THE JOURNAL OF INFECTIOUS DISEASES • VOL. 146, NO. 5 • NOVEMBER 1982
 0022-1899/82/4605-0007$01.09

The Epidemiology of Infections Due to *Neisseria meningitidis* and *Neisseria lactamica* in a Northern Nigerian Community

I. S. Blakebrough, B. M. Greenwood, H. C. Whittle, A. K. Bradley, and H. M. Gilles

From the Endemic Diseases Research Unit and the Department of Medicine, Ahmadu Bello University, Zaria, Nigeria; and the Department of Tropical Medicine, Liverpool School of Tropical Medicine, Liverpool, England

The epidemiology of infection due to *Neisseria meningitidis* and *Neisseria lactamica* was studied in a northern Nigerian community. A low meningococcal carriage rate was observed throughout the two-year survey. Initially, most meningococci isolated from nasopharyngeal carriers belonged to serogroup C or to serogroup Y. Following an outbreak of group A meningococcal disease, more group A meningococcal carriers were detected. Antibody studies indicated that infection with group A meningococci had been more widespread in the community than was suggested by regular carrier surveys. Carriage of meningococci was detected most frequently in children one to nine years of age. Children were identified as the first carriers in households more frequently than adults. The half-life of carriage was three months. The meningococcal carriage rate did not increase during the hot dry season when epidemics of meningococcal disease occur most frequently in Nigeria. *Neisseria lactamica* was isolated from the nasopharynx of children more frequently than were meningococci.

Over a large area of savanna Africa, extending from the Sudan in the east to the Gambia in the west, the pattern of meningococcal disease shows certain characteristic epidemiologic features [1]. One of these features is the tendency for major epidemics to occur once every five to 10 years. Thus, in northern Nigeria major outbreaks of meningococcal disease were recorded in 1949–1950, 1960–1962, 1969–1970, and 1977–1978. Many thousands of cases were recorded during each of these epidemics. The reasons for this regular epidemic cycle are not fully understood. It has been suggested that during major epidemics the majority of the population acquires antibodies to the epidemic strain as a consequence of a subclinical infection. Thus, a new epidemic can only start when a sufficiently large new nonimmune population has built up as a result of new births and migration. There is, however, little direct evidence to support this reasonable hypothesis.

Another characteristic of African meningitis epidemics is their tendency to start in the middle of the hot dry season and to end abruptly with the coming of the rains. The cause of this seasonal effect has not been determined. During meningitis epidemics in savanna Africa, meningococcal disease is seen most frequently in children five to nine years of age, a much later age of maximum incidence than that observed in Europe or the United States. Meningococci belonging to serogroup A have been responsible for most African epidemics, but some outbreaks have been caused by organisms belonging to serogroup B or to serogroup C.

Because most subjects infected with meningococci become asymptomatic nasopharyngeal carriers, but do not develop clinical meningococcal disease, the study of the epidemiology of meningococcal infection in a defined population should

Received for publication July 30, 1981, and in revised form June 8, 1982.

The present study was approved by the Ethical Committee of the Faculty of Medicine, Ahmadu Bello University, Zaria, Nigeria.

This work was supported in part by the United Kingdom Medical Research Council.

We thank the Galadiman Katsina, the village head of Yar Talata, the headmaster of Galadima Primary School in Malumfashi, the pupils of the Galadima Primary School, the people of Yar Talata, and B. D. Musa, Director of the Institute of Health, Ahmadu Bello University, Zaria, for support; Malam Dan-Azumi Musa for assistance in the field; Stephen Odeh for laboratory assistance; and Drs. J. D. Abbott, H. A. Feldman, and D. M. Jones for help in serotyping and testing for sensitivity to antimicrobial agents.

Please address requests for reprints to Dr. B. M. Greenwood at his present address: Medical Research Council Laboratories, Fajara, Banjul, the Gambia.

include carrier and serologic studies as well as case-finding surveys. Despite the importance of meningococcal infection as a cause of morbidity and mortality in countries of the African meningitis belt, few such studies have been undertaken in this region. Early studies in the Sudan, published in 1916–1932 [2–4], demonstrated high carriage rates in European troops stationed in the country, in prison inmates, and in the inhabitants of villages affected by an epidemic. Most strains isolated in the Sudan by Riding and Corkhill [4] belonged to serogroup B. Surveys undertaken at the time of the 1949–1950 epidemic in northern Nigeria showed a carriage rate of ~20% in healthy villagers [5]. Carriage was more frequent in the dry season than in the rainy season; most isolates belonged to serogroup B. When the area around the town of Katsina was resurveyed seven years later, a carriage rate of only 3% was found and most of the strains isolated could not be serotyped [1].

Twenty years later Sanborn et al. [6] noted a group A meningococcal carriage rate of 34% in an adjacent area of northern Nigeria during one of the first trials of meningococcal polysaccharide vaccines. An epidemic of group A meningococcal meningitis was taking place in northern Nigeria at the time of this survey. A much lower carriage rate of group A meningococci was found in a study carried out the previous year in Mali by Burian et al. [7]. Etienne [8] reported the results of a detailed study carried out in a village in Upper Volta. Nasopharyngeal swabs were collected from 95 subjects every two weeks throughout the year. The overall meningococcal carriage rate varied from 15% to 35%, and that of group A meningococci from 1% to 9%, but no obvious relationship between season and carriage was observed. A similar study was undertaken in eastern Nigeria by Njoku-Obi and Agbo [9]. Once again no seasonal variation in carriage rate was observed. However, eastern Nigeria is not subject to the marked seasonal climatic changes seen in northern Nigeria, and it lies outside the African meningitis belt.

Because of the paucity of detailed information on the epidemiology of meningococcal infection in the African meningitis belt, we have undertaken serial nasopharyngeal carrier and serologic surveys in a typical northern Nigerian village and in an urban primary school. The results of these surveys are reported in the present paper.

