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Preventive immunisation could reduce the risk of meningococcal epidemics in the African meningitis belt

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Control of meningitis epidemics is based on early case detection followed by mass campaigns of immunisation. However, this strategy showed severe inadequacies during recent outbreaks in Africa.

In Niamey, Niger, meningococcal vaccinations began in 1978 and detailed bacteriological and epidemiological surveillance of meningitis started in 1981. When vaccine coverage rates were higher than 50%, the prevalences of *Neisseria meningitidis* A meningitis were low in Niamey, although there was a concurrent epidemic in rural Niger. A massive outbreak of meningitis in Niamey in 1994–1995 followed a 6-year period during which the mean rate of vaccine coverage remained $<25\%$. The data indicate that, in the meningitis belt, preventive immunisation should avoid a great number of deaths and be less expensive than mass immunisation campaigns performed after epidemics have begun.

Epidemics of meningitis caused by *Neisseria meningitidis* remain a serious public-health problem in countries within the meningitis belt (Riou *et al.*, 1996; Hart and Cuevas, 1997; Tikhomirov *et al.*, 1997). The control of meningitis epidemics in this area is based on the early detection of the epidemics by weekly surveillance (WHO, 1995), followed by the treatment of cases and mass vaccination of target populations all around the focus of each epidemic. However, there were difficulties in the mobilisation of resources and the implementation of mass vaccinations during recent epidemics in West Africa, finally leading to an obvious failure of this method of control (Robbins *et al.*, 1997, 1998; Chippaux *et al.*, 1998).

The aim of the present study was to evaluate the role of preventive vaccination in restricting the development of meningitis epidemics in Niamey, Niger, during the last 15 years. The epidemiological and bacteriological data analysed were collected by the staff of the *Centre de Recherche sur les Méningites et les Schistosomoses* (CERMES), in Niamey, between 1981 and 1996.

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MATERIALS AND METHODS

Niamey, the capital of Niger, with an estimated 550 000 residents in 1995, is situated in the centre of the African meningitis belt. The annual changes in the population and age distribution over the period of interest were estimated from data collected in censuses in 1977 and 1988.

The bacteriology laboratory of the CERMES processes samples of cerebrospinal fluid (CSF) from the infectious-disease service of the National Hospital of Niamey (NHN), where all cases of suspected meningitis in Niamey are treated. All available information on the samples collected between 1 September 1981 and 30 June 1996 was gathered.

A case of bacterial meningitis (BM) was confirmed if: (1) *N. meningitidis*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, Enterobacteriaceae, or another bacterial pathogen was isolated from the CSF; (2) antigen from *N. meningitidis*, *S. pneumoniae*, or *H. influenzae* B was detected in the CSF by latex agglutination and/or counter-immunoelectrophoresis; (3) direct examination of the CSF revealed Gram-negative rods or cocci or Gram-positive cocci; and/or (4) the CSF contained >100 white blood cells/ml.

The clinical evolution of every confirmed case was read from the NHM's records. Morbidity and mortality were evaluated from these records and then compared, whenever possible, with the data obtained, through a mandatory reporting system, by the *Service National d'Information Sanitaire* (SNIS). The SNIS data are based on clinical reports and date back only to 1991, when national epidemiological surveillance began.

Information on meningococcal A/C vaccinations performed in Niamey was obtained either from the archives of the *Service des Grandes Endémies* (deposited at SNIS and covering the period from the end of 1977, when the vaccine first became available in Niger, to 1993), or from the files of the Expanded Programme of Immunisation (EPI; covering the period from 1993–date). Annual vaccine coverage was estimated from the total number of vaccinations performed by the health services and the mean (estimated) population of Niamey in the corresponding year.

RESULTS AND DISCUSSION

Cases of Bacterial Meningitis

The incidence of meningitis caused by *N. meningitidis* A in the population of Niamey is illustrated in Figure 1. Since 1930, eight epidemic waves have been observed, with a mean interval of 7.5 years (range = 3–10 years). Although the data for the years before 1985 are incomplete (as the report system was not fully operational), the cyclical trend in the incidence of meningitis in Niger appears similar to that seen in other West African countries (Moore, 1992).

