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Factors associated with pharyngeal carriage of *Neisseria meningitidis* among Israel Defense Force personnel at the end of their compulsory service

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SUMMARY

In this 1 year cross-sectional study of personnel being discharged from compulsory military service, an available database of health-related information was used to examine the association of meningococcal carriage with socio-demographic factors. A representative, systematic sample of 1632 personnel was interviewed and had throat cultures taken. The overall meningococcal carriage rate was 16%. Serogroups B and Y accounted for 76% and 13% of the isolates respectively. In univariate analysis, carriage was associated with male gender ($P < 0{\cdot}0001$), < 12 years school education ($P = 0{\cdot}002$), smoking ($P = 0{\cdot}014$), and service at a 'closed' base, reflecting greater interpersonal contact ($P < 0{\cdot}0001$). In multivariate analysis, only service on a closed base and male gender retained significance. School education of < 12 years remained significant for females only. Variables not associated with carriage included number of siblings, intensity of smoking, and use of the contraceptive pill. In this setting, meningococcal carriage was associated with the type of base on which soldiers served; and smoking was not an independent risk factor for carriage.

INTRODUCTION

Meningococcal disease is well recognized as a problem in military populations [1–4]. In the Israel Defense Force (IDF), outbreaks of meningococcal disease have been very infrequent and very localized [5]. Recent data have shown that the incidence of meningococcal disease fluctuates and that about 80% of the cases are caused by meningococcal serogroups other than serogroup B, and are thus preventable [6]. This is in contrast to the Israeli civilian population, in which most cases are due to serogroup B [7]. Israel is an area of generally low meningococcal disease activity with annual incidence rates of less than 2 per 100000 residents.

Many studies have addressed the issue of meningococcal carriage among recruits [1, 8–15], acquisition during military service [12, 14], and outbreak control [2, 3]. Carriage rates observed have varied widely, ranging from less than 20% [1] to well above 70% [16]. Previous studies of carriage and acquisition in the IDF carried out in the 1970s [8] indicated that carriage rates on recruitment varied from 6·9 to 24% for different platoons, that cumulative acquisition rates within 3–4 months of recruitment reached

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approximately 80% without accompanying disease, and that most acquired strains were of serogroup Y. The role of associated factors such as smoking, educational level, ethnic origin, etc. was not explored.

There are few studies concerning carriage of meningococci later on in military service. There are no data for the IDF, in which men serve for 3 years, and women for about 20 months. Pether and colleagues [14], found that carriage in a UK military establishment dropped from a high of 56% in soldiers serving less than 1 year to around 30% in those serving between 2 and 4 years, and to around 20% at more than 10 years of service. In a study of naval recruits, Fraser and colleagues [12] showed an increase in carriage from 30% at the start of service, to 71% after 9 months, when the study ended.

A framework has existed in the IDF for many years for gathering health-related data prospectively from personnel [17]. This afforded an opportunity to mount an investigation of meningococcal carriage in IDF personnel and relate it to information from the database. We designed a systematic 1 year cross-sectional study of military personnel leaving compulsory service. This work also represented part of a programme to gather basic epidemiological data regarding the occurrence of *N. meningitidis* in the IDF. In addition to estimating throat carriage rates, the study was intended to examine their association with socio-demographic factors and such behavioural variables as smoking and the use of oral contraceptives.

POPULATION AND METHODS

Period of the study

The study was carried out over 1 calendar year, from April 1993 to March 1994. No outbreaks of meningococcal infection occurred in the IDF during this period. There were 7 sporadic cases of meningococcal disease (data from the IDF Epidemiology Department), 5 due to serogroup C and 2 to serogroup Y with no identifiable epidemiological connection between the patients.

Population

Personnel being discharged after compulsory military service were included in this study. A systematic sample of soldiers entering and leaving the service has been included in ongoing epidemiological studies in the IDF for many years [17, 18]. The sample consists of a fixed proportion of soldiers, who are asked to agree in writing to be interviewed and have certain biological samples taken, such as blood specimens. The sample is considered to be representative of persons undergoing compulsory service in the IDF [17, 18]. During the study, 1632 soldiers were interviewed and had throat cultures taken, 912 males (56%) and 720 females (44%).

Socio-demographic and behavioural variables

Questionnaires were administered by trained interviewers, and for the purposes of this study included the following: the subject's age, number of siblings, the subject's years of schooling (< 12, $\geqslant 12$), the number of years of school education of the subject's father (< 12, $\geqslant 12$), the nature of the base to which the subject had been assigned during service as a measure of intensity of interpersonal contact and living conditions (closed bases on which soldiers live together for weeks at a stretch, and open bases where personnel work on the base and sleep at home), smoking, daily cigarette consumption, and smoking intensity (heavy > 15 cigarettes per day, medium 6–15 per day and light $\leqslant 5$ per day), use of contraceptive pills by women, and geographic-ethnic origin as defined by the place of birth of the subject's mother. Israel comprised one category; Europe, the Americas, Australia and South Africa were taken as representing the West, other African countries as Africa and the rest, including Turkey as Asia.