Materials and Methods

Study area. Preliminary surveys were undertaken in four villages within a 30-km radius of the town of Malumfashi in northern Nigeria. Malumfashi, which has a population of about 20,000, is a local-government center and an important trading base for surrounding villages. The main village survey was conducted in the village of Yar Talata which is situated 8 km east of Malumfashi. The climatic and geographic features of the Malumfashi district, which lies within the African meningitis belt, have been described in detail by Bradley et al. [10]. Within this region the dry season, during which epidemics of meningococcal disease may occur, lasts from October to April. During the wet season, which extends from May to September, ~1,000 mm of rain falls.

Meningococcal disease surveillance. The records of all patients admitted to Malumfashi General Hospital with a clinical diagnosis of meningitis during the period 1971–1979 were reviewed. A diagnosis of meningococcal meningitis was accepted if meningococci had been demonstrated in cerebrospinal fluid by Gram stain or by culture or if meningococcal antigen had been detected in cerebrospinal fluid by a latex agglutination test or by counterimmunoelectrophoresis. Because of the limited laboratory facilities at Malumfashi Hospital, bacteriologic investigations were not carried out for all patients with meningitis.

Subjects surveyed. Pupils attending Galadima Primary School, one of seven primary schools in the town of Malumfashi, were studied. In October 1977 the school had an enrollment of 631 pupils between four and 16 years of age; two thirds of the pupils were boys. In April and August 1976, nasopharyngeal swabs were collected from 107 and 104 pupils, respectively, as part of a preliminary survey of regional differences in the epidemiology of meningococcal infection in the district of Malumfashi. Plasma samples were collected from 36 pupils at this time. In October 1977, nasopharyngeal swabs were collected from all pupils attending the school. Further samples were collected in November 1977, January 1978, February 1978, and in June 1978 from all pupils found to be naso-

pharyngeal meningococcal carriers during the October 1977 survey. The child whose name followed that of the carrier on the school list acted as a control and was swabbed on each of these occasions. Finger-prick blood samples were collected from carriers and from control subjects in November 1977 and in June 1978.

Preliminary village surveys were carried out in April and August 1976. During these surveys, 402 and 393 pupils who were four to 16 years of age and who attended five primary schools in the Malumfashi district were studied. These preliminary surveys showed no seasonal variation in meningococcal carriage and no significant variations in meningococcal carriage or in mean group A or group C meningococcal antibody levels between villages.[1] Yar Talata was selected from among the villages surveyed as the site for a longitudinal study because it is near Malumfashi and because the population was cooperative. Nasopharyngeal swabs were collected from all available residents of Yar Talata in October 1976, January 1977, April 1977, and August 1977. Swabs were collected once a month from persons identified as carriers during the course of the surveys and from control subjects. After the main carrier survey, 140 pupils attending the village school were studied at intervals of two or three months for a further period of one year. In October 1976, plasma samples were collected from 382 (70%) of 545 inhabitants of Yar Talata. Second plasma samples were obtained from 113 of these individuals two years later.

Sample collection. Swabs were obtained from high on the wall of the posterior nasopharynx using charcoal-coated cotton wool swabs. Swabs were inoculated directly onto blood agar plates containing vancomycin (0.3 mg/100 ml) and polymyxin B (0.5 mg/100 ml). During the dry season the temperature in the Malumfashi area may exceed 40 C. Therefore, inoculated plates were stored in metal drums that were kept in insulated boxes to prevent overheating. Control cultures survived well when kept in the field under these conditions. Cultures were streaked across the agar plate immediately after their arrival at the base laboratory in Malumfashi, usually within 3–4 hr of the collection of swabs. Preliminary studies showed that recovery rates for meningococci obtained by this technique were at least as good as those obtained when Stuart's transport medium was used.

The reproducibility of the swabbing technique was investigated in a preliminary survey. Two hundred children were swabbed twice on the same morning by two investigators. Meningococci of the same serogroup were isolated from 10 children by both investigators; meningococci were isolated from three more children by one investigator or the other but not by both. Both investigators obtained negative swabs from the remaining 187 children.

Blood for antibody assays was drawn by finger-prick and collected in heparinized capillary tubes. Plasma was separated within 6 hr of the collection of the sample and stored at −20 C until tested.

Laboratory methods. Cultures which had been streaked onto blood agar plates were incubated in candle jars at 36.5 C for 18–24 hr. Colonies that were suspected of being positive were treated with Gram stain and tested with the oxidase reagent (tetramethyl-*p*-phenylenediamine). Gram-negative cocci which gave a positive oxidase reaction were subcultured onto Mueller-Hinton agar and incubated for an additional 18 hr at 36.5 C. If a pure growth was obtained, it was subcultured into cysteine trypticase agar sugars (glucose, maltose, sucrose, and lactose) and placed on a blood agar plate. A loopful of culture from the Mueller-Hinton agar plate was inoculated into *o*-nitrophenyl-β-D-galactopyranoside broth and incubated for 1 hr at 36.5 C. Strains which did not give a positive reaction to *o*-nitrophenyl-β-D-galactopyranoside were grouped by agglutination. Four drops of a saline suspension of bacteria were placed in wells of a World Health Organization plastic agglutination tray, and one drop of each of eight group-specific antisera (A, B, C, X, Y, Z, 29e, and W135) was added. These antisera, which had been prepared in rabbits, were provided by Dr. J. D. Abbott, Public Health Laboratory Services, Manchester, England. The pattern of agglutination was read after gentle shaking for 3 min. Sugar reactions were read after incubation for seven days. Strains that fermented glucose and maltose, but not sucrose or lactose, were accepted as meningococci.

Bacteria that gave a positive reaction to *o*-nitro-

[1] I. S. Blakebrough, "Epidemiological and Laboratory Studies of Meningococcal Infections in Nigeria," Ph.D. thesis, University of Liverpool, Liverpool, England, 1979.

phenyl-β-D-galactopyranoside and that fermented glucose, maltose, and lactose, but not sucrose, were identified as *Neisseria lactamica*. No attempt was made to group such strains or to determine their antimicrobial sensitivity.