Between 1981 and 1996, 7078 cases of BM were diagnosed at CERMES. Of these, 4081 (57.7%) were due to *N. meningitidis*, 934 (13.2%) to *S. pneumoniae*, 670 (9.5%) to *H. influenzae*, and 161 (2.3%) to other bacteria, particularly Enterobacteriaceae. No pathogen was identified in 1232 cases (17.4%). Although 3418 meningitis cases were diagnosed at the CERMES between July 1991 and June 1996, 3563 were reported to the mandatory reporting system of the SNIS for the same period. Taking the SNIS data as the 'gold standard', the overall sensitivity of the CERMES data for this period is therefore 96%.

The mean annual incidence of BM during the period of study was 113.2 cases/100 000 residents. Although the incidence of meningitis caused by other bacteria remained stable, the incidence of meningitis due to *N. meningitidis* fluctuated from year to year, with a mean annual incidence of 61.4 cases/100 000 and a range of 3.6–348.6 cases/100 000.

Two epidemics of bacterial meningitis have occurred in Niger since 1981, in 1986 and 1995. In the 1986 epidemic, although there were about 400 cases/100 000 inhabitants of rural areas (ranging from 350–500 cases/100 000, according to province), the attack rate in Niamey was much lower, at about 140/100 000—the threshold defining an

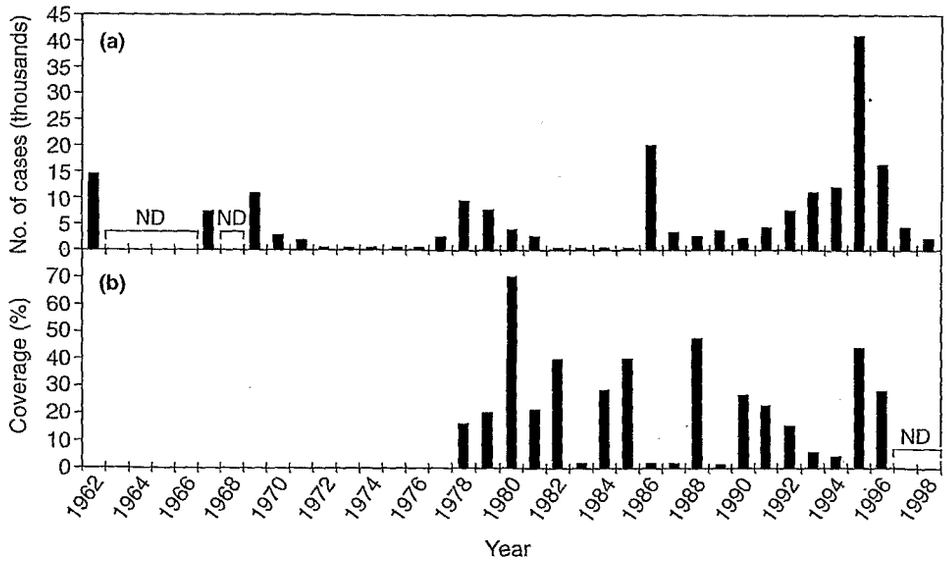

Fig. 1. Annual incidence of meningococcal meningitis in Niger (a) and vaccine coverage in Niamey, Niger (b), from 1962 to 1998. ND, No data available.

epidemic year (Campagne *et al.*, 1999). During the epidemic of 1995 the attack rates in Niamey (370 cases/100 000) and rural areas (435/100 000, with a range of 211–732/100 000) were fairly similar (Chippaux *et al.*, 1996).

The case–fatality rate, based on the CERMES and NHN data, was 20.5% overall, with high variations depending on the cause: 11.7% for *N. meningitidis*; 43.3% for *H. influenzae*; 52.7% for *S. pneumoniae*; and 54.1% for other bacteria.

Neisseria meningitidis of serogroup A was responsible for 85.6% of the cases of meningococcal meningitis. Serogroup C emerged between 1990 and 1993, representing 6.6% of the total cases in this period, and then disappeared. Serogroups W135 and X were always rare, apart from one focal outbreak of *N. meningitidis* X (Etienne *et al.*, 1990).

The incidence of *N. meningitidis* A was very low between 1981 and 1983, became much higher between 1984 and 1986, gradually decreased until 1993–1994, and then caused the 1995 epidemic (Fig. 2).