Laboratory methods

Throat cultures were collected in preference to pernasal specimens [19, 20], on synthetic swabs, and placed in Amies' transport medium [14, 21]. Samples were transferred to the laboratory of the National Centre for Meningococci at Tel Hashomer within 4 h, and immediately plated on a selective 5% blood agar medium containing 2·3 mg/l vancomycin and 2000 units/l of colistin as described previously [22]. Plates were incubated in 5% CO_2 for 5 days. Colonies of oxidase-positive, Gram-negative cocci were identified further using conventional methods [23]. Serogrouping of *N. meningitidis* was carried out by slide agglutination using sera selected from various commercial sources.

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Statistical methods

Data handling and calculations were carried out using the SAS (SAS Institute Inc., Cary, NC) and PEPI [24] statistical packages. Differences in proportions were tested by the χ^2 or two-tailed Fisher's exact tests, and differences in means by the *t* test. Odds ratios (OR) and 95% confidence intervals (CI) were calculated as appropriate. Variables found to be associated significantly with meningococcal carriage in the univariate analysis (alpha level 0·05) were evaluated by multiple logistic regression to control for confounding effects.

RESULTS

Table 1 indicates the frequency of isolation of *N. meningitidis* from the throats of IDF personnel, by serogroup. Almost 16% of those sampled were carriers. Carriage was significantly higher among males than females (19·1 *vs.* 11·9%; $P < 0{\cdot}0001$; OR 1·74; 95% CI 1·30–2·32). The average ages of carriers and non-carriers were similar: 21·9 and 22·0 years respectively for males, and 20·1 and 20·2 years respectively for females (means for all males and females were 22·0 ± S.D. 1·7, and 20·2 ± S.D. 0·6, respectively). The differences between male and female average ages was explained by the differences in length of service.

Socio-demographic factors

Carriage of meningococci was significantly associated with less than 12 years of school education ($P = 0{\cdot}002$). There was no association between the level of the father's education and pharyngeal carriage of *N. meningitidis* (Table 2).

Smoking was significantly associated with pharyngeal carriage of meningococci: 19% of current smokers were carriers *vs.* 14% of non-smokers ($P = 0{\cdot}014$; OR 1·42; 95% CI 1·06–1·91). Heavy, medium or light smoking did not influence the association ($P = 0{\cdot}38$). Carriers smoked an average of 14·5 ± 11·0 cigarettes per day, while non-carriers smoked 15·6 ± 10·5 ($P = 0{\cdot}37$).

The type of base at which an individual served was taken as an indicator of degree of contact with others and of living conditions (see Table 3). Prolonged and/or close contact between personnel, as indicated by service at a closed facility was associated with a higher carriage rate ($P < 0{\cdot}0001$).

Table 1. *Serogroup distribution of* N. meningitidis *carried by IDF personnel at discharge from service (n = 1632)*

Serogroup	No. of isolates	Carriage rate (%)	% of all isolates
A	2	0·1	0·8
B	198	12·1	76·2
C	4	0·2	1·5
Y	33	2·0	12·7
Other	1	0·1	0·4
Ungroupable	22	1·3	8·4
Total	260	15·9	100·0

Table 2. *Association of educational level with pharyngeal carriage of* N. meningitidis

	Soldier's education*			Father's education†		
Education	*n*	Carriers	%	*n*	Carriers	%
< 12 years	171	41	24·0	476	77	16·2
⩾ 12 years	1459	218	14·9	939	148	15·8
Total	1630	259	15·9	1415	225	15·9

* $P = 0{\cdot}002$, OR 1·80 (95% CI 1·21–2·67).
† $P = 0{\cdot}840$.

Table 3. *Association of type of base with pharyngeal carriage of* N. meningitidis

Type of base*	*n*	Carriers	%
Closed base†	617	128	20·8
Open base†	900	119	13·2
Other	113	13	11·5
Total	1630	260	16·0

* Closed, soldiers live on the base for weeks at a time; open, work on the base, sleep at home.
† $P < 0{\cdot}0001$; OR 1·72 (95% CI 1·29–2·28).

Of 720 women in the study, nearly 14% of those using the contraceptive pill (60/435) were carriers compared with 9% of those not on the pill (26/285). This finding was not statistically significant ($P = 0{\cdot}059$ by the two-tailed Fisher exact test; OR 1·59 with 95% CI 0·96–2·67).