The antimicrobial sensitivities of a portion of meningococcal isolates were investigated. Pure cultures grown on Mueller-Hinton broth were inoculated onto Mueller-Hinton agar plates containing various concentrations of sulfadiazine or onto blood agar plates containing various concentrations of penicillin. The MIC was considered to be the lowest concentration of the antimicrobial agent that prevented the growth of ⩾10 colonies.

Selected strains of meningococci were freeze-dried in horse serum supplemented with 5% glucose and sent to Dr. J. D. Abbott or to Dr. H. A. Feldman, State University of New York, Syracuse, for confirmation of their serogroup and sulfonamide-sensitivity. The results of our tests for serogroup and for sulfonamide-sensitivity were concordant with those obtained for 61 of the 68 isolates sent to either England or the United States.

An HA technique was used to measure meningococcal antibodies. Human group O erythrocytes were washed in phosphate-buffered saline at pH 7.2 and stored at 4 C in Alsever solution for two to three days before coating with meningococcal polysaccharide. An aliquot of a 2.5% suspension of red blood cells in phosphate-buffered saline (pH 6.9) was incubated for 30 min at 37 C with an equal volume of group A meningococcal polysaccharide vaccine (Institut Mérieux, Lyon, France) at a concentration of 1.25 mg/100 ml or with an equal volume of group C meningococcal polysaccharide vaccine (Mérieux) at a concentration of 2.5 mg/100 ml. Coated erythrocytes were washed three times in phosphate-buffered saline (pH 6.9) and suspended at a concentration of 0.5% in this buffer supplemented with 0.5% absorbed, inactivated, normal rabbit serum. One drop of the red blood cell suspension was added to twofold dilutions of heat-inactivated plasma in microtiter plates. The plates were incubated for 2 hr at room temperature (~24 C) and then overnight at 4 C. The highest dilution of plasma that showed agglutination of the red blood cells when examined by the naked eye was taken as the antibody titer. Results are expressed as a reciprocal of this $\log_2$ titer. All samples were tested within two months of collection. The consistent results obtained with control samples included with each batch of test samples confirmed the comparability of assays carried out on different occasions.

Results

Meningococcal disease at Malumfashi. During the period 1971–1976, few cases of meningococcal disease were seen at Malumfashi General Hospital, but in 1976, 20 patients with probable meningococcal meningitis were admitted. Samples of cerebrospinal fluid were obtained from eight of the patients and were tested for bacterial antigens; group C meningococcal antigen was found in six of the samples. In the early part of 1977 and in 1978, Malumfashi was affected by two major epidemics of group A meningococcal meningitis which involved much of northern Nigeria [11]. Approximately 100 patients with a clinical diagnosis of meningococcal meningitis were admitted to Malumfashi General Hospital in 1977; a laboratory diagnosis of group A meningococcal infection was established in 59 of the 66 patients from whom cerebrospinal fluid was obtained. The majority of these patients came from within the town of Malumfashi. This epidemic subsided during the 1977 wet season.

Another outbreak occurred during the following dry season and ~500 patients with meningococcal disease were admitted to Malumfashi General Hospital during 1978. Cerebrospinal fluid was obtained from 270 of these patients; 170 samples contained group A meningococci or group A meningococcal antigen, four samples yielded other bacteria, and 93 samples were sterile or antigen-negative. Only 17% of the 272 patients with probable meningococcal meningitis seen in 1978 from whom a detailed history was obtained came from Malumfashi; the remainder came from surrounding villages. No cases of meningococcal disease were identified among pupils attending Galadima Primary School during either 1977 or 1978, and no cases were detected in Yar Talata although cases of meningococcal disease occurred in surrounding villages.

The temporal relationship between the bacteriologic and serologic surveys undertaken in Galadima Primary School and in Yar Talata and the admissions to Malumfashi Hospital of patients with meningitis is shown in table 1.

Carriage of Neisseria meningitidis and N. lacta-

Table 1. Temporal relationship between the number of patients admitted to Malumfashi General Hospital with a clinical diagnosis of meningococcal meningitis and the epidemiologic surveys conducted in Galadima Primary School and the village of Yar Talata, northern Nigeria.

	Type of survey (survey no.)			Patients	
Year	Preliminary	Galadima	Yar Talata	No.*	Serogroup†
1975	. . .	. . .	. . .	20	C > A
1976	Carrier and serologic during dry and wet seasons	Carrier (1), serologic (1)	Cross-sectional carrier (1), serologic (1)	25	A
1977	. . .	Longitudinal carrier	Cross-sectional carrier (2–4)	100	A
1978	. . .	Longitudinal carrier, serologic (2)	Schoolchildren, serologic (2)	500	A
1979	. . .	. . .	. . .	<10	Unknown

* Approximate figures from hospital records.
† Only a portion of samples were serogrouped.

mica at Galadima Primary School. During the preliminary surveys undertaken in April and August 1976, eight of 107 pupils and seven of 104 pupils, respectively, were found to be carrying meningococci. Seven isolates belonged to serogroup C, five to serogroup Y, two to serogroup A, and one to serogroup B.

In October 1977, six months after the first outbreak of meningococcal disease in Malumfashi, nasopharyngeal swabs were collected from all 631 pupils attending the school. Fifty-eight (9%) of the pupils were identified as meningococcal carriers; 42 (72%) of the isolates of meningococci belonged to serogroup A, seven (12%) belonged to serogroup C, five (9%) to serogroup Z, two (3%) to serogroup Y, and one (2%) to serogroup B. One isolate could not be typed. Fifty-seven (9%) of the children were found to be carrying *N. lactamica.*

During the eight-month period of observation, October 1977–June 1978, seven of the 58 meningococcal carriers identified during the first survey acquired meningococci of a different serogroup from the original isolate, and five of 58 control pupils who were not carriers during the first survey became meningococcal carriers. These acquisition rates did not differ significantly.

The rates of loss of carriage of group A meningococci and of meningococci belonging to other serogroups are shown in figure 1. The t½ of carriage of group A meningococci was one month and the t½ of carriage of meningococci belonging to other serogroups was three months. At one month and at three months the rate of loss of carriage was significantly different between the two groups ($P < 0.05$ and $P < 0.02$, respectively).