Vaccination

Between 1978 and 1992, vaccinations performed by mobile teams accounted for 95% of the vaccine coverage. Two strategies were used by the teams: mass vaccinations of the general population (100 000–200 000 people/year, carried out in 1980, 1982, 1985, 1988, 1990 and 1991, at the beginning of each dry season); and selective vaccinations, of schoolchildren only (40 000–70 000 children/year, carried out in 1978, 1981, 1984 and 1992). Vaccinations in mother-and-child health centres (MHC) represented 4% of the vaccinations and those carried out in the International Vaccination Centre accounted for $<1\%$. Very few vaccinations were performed in the private sector.

The rates of vaccine coverage decreased gradually from 1985 until 1993, with coverage in 1992 and 1993 falling below 5% (Fig. 1). Only 25 000 vaccinations were performed in 1993 and most of these were in the MHC. Since 1993, the EPI has taken charge of meningococcal vaccinations and vaccines have been administered either at MHC (each per-

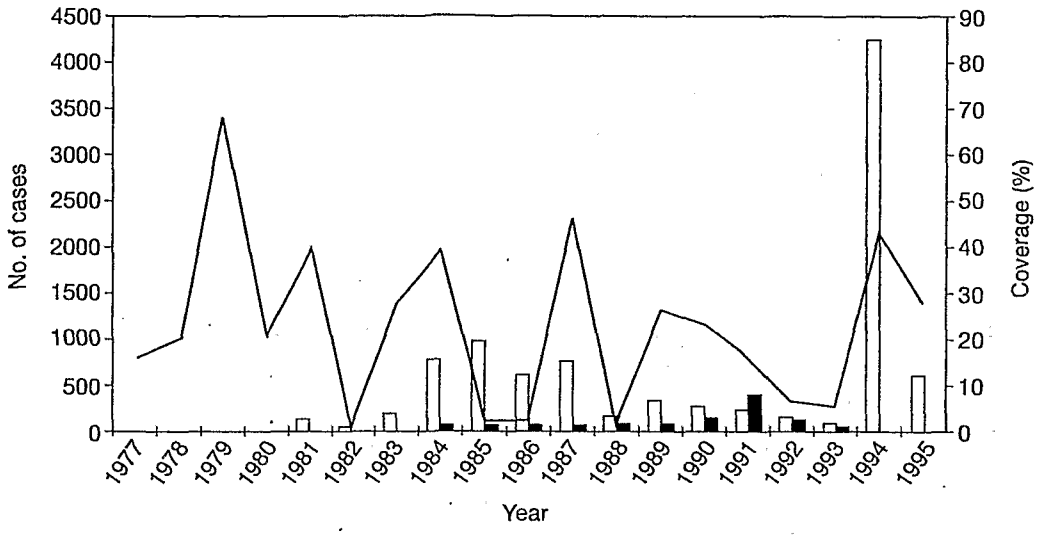

Fig. 2. Vaccine coverage (—) and incidences of meningococcus A (□) and C (■) in Niamey from 1977 to 1996.

son vaccinated being charged the cost price—about U.S.$0.5) or through mass vaccinations (free of charge) when, in 1994–1995, there was an epidemic alert. Information on the mass vaccination during 1994–1995 is incomplete but about 200 000 people were vaccinated. Vaccine coverage between 1978 and 1996 was very irregular (Fig. 2) and was particularly poor between 1988 and 1994, despite mass campaigns (1990 and 1991) and selective vaccinations (1992).

General Discussion

The numbers of vaccinations carried out in Niger may have been over-estimated in the present study because the estimates make no allowance for loss of the doses of vaccine on their way to the target populations (perhaps as much as 5% during the mass campaigns). However, as the numbers of people living in Niamey may have been under-estimated by a similar percentage (because of immigration from rural areas affected by political unrest in northern Niger), the present estimates of vaccine coverage may be fairly accurate.