No difference could be shown in carriage rates among soldiers of Israeli (16·6%), Western (16·7%), Asian (13·9%) or African (15·4%) extraction. The number of siblings showed no association ($P = 0{\cdot}629$) with carriage rates: 15·3% in personnel with fewer than 2 siblings ($n = 354$), 16·7% in those with 2–3 ($n = 949$) and 14·6% in those with 4 or more ($n = 329$).

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Table 4. *Multivariate analysis of variables significantly associated with meningococcal carriage in univariate analyses*

Associated variable	*P* value in univariate analysis	Unadjusted OR (95% CI)	*P* value in multiple logistic regression	OR (95% CI)
All personnel				
Male gender	< 0·0001	1·74 (1·30–2·32)	0·009	1·49 (1·11–2·01)
Closed base	< 0·0001	1·72 (1·29–2·28)	0·002	1·58 (1·19–2·09)
< 12 years school	0·002	1·80 (1·21–2·67)	0·119	1·39 (0·92–2·11)
Current smoking	0·014	1·42 (1·06–1·91)	0·244	1·19 (0·89–1·60)
Women				
Closed base	0·314	1·28 (0·77–2·11)	0·279	0·77 (0·47–1·24)
< 12 years school	0·005	3·89 (1·26–11·55)	0·011	3·78 (1·36–10·49)
Current smoking	0·569	1·16 (0·68–1·95)	0·789	0·93 (0·56–1·55)
Men				
Closed base	0·001	1·77 (1·23–2·56)	0·002	1·77 (1·24–2·51)
< 12 years school	0·149	1·36 (0·88–2·10)	0·480	0·85 (0·65–1·34)
Current smoking	0·061	1·38 (0·97–1·96)	0·212	1·26 (0·88–1·86)

Multivariate analysis (Table 4)

In the multiple logistic regression analysis, the association of closed bases with meningococcal carriage remained significant ($P = 0·002$) as did that of male gender ($P = 0·009$). The associations with smoking ($P = 0·244$) and lower educational level ($P = 0·119$) were no longer significant.

There were potentially confounding differences between male and female personnel, which prompted a separate analysis by gender. Women served for a shorter period than men, so that their exposure to meningococci was different. They were also less likely than men to serve in combat roles, which may also have affected their exposure or perhaps their susceptibility to colonization. Women in the IDF were significantly less likely to have < 12 years of education than men, since women exempted from service were frequently those with < 12 years of schooling [18]. This was consistent with our study (2·5 *vs.* 17%, $P < 0·0001$, data not shown). Fewer women served on closed bases (30·6 *vs.* 49·1%, $P < 0·0001$) or smoked (26·5 *vs.* 35·8%, $P = 0·0001$).

Separate univariate analysis of the variables associated with meningococcal carriage for males ($n = 912$) and females ($n = 720$) was performed (data not shown). While for males the type of base remained significant ($P = 0·001$; OR 1·77; 95% CI 1·23–2·56), the associations with smoking ($P = 0·061$; OR 1·38; 95% CI 0·97–1·96) and lower education ($P = 0·149$; OR 1·36; 95% CI 0·88–2·10) were not confirmed. For females, the associations with smoking ($P = 0·569$; OR 1·16; 95% CI 0·68–1·95) and type of base ($P = 0·314$; OR 1·28; 95% CI 0·77–2·11) became non-significant, while that with lower educational level remained significant ($P = 0·005$; OR 3·89; 95% CI 1·26–11·55). Multiple logistic regression analysis of the same variables produced similar results.

DISCUSSION

Pharyngeal carriage of *N. meningitidis* was detected in 15·9% of military personnel at the end of their compulsory service. Serogroup B predominated (76%), with serogroup Y being encountered much less frequently (13%) and serogroups A and C together making up only 2%. During the study period, serogroup B caused 59% of laboratory-confirmed cases in Israel, 30% being due to serogroup C (unpublished data from the National Centre for Meningococci). Of the 7 cases which occurred in the IDF during the study period, 5 were caused by organisms of serogroup C and 2 by serogroup Y. There was thus no clear connection between carriage and disease in the IDF, though data would be needed from recruits in the early part of their service to rule this out properly. In the previous study of carriage in the IDF [8] serogroup Y was the commonest isolate, though the serogroup distribution at the time of recruitment was not given. It was made clear, however, that serogroup Y became more frequent with follow-up cultures.

