 191) originated in the West Rand.

Table II. Geographical distribution of *Neisseria meningitidis* cases

Region	Total		SAIMR-confirmed	
	N	%	*N*	%
West Rand	103	54	33	42
Central Witwatersrand	73	38	38	48
East Rand	12	6	8	10
Pretoria	3	2		
Total	191	100	79	100

The reason why there were more West Rand cases in the total group compared with the laboratory group is because early isolates from the West Rand were not sent to the SAIMR reference laboratory for typing.

Of the 70 cases on the Gauteng list 41 (59%) were from the mines.

Outcome

Ten of the 70 cases of known outcome died, yielding a case fatality rate of 14%.

Typing of isolates

Serogrouping of the SAIMR isolates revealed that 65 strains belonged to serogroup A (76%) (Table III), with a smaller number of serogroup B and Y cases. Forty-nine isolates (58%) formed a cluster on DNA fingerprinting and were identified as

Table III. Typing results of *Neisseria meningitidis* isolates

Serogroup	DNA fingerprint type*	No. of isolates	No. of isolates in serogroup
A	1 (clone I-1)	49	65 (76%)
A	2 (clone III-1)	12	
A	3	2	
A	4	1	
A	5	1	
B	6	1	8 (9%)
B	7	1	
B	8	1	
B	9	1	
B	10	1	
B	11	1	
B	12	1	
B	13	1	
C	14	1	1 (2%)
W-135	6	1	2 (2%)
W-135	3	1	
Y	1	1	9 (11%)
Y	15	7	
Y	16	1	
Total			85 (100%)

* Typing using combination of AP-PCR and ribotyping.

Fig. 3. Map of Gauteng showing distribution of N. meningitidis *group A clones, July - December 1996. ▲ = Clone I-1 cases mainly in western part of Gauteng. ■ = Clone III-1 cases mainly in central Johannesburg. The boundary lines in the map define the regions of Gauteng.*

belonging to the clone I-1 (Table III), while a second large cluster comprising 12 isolates (14%) belonged to clone III-I. DNA typing also revealed the presence of a cluster of 7 isolates in serogroup Y and a large number of unrelated strains.

All meningococci were sensitive to penicillin with MICs of $< 0.05\ \mu g/ml$.

The geographical distribution of clone I-1 and clone III-1 is illustrated in Fig. 3. The majority of clone I-1 cases were in the Bekkersdal, Westonaria and Randfontein (West Rand) areas adjoining the mines, while a secondary group was in Alexandra (central Witwatersrand). Most of the cases of clone III-1 were in central Johannesburg, with a few in Soweto.

Discussion

Criteria for defining epidemics have been set by the WHO.[19] In highly endemic areas, including the meningitis belt of Africa, a rate of 15 cases per 100 000 per week over 2 consecutive weeks is taken to be an epidemic. Where epidemics are uncommon, the threshold defined is a three- to fourfold increase in the number of cases compared with those occurring in the same time period in previous years, or a doubling of the number of cases from one week to the next for a period of 3 weeks. An additional marker of epidemic conditions is an increasing proportion of cases in individuals older than 4 or 5 years of age.[19,20]

Only the 118 official notifications for the year 1996 can be compared with other years. The number of cases reported to the Gauteng Health Department for the year 1996 clearly qualifies as being of epidemic proportions, as it was more than three times higher than the 24 and 37 cases reported during 1994 and 1995, respectively. The majority of patients were under 30 years of age but older than 4 years. This is a further criterion that qualifies the outbreak as an epidemic and is consistent with the pattern that has been observed in epidemic sub-saharan African meningococcal cases.

The source of the main epidemic was the mines on the West Rand, with the first case in this particular epidemic recorded on 1 July 1996. This is not surprising, as meningococcal meningitis is known to spread rapidly in closed communities such as are found in army barracks, hostels, prisons and mines.[7]

The serotyping of the epidemic was valuable in indicating different serotypes causing disease. The non-A serotypes were randomly distributed throughout the province, while group A strains occurred in fairly well-defined areas of Gauteng. The group A clone I-1, which is not new to South Africa, was highly concentrated in the West Rand, apparently having arisen in the mines. The group A clone I-1 clearly caused the outbreak in the mines, but as comprehensive DNA fingerprinting was not available, the number of cases not belonging to this clone is unknown. The cases occurring in the West Rand belonged almost exclusively to this clone. Clone I-1 also occurred in other areas of Gauteng, but to a lesser extent.

The proven presence in 1996 of group A clone III-1 in the Johannesburg central business district is a matter for concern.

This strain has been documented for the first time in South Africa; as it is a cause of major epidemics worldwide, it needs to be closely monitored.

Only 43% of the cases were notified. This figure suggests that there are problems in the notification system, starting at the source of notification. A further 29% of cases was reported to the Gauteng Health Department, but official notification forms were not submitted. It would seem that some health workers might have confused the list required by Gauteng with the need for notification. This distinction needs to be explained fully in future outbreak management.

Early in the epidemic the number of cases in Bekkersdal was disturbing. The Gauteng Health Department had to consider whether or not vaccination was necessary; however, the number of cases in this community subsequently declined and this intervention was not undertaken. The affected mines on the West Rand did vaccinate their employees (Dr P Lowe — personal communication). This action was warranted as the WHO recommends vaccination during epidemics, especially in areas where the epidemic is maximal.[19] Extension of a vaccination campaign to surrounding areas is necessary if infection rates exceed 5 cases per 100 000 people.

RECOMMENDATIONS

The spread of meningococcal disease in high-risk areas such as mines, prisons and army barracks is well documented. Effective tetravalent (A, C, Y, W-135), bivalent (A, C) and monovalent (A) vaccines are available and vaccination is advisable. The WHO recommends chemoprophylaxis to close contacts of persons sharing the same housing, particularly room-mates in households, institutions or barracks.[19] However, during epidemics the WHO does not recommend mass chemoprophylaxis.

In a closed community such as a mine, where large numbers of people are housed, vaccination should be resorted to if an epidemic of meningococcal meningitis preventable by a vaccine occurs. Chemoprophylaxis of close contacts should be instituted during the early stages of the outbreak.

Regular immunisation of new mine recruits should be considered by mine authorities depending on frequency of cases and outbreaks. All health workers dealing with meningococcal meningitis cases should be advised about vaccination.

Health workers require education, monitoring and feedback on the official notification system currently operating in South Africa. National, provincial and local surveillance systems should be established to monitor trends and recognise new epidemics. To be effective, outbreak control must be timeous and thorough. Proven cases of meningococcal meningitis should be reported telephonically to local authority health departments as a matter of urgency so that appropriate control measures can be implemented.

DNA typing of bacterial isolates should be performed in a central laboratory and monitored on a regular basis; in the face of an epidemic this process should be intensified. The fact that clone III-1 has been shown to be present in South Africa makes it mandatory that any sign of an outbreak should be identified as soon as possible. Group A vaccines will protect against all group A strains, including those belonging to clone III-1.

Antimicrobial susceptibility testing has shown meningococcal strains in Gauteng province to be sensitive to penicillin (< 0.05 μg/ml) (SAIMR data). Decreased susceptibility has been documented in a number of isolates in South Africa and intermediately resistant strains with values as high as 1.01 μg/ml have been reported.[21] Although such resistant meningococcal strains have been reported infrequently to date, clinicians should be alert to the possibility of their occurrence in unexplained treatment failures. Continued surveillance for increasing penicillin resistance should therefore be instituted and trends should be carefully monitored.

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