Meningococcal antibody levels at Galadima Primary School. Levels of antibodies to group A and group C meningococci in pupils attending Galadima Primary School before and after two outbreaks of group A meningococcal disease in the district of Malumfashi are shown in figure 2. The mean titer of antibody to group A meningococci increased significantly between 1976 and 1977 ($P < 0.01$) but showed no further increase the following year. Similarly, the percentage of subjects with reciprocal titers of ≥ 2 $\log_2$, increased

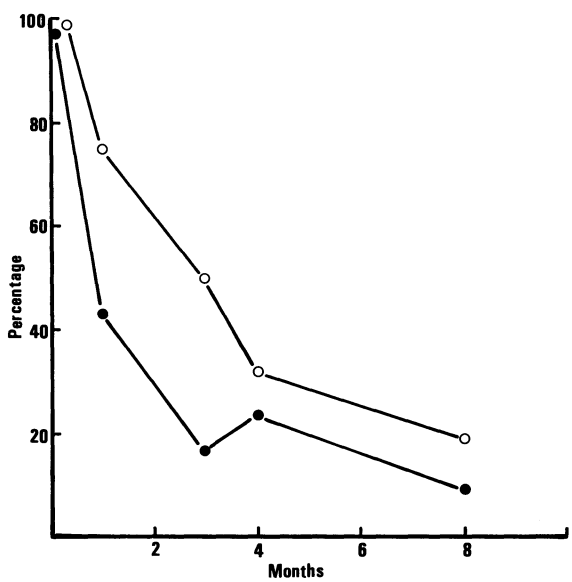

Figure 1. The percentage of schoolchildren among those identified as meningococcal carriers who were positive for group A meningococci (n = 42) (●) or for meningococci of other serogroups (n = 16) (○) at various times.

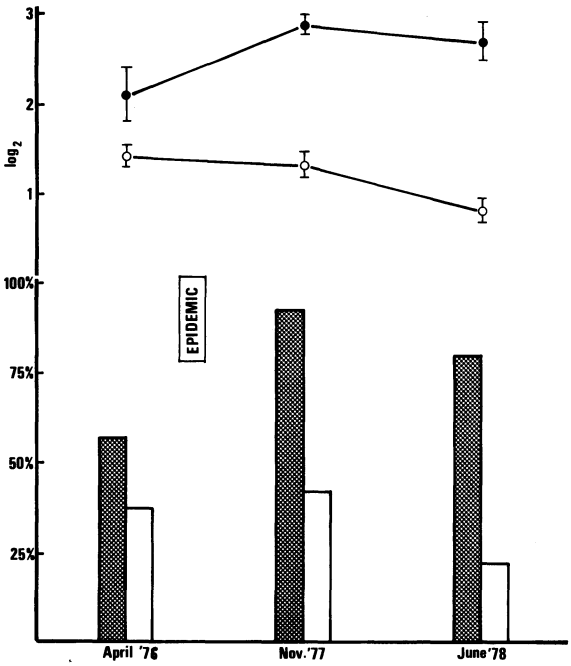

Figure 2. The mean ± SEM $\log_2$ reciprocal titers of antibody to group A meningococci (●) and to group C meningococci (○) in schoolchildren from Malumfashi, Nigeria, before and after an outbreak of group A meningococcal disease. Histograms indicate the percentages of subjects with reciprocal titers of ≥2 $\log_2$ of antibody to group A meningococci (▨) or antibody to group C meningococci (□). Thirty-six, 97, and 92 children were studied in 1976, 1977, and 1978, respectively.

from 58% in 1976 to 93% in 1977 ($P < 0.001$). The mean titer of antibody to group C meningococci decreased progressively from 1976 to 1978. The difference in mean titer between 1976 and 1978 was statistically significantly ($P < 0.02$).

The mean (± SEM) reciprocal titer of antibody to group A meningococci in 36 pupils who had been identified as carriers of group A meningococci one month before blood samples were collected was 3.2 ± 0.2 $\log_2$; this value was significantly higher than the mean titer of antibody to group A meningococci of 2.7 ± 0.1 $\log_2$ recorded in 55 pupils who were not meningococcal carriers ($P < 0.02$). Six pupils who were carriers of group C meningococci had a much higher mean titer of antibody to group C meningococci than the 55 pupils who were not meningococcal carriers (3.7 ± 0.4 $\log_2$ vs. 1.2 ± 0.2 $\log_2$; $P < 0.001$).

Meningococcal carriage in Yar Talata. The influence of age, sex, and season. The total population of Yar Talata, which varied from 520 to 570 during the course of the study, was surveyed on four occasions during the period from October 1976 to July 1977. At each survey, samples were obtained from 92%–96% of the population. The overall carriage rate varied little from survey to survey (table 2), and it was not affected by season. Most meningococci isolated during the first survey belonged to serogroup C or to serogroup Y, and

Table 2. Carriage of *Neisseria meningitidis* and *Neisseria lactamica* at four times of the year in Yar Talata, a village in northern Nigeria.

	No. (%) positive			
Presence of	October 1976 (n = 518)	January 1977 (n = 525)	April 1977 (n = 501)	July 1977 (n = 505)
N. lactamica	NT*	NT*	38 (10.2)†	39 (7.7)
N. meningitidis	17 (3.6)	20 (3.8)	18 (3.6)	17 (3.4)
Serogroup				
A	. . .	. . .	1	9
B	. . .	1	. . .	. . .
C	6	4	3	. . .
X	. . .	. . .	1	. . .
Y	5	5	5	1
Z	2	7	5	3
29e	1	2	1	1
W135	. . .	. . .	. . .	. . .
NG‡	3	1	2	3

NOTE. An epidemic of group A meningococcal disease occurred in the region from February to May 1977.

* NT = not tested.

† Of the samples taken in April 1977, only 372 were analyzed for *N. lactamica*.

‡ NG = nongroupable.