The cyclical character of *N. meningitidis* incidence in the population may reflect changes in climate, bacterial virulence (Riou *et al.*, 1996) and/or the immune status of the human population. Climatic factors are probably more responsible for the seasonal recurrence of meningococcal infection that for the multi-year cycle (Lapeyssonie, 1963). There is no epidemiological evidence to indicate that the strain of bacterium responsible for the 1995 epidemic, *N. meningitidis* A:4:P1.9 clone III-1 (Riou *et al.*, 1996), is any more virulent than the strains circulating earlier (Lapeyssonie, 1963; Greenwood *et al.*, 1979). Although the spread of clone III-1 beyond the meningitis belt may be an indication that it is more epidemiogenic than earlier strains, it may equally reflect changes in socio-economic and climatic factors.

According to Lapeyssonie (1963), an epidemic begins when sufficient subjects are susceptible and ends, in the absence of any intervention, with the disappearance of receptive subjects (Hassan-King *et al.*, 1988). The immunological factors involved in the epidemics are probably complex. Antigenic variation in *N. meningitidis* could play a role in the propagation of pandemics (Moore, 1992). However, vaccination or natural contact with

N. meningitidis polysaccharides induces immunity to every strain belonging to the same serogroup, even though the immunity is short-lasting (Ceesay *et al.*, 1993; Reingold *et al.*, 1985). Collective immunity, acquired after vaccination or natural contact with *N. meningitidis*, could therefore be an essential factor in protecting a population from epidemics of meningococcal meningitis. Two features of the present data indicate that this so:

(1) the 1984–1986 and 1994–1995 epidemics of meningococcal meningitis affected all of Niger. However, in Niamey, these two outbreaks differed from one another, both in the overall incidence of disease (higher in 1994–1995 than in 1984–1986) and in the way incidence increased (much more sudden in 1994–1995 than in 1984–1986). The relatively slow increase in incidence in 1984–1986 was probably the result of high rates of vaccine coverage in 1980–1982 (Fig. 2). This good vaccine coverage may not only have delayed the development of an epidemic but may also have greatly reduced the severity of the 1985–1986 epidemic in Niamey (compared with that seen in rural areas at the same time). The period of poor vaccine coverage (1992–1993) presumably led to poor collective immunity and the subsequent explosion in the incidence of *N. meningitidis* A meningitis in 1994–1995.

(2) cases of *N. meningitidis* A meningitis almost disappeared prior to each epidemic episode. This drop in incidence, also observed in the years preceding the epidemic in Zaria, Nigeria, in 1977–1978 (Greenwood *et al.*, 1979), would cut natural exposure to the meningococcus and, therefore, individual immunisation. (The apparent disappearance of *N. meningitidis* A was not due to detection bias, as the prevalences of other bacteria in the CSF samples remained relatively stable.)

The current strategy for the control of epidemics of bacterial meningitis—surveillance, and vaccination only when there is an epidemic alert—seems unsatisfactory (Perkins *et al.*, 1998). Although epidemiological surveillance is functional in most African countries, the use of a general threshold of incidence needed to trigger an epidemic alert, as recommended by the World Health Organization, remains controversial (Varaine *et al.*, 1997). Chippaux *et al.* (1998) proposed that epidemiological studies must be carried out so that a different, more appropriate threshold can be established for each of the various climates and demographic conditions within the meningitis belt. Although Perkins *et al.* (1998) claimed otherwise, mass vaccination campaigns have been recommended and attempted since meningococcal vaccine became available in the mid-1970s, albeit with little success (Robbins *et al.*, 1997). Mass vaccination is expensive and not very cost-effective (Varaine *et al.*, 1997). It is unlikely that meningococcal vaccination will be added to the EPI, as a preventive immunisation strategy, because of the young age of the subjects targetted by the programme (Wenger *et al.*, 1997). Other strategies have therefore to be set up, taking cost recovery into account when applicable. For example, immunisation campaigns based on mobile teams might be recommended in focus points such as schools, markets, and camps. This strategy appears to have been very successful in Benin, where it has been implemented since 1988 (Hassan *et al.*, 1998): no epidemic has occurred in northern Benin, which lies within the meningitis belt, since 1989, whereas all neighbouring countries were struck by epidemics between 1993 and 1998.

While waiting for the conjugated, meningococcal A/C vaccine, whose immunological superiority is no longer in doubt, the regular utilisation of the polysaccharide vaccine would probably significantly reduce meningitis-attributable mortality in the meningitis belt of Africa.

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