Bull. Org. mond. Santé
Bull. Wld Hlth Org. } 1971, **45**, 275-278

Meningococcal Infections*

1. Prevalence of Serogroups Causing Disease in US Army Personnel in 1964–70

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Examination of large numbers of strains of meningococci associated with systemic disease in US Army personnel over a 7-year period has shown a changing pattern of serogroup prevalence and an increasing proportion of sulfadiazine-resistant organisms. These findings underline the failure of sulfadiazine prophylaxis and the necessity of applying a specific vaccine to this population. Knowledge of this kind from other populations will be required in order to provide appropriate control measures—vaccine or chemoprophylaxis.

Dissemination of sulfonamide-resistant meningococci, initially described in US military camps in California (Gauld et al., 1965; Millar et al., 1963), has subsequently been found in civilian and military populations throughout the world (Alexander et al., 1968; Vandekerkove et al., 1969; Vassiliadis, Kanellakis & Papadakis, 1969). Since 1964 US Army populations have been followed closely to determine the prevalence of resistant meningococci. This was accomplished in part by establishing a reference centre at the Walter Reed Army Institute of Research to which isolates from meningococcal illnesses were submitted for final identification. A previous report, which summarized these data up to the early part of 1967, showed a changing prevalence of serogroups and a high incidence of sulfadiazine resistance, and also described several new serogroups (Evan, Artenstein & Hunter, 1968).

The present report extends these observation to May 1970 and patterns of serogroup prevalence and sulfadiazine resistance are more clearly documented. In addition, selected data from nasopharyngeal carrier surveys, obtained in US Army recruit camps, are presented for comparison with results from " case " strains.

METHODS

Origin of strains

Army medical treatment centres throughout the world transmitted presumptive cultures of *Neisseria meningitidis* to the Walter Reed Army Institute of Research on agar slants. The great majority of strains were obtained from recruit training centres in continental USA. Most of the isolates came from blood or cerebrospinal fluid but a few were cultured from joint aspirates, sputum, or tissue obtained *post mortem*.

Identification of strains

The methods for serogrouping, carbohydrate fermentations, and sulfadiazine sensitivity tests were those previously described by Evans, Artenstein & Hunter (1968). Nasopharyngeal carrier surveys were performed by methods already reported (Artenstein et al., 1967).

RESULTS

Between 1 January 1964 and 15 May 1970, 1 745 cultures were identified as strains of *N. meningitidis*. Each year over 90% of cultures were classified as serogroups B or C (Table 1). Group A strains were exceedingly rare during this period. Of 12 such strains only 1 was isolated from a patient with an illness acquired in continental USA. Only 4 nongroupable strains were noted in this series. They occurred during the first year of the study; none has been found among the last 1 400 strains examined.

Group B strains predominated during the first 3 years of the study (Table 2). Subsequently, group C strains have increased in number to the current proportion of 96%.

Sulfadiazine resistance of these " case " strains is shown in Table 3. (A level of resistance of 1 μg/ml was chosen since sulfonamide chemoprophylaxis has been unsuccessful at this level.) Resistance among group B strains has varied only slightly during the

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Table 1. Prevalence of meningococcal serogroups causing systemic infections, 1964-70

Serogroup	1964	1965	1966	1967	1968	1969	1970[a]
A	5	3	1	1	0	1	1
B	259	153	226	53	37	37	5
C	29	22	40	81	275	309	150
Y	2	3	12	11	10	7	0
29 E	1	0	0	0	1	0	0
135	0	0	2	2	2	0	0
non-groupable	4	0	0	0	0	0	0
totals	300	181	281	148	325	354	156

[a] To 15 May only.

Table 2. Changing prevalence of serogroups B and C as causes of disease

Serogroup	Percentage of total strains in the following years:						
	1964	1965	1966	1967	1968	1969	1970[a]
B	86.4	84.5	80.4	35.8	11.4	10.4	3.2
C	9.7	12.3	14.2	54.7	84.6	87.3	96.2
other	4.0	3.3	5.3	9.4	4.0	2.2	0.6

[a] To 15 May only.

Table 3. Percentage of strains of serogroups B and C showing sulfadiazine resistance to 1 μg/ml or larger doses of sulfadiazine

Serogroup	1964	1965	1966	1967	1968	1969	1970[a]
B	65	57	71	65	49	49	20
C	7	12	63	86	96	98	96

[a] To 15 May only.

6 full years of study, from 49% to 71% of strains each year being resistant to the drug. Group C strains have shown a different pattern of sulfadiazine resistance. During the first 2 years of the study, when few group C strains were found, most were inhibited by low concentrations of sulfadiazine. As group C infections became more prevalent, the proportion of strains resistant to sulfadiazine increased strikingly; since 1968 over 96% of group C strains recovered each year have been resistant.

Strains of serogroups Y, 29E, and 135 have occurred in small numbers each year. Sulfadiazine resistance patterns in these strains are shown in Table 4. Although some resistant Y strains were found, the majority of cultures of these serogroups have been sensitive to sulfadiazine.