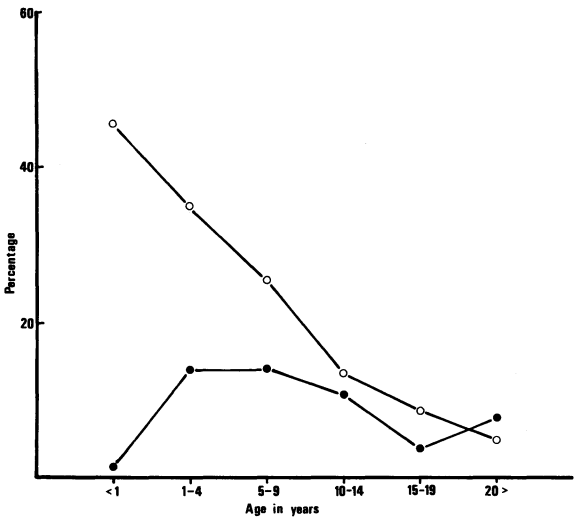

Figure 3. The age distribution of carriers of *Neisseria meningitidis* (●) and *Neisseria lactamica* (○) in the population of a village in northern Nigeria. The population ranged from 520 to 570 during the study.

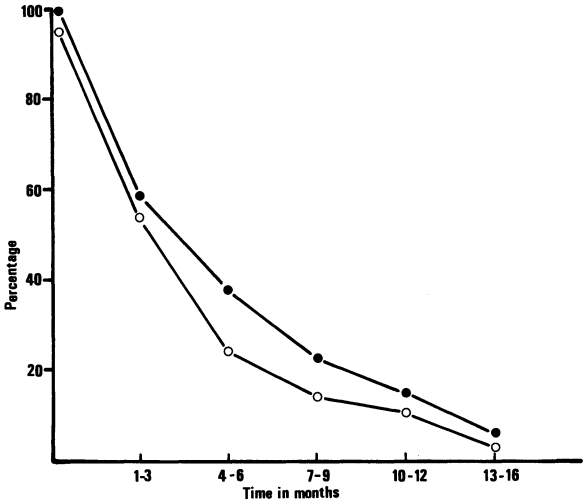

Figure 4. The percentage of subjects in a village in northern Nigeria who were identified as nasopharyngeal carriers and who were positive for *Neisseria meningitidis* (n = 68) (●) or *Neisseria lactamica* (n = 55) (○) at various times after the initial identification.

no organisms belonging to serogroup A were identified. However, the majority of strains isolated during the last survey were group A meningococci. The age distribution of carriers identified during the four surveys is shown in figure 3. The prevalence of carriage among males (29 of 256) was not significantly different from the prevalence of carriage among females (21 of 287).

After the main longitudinal survey, carriage was monitored for an additional year in 143 pupils attending the village school. Seventeen (12%) of the children carried meningococci at some time during this period, an acquisition rate of 0.35% per month. Eight isolates belonged to serogroup A. The overall carriage rate obtained during individual surveys of these schoolchildren ranged from 1.4% to 7.7%, but no significant variation in carriage rate was observed between seasons.

Duration of meningococcal carriage. Individuals identified as carriers during one of the main surveys were retested at monthly intervals for a subsequent period of 12–24 months. Because some people were away from the village for part of the year and because some were unwilling to be tested repeatedly, not all serial samples were obtained. However, samples were obtained from at least 50% of the subjects at each monthly survey. The rate at which carriers lost meningococci from the nasopharynx is indicated in figure 4. The t½ of meningococcal carriage is three months. Gaps of several months separated two isolations of meningococci of the same serogroup in some subjects, suggesting that such individuals had been harboring meningococci in the nasopharynx for a prolonged period, despite the fact that several intervening negative swabs had been obtained. The duration of carriage was not influenced by the age of the carrier.

Spread of meningococci within households. The age and sex distributions of the first carrier detected in a household are indicated in table 3. Children <10 years of age were identified as first carriers significantly more frequently than older children or adults ($\chi^2 = 5.8$; $P < 0.02$). Among adults (subjects ⩾15 years of age), males were identified as first carriers significantly more frequently than females ($\chi^2 = 7.0$; $P < 0.01$).

A meningococcal carrier was identified in 22 households during the first survey of the entire village. The meningococcal acquisition rate among the 129 household contacts of these carriers was 1.6% per month. This figure is higher than the acquisition rate of 0.7% per month observed among the members of households in which no carriers were identified during the first survey, but the difference is not statistically significant ($P > 0.1$). Only two of 14 carriers who were identified during the first survey and followed throughout the one-

year study period acquired meningococci of a different serogroup. This acquisition rate was comparable to that observed among the 504 subjects who were not carriers at the time of the first survey, 43 of whom subsequently became carriers.

Sensitivities of meningococcal isolates to sulfonamide and penicillin. Fifty-three randomly selected isolates of meningococci were tested for their sensitivity to sulfadiazine and to penicillin. Forty-three (81%) of the strains were resistant to sulfadiazine with an MIC of ≥5 mg/100 ml. Seven of the eight sulfadiazine-sensitive strains belonged to serogroup Z. All isolates were sensitive to penicillin at a concentration of 0.01 mg/100 ml.

Carriage of N. lactamica in Yar Talata. The carriage rate of *N. lactamica* detected during two of the four surveys of Yar Talata is indicated in table 2. During each of these surveys the carriage rate of *N. lactamica* was higher than the carriage rate of *N. meningitidis*. Carriage rates in a smaller subsample investigated monthly from August 1977 to April 1978 ranged from 9.8% to 17.5%. The age distribution of carriers of *N. lactamica* is shown in figure 3. Young subjects carried *N. lactamica* more frequently than meningococci. No sex difference in the carriage of *N. lactamica* was observed. The duration of carriage of *N. lactamica* was similar to that observed among carriers of meningococci (figure 4).

No correlation was found between carriage of *N. lactamica* and carriage of meningococci. Four hundred two subjects did not carry either organism during the one-year study period, 73 subjects carried *N. lactamica* alone, 52 carried meningococci alone, and 16 carried both organisms. The last figure does not differ significantly from the number (11) expected by chance ($P > 0.05$).