The carriage rates estimated in this study are relatively low in comparison with some studies in military populations. Fraser and colleagues [12] found

30% carriage among naval recruits aged 15–16 years. They showed a lower rate of 18% in the 17–20 year age group. Melton and colleagues demonstrated much higher rates: 54% in males, though only 18% in females [25]. They noted that their subjects were swabbed during their first week at a Naval Hospital Corps School, after attending recruit camps. They noted further that carriage rates varied by recruit camp of origin, varying from 26 to 63%. Blackwell and colleagues [9] found an overall rate in recruits of 25%, with 18% in one camp and 30% in another. Thus there are clearly differences between various groups of subjects, even in the same countries. A closer look at our results shows that men completing service on closed bases had a carriage rate if 24·1%. Age is also an important variable within groups. It should be emphasized that the subjects in the present study were not recruits, but rather personnel ending long terms of service.

Might direct plating of throat swabs have yielded higher carriage rates? This method could not be used in the present study for logistic reasons. In an investigation on a kibbutz in northern Israel in which direct plating was used [22], meningococcal carriage rates were 13, 12 and 12% on separate samplings over 3 years in the 16–20 years age group and 9, 12 and 3·4% in 21-to 30-year-olds. By comparison, volunteer workers from other countries who were resident temporarily on the kibbutz and were sampled at the same sessions had much higher carriage rates: 22, 40 and 30% over the 3 study years. Almost all the volunteers were aged between 18 and 30 years.

The use of Amies' medium with a minimal delay before plating on a selective medium in the laboratory was based on our own previous studies and that of Pether and colleagues [14, 21]; collection, transport and laboratory processing conditions were uniform throughout the study.

Four of the variables we studied were significantly associated with meningococcal carriage in the univariate analyses: male gender, closed as opposed to open bases (as a measure of the degree of interpersonal contact and other factors possibly facilitating transmission of infectious agents), smoking, and an incomplete (< 12 years) school education, which has been used as a measure of lower socioeconomic status [18]. Gender and smoking are well recognized risk variables, and control of smoking has even been proposed as a preventive measure for meningococcal disease [26].

Statistical scrutiny of the four variables in a multiple logistic regression model suggested that the association of carriage with smoking might not be independently significant in the setting of this study (Table 4). A similar observation was made by Davies and colleagues [27] in a study of risk factors for carriage. They found that increasing age (not feasible in our study), female sex, and manual social class, remained significant in multivariate analysis, while personal smoking, regular discotheque attendance and rhinorrhea did not.

Our study did not address the issue of passive smoking, which has been found to be important in some studies [28]. Despite this and the common perception in the literature, our results indicate that smoking may be less prominent as a risk factor in Israeli military bases than in other environments.

The male predominance we found in pharyngeal carriage is consistent with the literature [8, 25]. Melton and colleagues [25] studied this sex difference in US naval recruits, and concluded that the role of gender was probably a function of differences in exposure. We found that the gender difference was evident on closed bases (24·1% for men *vs*. 14·2% for women; $P = 0·004$; OR 1·92; 95% CI 1·20–3·08), but not statistically significant on open bases (15·2% for men *vs*. 11·5% for women; $P = 0·097$; OR 1·39; 95% CI 0·92–2·08).

The interactions between these carriage-associated variables is not clear. The association between smoking and educational level in the IDF is known [18]. Our data showed that about twice as many individuals with < 12 years of schooling, both men and women, were current smokers as compared with those who had ⩾ 12 years of education: 62 *vs*. 30% for men ($P < 0·0001$), and 56 *vs*. 26% for women ($P = 0·005$). In a study population of IDF personnel discharged from service in 1988, Kark and Laor [18] found very similar proportions: 71 *vs*. 35% for men, and 56 *vs*. 26% for women. It is also unclear why < 12 years of school education might be more important in females than in males, as suggested by the multivariate analysis.

Carriage of certain bacteria has been shown to be influenced by hormonal status in women [29]. An association between the use of the contraceptive pill and pharyngeal carriage of meningococci in women did not reach significance in this study. The measure of contraceptive pill use employed in this study (yes–no) was very crude, and a more careful analysis would be needed to elucidate the question of any endocrinological association.

In previous studies in the IDF, the number of siblings and geographic or ethnic origin have been

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significantly associated with antibody levels to hepatitis A virus (HAV) [30, 31], *Shigella sonnei* infection [32] and cytomegalovirus infection [33]. In these situations, the importance of siblings related essentially to exposure to the infectious agent before the start of military service. We found no association of these variables with current asymptomatic infection by *N. meningitidis*.

In all, pharyngeal carriage of meningococci in IDF personnel completing their service showed no very unusual features. The data which have become available from the relatively large population studied here have thrown some light on the complexities of the associations of carriage with such key variables as gender, educational level, living conditions and smoking. Further studies are necessary to improve our understanding of these interactions. Two reasonable conclusions have emerged from this study: that service on a closed base is clearly associated with meningococcal carriage, possibly reflecting a greater intensity of contact between individuals; and that active smoking may be less prominent as a risk factor for carriage in the population and setting studied here, where other variables may be of greater importance.

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