Carrier surveys in various recruit training centres have been performed at frequent intervals since 1964. The limitations on interpretation of carrier rates in relation to disease incidence and other epidemiolo-

Table 4. Sulfadiazine sensitivity of meningococcal serogroups Y, 29E and 135

Serogroup	No. of strains with indicated minimal inhibitory concentration of sulfadiazine (μg/ml)					
	⩽ 0.5	1	5	10	50	100
Y	35	0	1	4	5	0
29E	2	0	0	0	0	0
135	5	1	0	0	0	0
non-groupable	3	0	0	0	0	1

gical problems are illustrated by the selected surveys shown in Table 5. These studies were performed at three different recruit training camps in the eastern USA over a 2-week period. The data show that not only does one camp differ from another but, even within a camp, companies that trained in parallel (i.e., started at same time, followed identical schedules, and had identical living quarters) showed different patterns of meningococcal dissemination.

The number of cases of meningococcal disease in each camp did not correlate well with the survey data. Moreover, although all the illnesses were caused by group C meningococci, many other serogroups and non-groupable strains were found in carriers.

DISCUSSION

Group A meningococci were uncommon in military populations in the USA during the period from 1964 to 1970. The same finding has been reported for civilian populations in the USA (Bennett & Young, 1969). In other parts of the world, however, group A strains have continued to be responsible for epidemic meningitis; this has been especially true in Africa (*WHO Chronicle*, 1969). The shift in prevalence of serogroups causing disease from primarily group B strains to an overwhelming predominance of group C strains has occurred as a natural phenomenon, as have the periodic outbreaks of disease caused by group A strains in the 20th century (Aycock & Mueller, 1950).

The relative infrequency of serogroups Y, 29E, and 135, as well as of non-groupable strains, as causes of systemic disease suggests that these serogroups are lacking in virulence. Although strains identified as 135 have not been common in carriers, Y, 29E, and non-groupable strains have been rather frequently cultured from carriers in US Army training centres (Artenstein et al., 1967). In addition, there is some evidence that there may exist a high level of natural immunity to disease caused by these serogroups in the adult population. Goldschneider,

Table 5. Meningococcal carrier rates and number of illnesses in basic trainees in samples of approximately 100 men in the 6th or 7th week of the training cycle. All patients had group C disease. The average recruit population varied from 7000 to 9000 men at each post

Post	Date	Unit	Positive (%)	No. of strains of indicated serogroup					No. of meningitis cases	
				B	C	Y	29E	NG[a]	Jan.	Feb.
Fort Dix	20 Jan. 1970	C-4-3	41	0	15	1	13	18		
		E-5-2	33	1	15	5	4	8	4	6
		B-5-2	46	5	11	8	6	16		
Fort Knox	28 Jan. 1970	C-16-4	32	2	15	3	2	10		
		A-16-4	29	1	2	1	16	9	0	5
		D-16-4	24	3	2	8	4	7		
Fort Bragg	3 Feb. 1970	A-4-1	21	0	0	8	6	5		
		C-3-1	11	1	2	0	4	4	0	2
		C-2-1	32	2	19	3	3	5		

[a] NG = non-groupable.

Gotschlich & Artenstein (1969) found that over 90% of army recruits possessed bactericidal antibodies against a group Y organism at the time they were inducted into military service. Thus the lack of clinical virulence of group Y strains may be related to the frequent occurrence of serum antibodies against them. It is not clear whether these antibodies are induced by carrier infections with heterologous serogroups of meningococci containing cross-reactive antigens or by homologous strains that lack virulence factors. Until some method of testing for virulence among meningococcal strains is developed, this particular problem will remain unsettled.

The data presented in this report demonstrate that sulfonamide-resistant organisms have been the most frequent causes of systemic meningococcal disease since 1967. This pattern has emerged despite the fact that sulfadiazine prophylaxis was abandoned in army training centres in 1964 except for research purposes. Other antibacterial agents have failed to control outbreaks of disease although new compounds are being tested for this purpose (Sanders & Deal, 1970). However, the development of non-toxic, highly immunogenic polysaccharide vaccines (Artenstein et al., 1970; Gotschlich, Goldschneider & Artenstein, 1969) offers hope that control of meningococcal disease will once again be possible.

RÉSUMÉ

INFECTIONS MÉNINGOCOCCIQUES: 1. PRÉVALENCE DES SÉROGROUPES RESPONSABLES DE LA MALADIE PARMI LE PERSONNEL DES FORCES ARMÉES DES ÉTATS-UNIS D'AMÉRIQUE (1964/70)

De janvier 1964 à mai 1970, 1745 cultures de spécimens pathologiques recueillis chez des militaires américains atteints d'une infection à *Neisseria meningitidis* ont été examinées au Walter Reed Army Institute of Research, à Washington.

Seules 12 souches du groupe A ont été identifiées pendant cette période. Jusqu'en 1966, les souches du groupe B ont été les plus fréquemment rencontrées, tandis que la prévalence des méningocoques du groupe C s'accroissait après cette date pour représenter en 1970 96% des isolats. Chaque année, on a découvert quelques rares souches appartenant à d'autres sérogroupes (Y, 29E, 135).

Dans les souches du groupe B, les caractéristiques de la résistance à la sulfadiazine sont restées relativement stables. De 1964 à 1969, la proportion des isolats résistants à 1 μg/ml du produit a varié de 49 à 71%. La résistance des méningocoques du groupe C s'est accrue dans la même mesure que leur prévalence, et depuis 1968, plus de 96% des souches de ce groupe isolées chaque année étaient résistantes.

Des enquêtes sur les porteurs de méningocoques ont été faites dans trois centres d'entraînement de recrues. Elles ont montré de fortes variations du nombre des porteurs et de la fréquence des divers sérogroupes, sans rapport avec l'incidence de la maladie.

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