Meningococcal antibody levels in Yar Talata. Blood samples were collected from 382 (70%) of the inhabitants of Yar Talata at the time of the first carrier survey in October 1976. The distribution by age of the group A and group C meningococcal HA antibody levels found in these samples is shown in figures 5 and 6. No sex difference in antibody levels was found.

Two years after the first serologic survey, further samples were obtained from 113 subjects. Assay of these samples showed that a rise in the mean titer of antibody to group A meningococci had occurred in all age groups, except in children two to four years of age (figure 5). There was little change in the mean titer of antibody to group C meningococci between surveys (figure 6). Paired samples were obtained from 82 subjects; 39 had higher titers of antibody to group A meningococci in the second sample than in the first. Increases in titer ranging from twofold to 64-fold (mean, sixfold) were observed in five of six subjects who had been demonstrated to be carriers of group A meningococci at some time during the two-year observation period.

Discussion

Preliminary surveys undertaken in 1976 showed no significant differences in the meningococcal carriage rate or in the mean titers of antibody to group A or group C meningococci among pupils attending five primary schools within or around the town of Malumfashi in northern Nigeria. Thus, it is likely that the pattern of meningococcal infection found in Yar Talata, the village selected as the main study area, was representative of the epidemiology of meningococcal infection in the Malumfashi area as a whole.

Little change in the overall carriage rate of meningococci was observed in either Yar Talata or in Galadima Primary School in Malumfashi during the two-year period of observation. At Yar Talata the overall meningococcal carriage rate was

Table 3. The age and sex distribution of persons identified as first carriers of *Neisseria meningitidis* in households in Yar Talata, a village in northern Nigeria.

	Age in years					
Sex	0–4	5–9	10–14	15–19	20+	Total
Male	4/55	6/42	2/29	2/17	11/113	25/256
Female	4/42	7/45	1/35	1/30	3/127	16/279
Total (%)	8/97 (8.2)	13/87 (14.9)	3/64 (4.7)	3/47 (6.4)	14/240 (5.8)	41/535 (7.7)

NOTE. Data are no. of first carriers/no. of subjects. Coprimary carriers have been excluded.

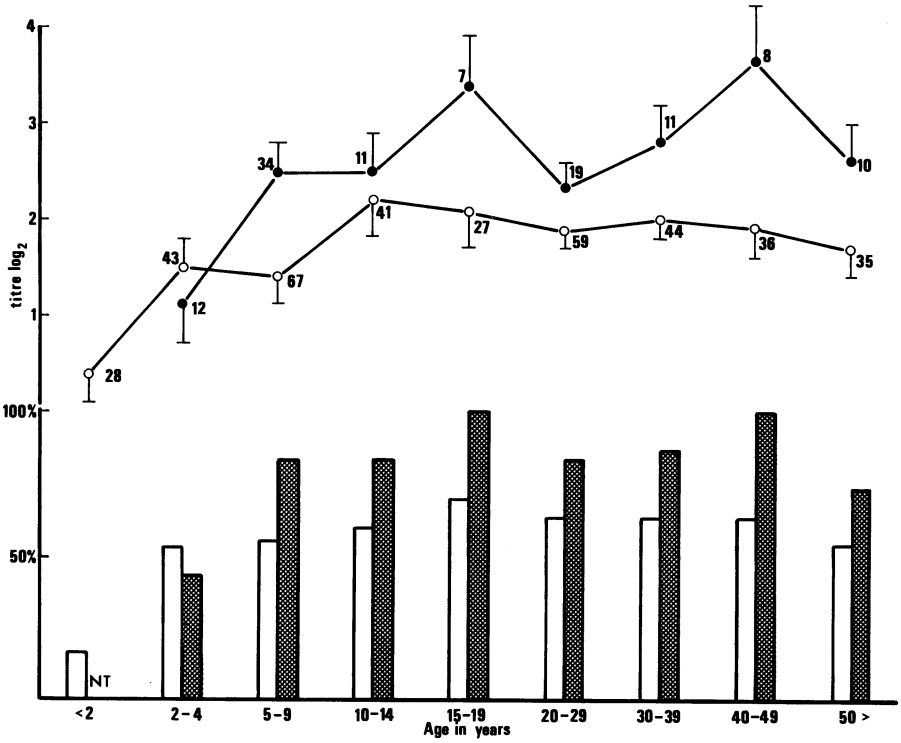

Figure 5. The mean ± SEM of titers of antibody to group A meningococci in the population of Yar Talata, a village in northern Nigeria, during October 1976 (○) and June 1978 (●). The figures indicate the number of observations made. Histograms indicate the percentages of subjects with reciprocal titers of antibody of ≥ 2 $\log_2$ in 1976 (□) and in 1978 (▨). NT = not tested.

3%–4%, and among pupils at Galadima Primary School it was 3%–9%. However, a significant change was observed in the serogroup of meningococci isolated from nasopharyngeal carriers in both populations during the course of the study. During surveys undertaken in 1976, group C and group Y organisms were identified most frequently and few isolates belonged to serogroup A. The high proportion of group C strains isolated in 1976 is in keeping with the fact that a number of patients with group C meningococcal meningitis had been admitted to Malumfashi General Hospital during the previous year.

In the early part of 1977, the Malumfashi area, in common with much of northern Nigeria, was affected by a severe outbreak of group A meningococcal disease. Although no clinical cases of meningococcal infection were identified in either Yar Talata or in Galadima Primary School, an increase in the carriage rate of group A meningococci was observed in both communities and reached maximum values of 1.8% and 6.7%, respectively. The maximal carriage rate of group A meningococci recorded at Yar Talata was similar to the overall carriage rate of 2.6% recorded in the city of Zaria, 80 km south of Malumfashi, which was also severely affected by the 1977 epidemic [12]. Thus, this epidemic was not accompanied by a high overall carriage rate of the epidemic strain in the general population as was a previous epidemic of group A meningococcal disease in northern Nigeria [6].

The increase in the proportion of group A meningococci isolated from carriers in Yar Talata followed the outbreak of meningococcal disease in the Malumfashi area, and serial studies undertaken in the village gave no warning of the epidemic which, on the basis of a 10-year epidemic cycle, was two or three years earlier than expected. The development of an effective early warning system for epidemics of meningococcal disease would be a major advance. Our findings suggest that continuous monitoring of meningococcal carriage rates would not be a sufficiently sensitive

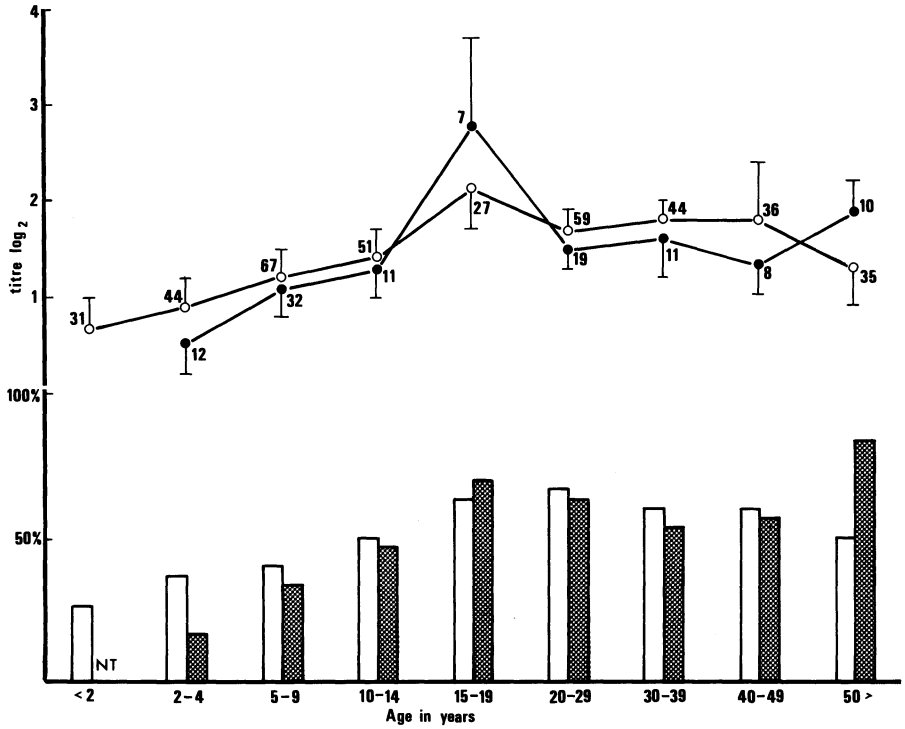

Figure 6. The mean ± SEM of titers of antibody to group C meningococci in the population of Yar Talata, a village in northern Nigeria, during October 1976 (○) and June 1978 (●). The figures indicate the number of observations made. Histograms indicate the percentages of subjects with reciprocal titers of antibody of ⩾2 $\log_2$ in 1976 (□) and in 1978 (▨). NT = not tested.

tool for predicting epidemics unless some marker for meningococcal virulence could be identified.

Serologic studies undertaken at Yar Talata and at Galadima Primary School indicated that infection with group A meningococci was more widespread in 1977 than was suggested by carrier studies. At Galadima Primary School the mean titer of antibody to group A meningococci increased significantly between 1976 and 1977, and the number of pupils with reciprocal titers of ⩾2 $\log_2$ nearly doubled during this period. Serologic surveys carried out in Yar Talata in October 1976 and two years later showed an increase in the titer of antibody to group A meningococci in all but the youngest children. One half of the villagers from whom paired samples had been obtained showed an increase in titer of antibody to group A meningococci between the first and the second survey. Thus, it is likely that as much as one half of the population of the village (250 subjects) was infected with group A meningococci for a sufficient period to produce booster immunization, even though only 14 carriers of group A meningococci were identified in the village during the two-year observation period.

The combined results of carrier and serologic studies suggest that infection with group A meningococci was widespread in both Yar Talata and in Galadima Primary School during 1977 despite the fact that no clinical cases of meningococcal disease were recorded in either of these communities at the time. A few cases could have occurred at Galadima Primary School and escaped detection if students affected by meningococcal disease did not seek treatment at Malumfashi General Hospital. We are confident that no cases of meningococcal disease occurred at Yar Talata, which was kept under close surveillance.

Group A meningococcal disease occurred among pupils at other primary schools in Malumfashi and in villages near Yar Talata, so that it is likely that the group A organisms identified in these communities at the time of the epidemic belonged to the epidemic strain. However, it is possible that sever-

al strains of group A meningococci began to circulate in the Malumfashi area at the same time, that only some of these were virulent, and that the populations of Yar Talata and of Galadima Primary School were spared infection by the virulent strain. An attempt was made to investigate this possibility by comparing the antigenic characteristics of strains of group A meningococci isolated from patients and carriers at the beginning and at the end of the 1977 epidemic. No heterogeneity was detected among group A isolates by HA or by bactericidal assays.[2] Unfortunately, polyacrylamide gel electrophoresis of protein and lipopolysaccharide extracts of these isolates could not be performed.

Analysis of the pattern of meningococcal carriage in Yar Talata showed an acquisition rate of 1.6% per month in households with a carrier and an acquisition rate of 0.7% per month in households without a carrier. Both of these figures are higher than the acquisition rate of 0.5% per month reported in an American community by Greenfield et al. [13] and higher than the acquisition rate of 0.3% per month recorded in American children by Gold et al. [14]. Nevertheless, the spread of meningococci in Yar Talata was much slower than that of many other infectious agents. Meningococcal carriage was found most frequently in children, and children were identified as first carriers within a household more frequently than adults. These findings, together with the observation that in northern Nigeria meningococcal disease is seen most frequently in children 5–14 years old [11], suggest that in northern Nigeria meningococcal infection is usually spread from child to child. This pattern of infection differs from that recorded in the United States [13] and Brazil [15] where adult males are thought to be the main introducers of the infection into a household.

The preliminary surveys and studies carried out in Yar Talata over a two-year period showed no seasonal variation in meningococcal carriage in either a nonepidemic or in an epidemic year. Season had no influence on rates of acquisition of meningococci at Yar Talata. Thus, our findings are in agreement with those of Etienne [8] who found no seasonal variation in carriage during a one-year period of observation in a village in Upper Volta. It is therefore unlikely that the occurrence of epidemics of meningococcal disease in savanna Africa during the dry season is determined by climatic factors which favor the spread of meningococci from person to person at that time of year. Rather, it appears that the low absolute humidity and high temperature of the dry season favor the occurrence of meningococcal disease, as opposed to asymptomatic meningococcal infection, perhaps by damaging the local defense mechanisms of the nasopharynx.

The t½ of meningococcal carriage found at both Yar Talata and at Galadima Primary School was three months. However, this figure is likely to be an underestimate of the true duration of meningococcal carriage in this community because several negative swabs were obtained between two positive cultures in a number of subjects. Greenfield et al. [13] devised a method for determining the mean duration of menincogoccal carriage which takes account of the phenomenon of "missed cultures." When their technique was applied to our data for Yar Talata, a mean duration of carriage of 5.6 months was obtained, a figure considerably less than the value of 9.6 months obtained in their study. However, it is similar to the value of 4.1 months obtained in a study of American children six to eight years old by Gold et al. [14] using a system of life-table analysis.

Although *N. lactamica* rarely causes clinical disease, the epidemiology of infection with this organism is of interest because nasopharyngeal colonization by *N. lactamica* can induce the formation of antibodies which are bactericidal for group A, group B, or group C meningococci. Gold et al. [14] showed that in Danbury, Conn., the carriage rate of *N. lactamica* increased from 4% in infants three months of age to a maximum of 21% in children 18–24 months of age. Thereafter the carriage declined progressively to reach a value of only 2% in children 14–17 years of age. At Yar Talata, carriage rates for *N. lactamica* were higher in young children than those observed in the Danbury study (>25% in children <10 years of age), and the carriage rate declined less rapidly with age than in the United States. At Yar Talata the carriage rate of *N. lactamica* among children 10–14 years of age was ~15%, whereas at Danbury carriage was observed in only ~4% of children of this age. The epidemiologic significance of a high carriage rate of *N. lactamica* in Nigerian infants and of the persistence of carriage into later childhood is uncer-

[2] See footnote 1.

tain. Carriers of both *N. lactamica* and meningococci were found in the number expected by chance on the basis of the overall carriage rate of the two organisms in the community. Thus, it appears that carriage of *N. lactamica* does not prevent local colonization of the nasopharynx with meningococci. Carriage of *N. lactamica* may have played a part in protecting against systemic meningococcal infection, as described by Gold et al. [14], but a high *N. lactamica* carriage rate was found in Nigerian children 5–14 years of age, the group most at risk of contracting systemic meningococcal disease.

References

1. Lapeyssonnie, L. La méningite cérébro-spinale en Afrique. Bull. W.H.O. 28(Suppl.):3–114, 1963.
2. Chalmers, A. J., O'Farrell, W. R. Preliminary remarks upon epidemic cerebrospinal meningitis as seen in the Anglo-Egyptian Sudan. J. Trop. Med Hyg. 19:101–116, 1916.
3. Davis, L. J. A bacteriological investigation of epidemic cerebrospinal meningitis in the southern Sudan. Trans. R. Soc. Trop. Med. Hyg. 24:617–622, 1931.
4. Riding, D., Corkhill, N. L. Prophylactic vaccination in epidemic meningococcal meningitis. J. Hyg. (Lond.) 32:258–267, 1932.
5. Horn, D. W. The epidemic of cerebrospinal fever in the northern provinces of Nigeria, 1949–1950. Journal of the Royal Sanitary Institute 71:573–588, 1951.
6. Sanborn, W. R., Benčjć, Z., Cvjetanović, B., Gotschlich, E. C., Pollock, T. M., Sippel, J. E. Trial of a serogroup A meningococcus polysaccharide vaccine in Nigeria. Progress in Immunobiological Standardization 5:497–505, 1972.
7. Burian, V., Fofana, Y., Sow, O. Etude des *Neisseria meningitidis* isolés en République du Mali en 1970. Bull. W.H.O. 51:495–500, 1974.
8. Etienne J. Portage rhinopharyngé de méningocoques en Haute Volta. *In* Table ronde sur l'immunoprophylaxie de la méningite cérébrospinale. Fondation Mérieux, Lyon, France, 1973, p. 75–81.
9. Njoku-Obi, A. N., Agbo, J. A. C. Meningococcal carrier rates in parts of eastern Nigeria. Bull. W.H.O. 54:271–273, 1976.
10. Bradley, A. K., Gilles H. M., Shehu, U. Malumfashi endemic diseases research project. I. Some ecological and demographic considerations. Ann. Trop. Med. Parasitol. 71:443–449, 1977.
11. Greenwood, B. M., Bradley, A. K., Cleland, P. G., Haggie, M. H. K., Hassan-King, M., Lewis, L. S., Macfarlane, J. T., Taqi, A., Whittle, H. C., Bradley-Moore, A. M., Ansari, Q. An epidemic of meningococcal infection at Zaria, northern Nigeria. I. General epidemiological features. Trans. R. Soc. Trop. Med. Hyg. 73:557–562, 1979.
12. Hassan-King, M., Greenwood, B. M., Whittle, H. C., Abbott, J. D., Sutcliffe, E. M. An epidemic of meningooccal infection at Zaria, northern Nigeria. III. Meningococcal carriage. Trans. R. Soc. Trop. Med. Hyg. 73: 567–573, 1979.
13. Greenfield, S., Sheehe, P. R., Feldman, H. A. Meningococcal carriage in a population of "normal" families. J. Infect. Dis. 123:67–73, 1971.
14. Gold, R., Goldschneider, I., Lepow, M. L., Draper, T. F., Randolph, M. Carriage of *Neisseria meningitidis* and *Neisseria lactamica* in infants and children. J. Infect. Dis. 137:112–121, 1978.
15. Munford, R. S., Taunay, A. de E., de Morais, J. S., Fraser, D. W., Feldman, R. A. Spread of meningococcal infection within households. Lancet 1:1275–1278, 1974.