Impact of a mass vaccination campaign against a meningitis epidemic in a refugee camp

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Summary Serogroup A meningococcus epidemics occurred in refugee populations in Zaire in August 1994. The paper analyses the public health impact of a mass vaccination campaign implemented in a large refugee camp. We compared meningitis incidence rates from 2 similar camps. In Kibumba camp, vaccination was implemented early in the course of the epidemic whilst in the control camp (Katale), vaccination was delayed. At a threshold of 15 cases per 100 000 population per week an immunization campaign was implemented. Attack rates were 94 and 134 per 100 000 in Kibumba and Katale respectively over 2 months. In Kibumba, one week after crossing the threshold, 121 588 doses of vaccine were administered covering 76% of all refugees. Vaccination may have prevented 68 cases (30% of the expected cases). Despite its rapid institution and the high coverage achieved, the vaccination campaign had a limited impact on morbidity due to meningitis. In the early phase in refugee camps, the relative priorities of meningitis vaccination and case management need to be better defined.

keywords meningitis, bacterial meningitis, meningococcal meningitis, *Neisseria meningitidis*, epidemics, outbreaks, epidemiology, vaccination, active immunization, refugees

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Introduction

Serogroup A meningococcus is the most frequent cause of acute bacterial meningitis (ABM) epidemics in Africa (Galazka 1982; Greenwood 1987; Moore 1992; Peltola 1983). This serogroup can cause severe epidemics whose attack rates tend to be higher than for other serogroups (Moore *et al.* 1990). While the efficacy of group A meningococcal vaccine was proved (Erwa *et al.* 1973; Peltola *et al.* 1977; Reingold *et al.* 1985), the immunity it confers is of limited duration; in young children it lasts less than 3 years (Reingold *et al.* 1985) and protection is poor in infants (Galazka 1982; Schwartz *et al.* 1989). For these reasons, meningococcal vaccine has not been added to routine childhood immunization programmes (Galazka 1982; Reingold *et al.*, 1985; Wright 1989).

Mass vaccination campaigns seem to be able to curtail epidemics (Binkin & Band 1982; Cadoz 1984; Cochi *et al.* 1987; Greenwood 1984; Mohammed & Zaruba 1981; Spiegel *et al.* 1993)

Table 1 Population characteristics in Kibumba and Katale camps, July and August 1994

	Kibumba	Katale
Population number at the end of July	180 000	80 000
Population less than 5 years of age (%)	17	17
Proportion of refugees who died during the first 3 weeks of the camp existence (%)	7.3	8.3
Average crude mortality rate per 10 000 per day at mid-August	5.2	4.3
Malnutrition prevalence amongst children less than 5 years of age (%)	20.1	23.1
Available surface per person (m^2)	below 10	below 10
Prevaccination attack rates per 100 000 (week 1 to 4)	43.3	41.1

and may be cost-effective (Cochi *et al.* 1987). However, to be effective, mass vaccination campaigns need to start early in the course of the epidemic (Cadoz 1984; Greenwood 1984). As ABM has become endemic in most of Africa's meningitis belt, it is difficult for public health practitioners to determine whether one is facing the start of an epidemic or a fluctuation of the usual baseline number of cases. In Burkina Faso an incidence rate of 15 cases per 100 000 population per week averaged over 2 consecutive weeks has been found to be of a high positive predictive value regarding subsequent epidemics. This incidence rate was later used as a threshold for declaring an epidemic in sub-Saharan Africa (Moore *et al.* 1990b; 1992; WHO 1995) although the authors of the initial study specified that it should be evaluated in different settings (Moore *et al.* 1992).

Displaced populations are at high risk for ABM outbreaks, with serogroup A meningococcus as the most frequent cause (Moore *et al.* 1990b). The threshold of 15 cases per 100 000 people per week averaged over 2 weeks was recommended as the decisive criterion for declaring an epidemic and instituting an immunization programme among refugee populations in camps. According to current recommendations, mass vaccination campaigns should be implemented within 4–8 weeks of an epidemic's onset in order to have an impact on its course (Moore *et al.* 1990b). Data on epidemics in refugee settings are scarce and health policy is based on data taken from non-camp situations. Disease dynamics and the impact of mass vaccination campaigns may vary in refugee populations, whose living conditions are usually characterized by overcrowding and low

sanitary standards. The paper describes meningococcus A epidemics in two Rwandan refugee camps in Zaire in August 1994 and analyses the public health impact of the mass vaccination campaign carried out in one of them.

Materials and methods

Setting

The refugee camps Kibumba and Katale were formed after the massive influx of displaced persons (between 500 000 and 800 000) from Rwanda into the Goma region, north-eastern Zaire, in mid-July 1994. The camps were located 30 km apart in the mountainous Kivu lake area which has an average annual rainfall of 1200 ± 300 mm (Wills *et al.* 1986). A long dry season occurs between June and August, another short one in January and February. Even the dry seasons can be fairly wet; in 1994, rainfall intensified from early August. The average annual temperature is 19°C.

Both camps were extremely overcrowded: the available surface area per person of less than 10 m^2 was far below the recommended minimum of 30 m^2 (UNHCR 1986). Housing conditions were extremely precarious in both camps. Three epidemics occurred between mid-July and mid-August 1994; cholera, shigellosis and meningococcal A meningitis. Health conditions (Table 1) among both camp populations were comparable and very poor (Goma Epidemiology Group 1995). Various aid agencies provided hospital and outreach health services to the refugees.

Study population

Population figures were estimated from aerial photographs taken in early August combined with population counts in randomly chosen high and low density areas. Population figures at the time were 180 000 in Kibumba and 80 000 in Katale. From early September, a part of the refugees were progressively moved from Kibumba to a new setting, Kahindo. The number of refugees leaving Kibumba was registered by the Office of the UNHCR and used to adjust Kibumba population figures. In Katale the population increased after a late arrival of refugees, giving a new estimate of 110 000 on 21 August 1994. The age distributions of both populations were comparable.

Epidemiological surveillance and case definition

A surveillance system was established in both camps. The case definition for computation of ABM incidence was 'all suspect cases admitted to the camp hospitals with bacteriological confirmation of meningococcus in the cerebrospinal fluid'. Cases were no longer bacteriologically confirmed during the final 3 weeks in Kibumba. In order to compute incidence for these weeks, the proportion of positives from the previous 6 weeks (number of bacteriologically confirmed cases as a proportion of the submitted cerebrospinal fluid) was applied to the weekly number of reported cases. Katale cerebrospinal fluid samples were submitted to either the Bioforce or the Israeli hospital laboratories. Most samples from Kibumba were submitted to Bioforce, only a few to the Israeli hospital laboratory. The extrapolation was based on the proportion of positives from the Bioforce laboratory. The threshold for an ABM epidemic was set by the Goma Epidemiology Group (1995) at 15 confirmed meningitis cases per 100 000 per week for each refugee camp in the Goma region. Case fatality rates (CFR) were determined with data from the in-patient registration system instituted in the camps. Deaths of patients with an admission diagnosis of meningitis were registered as deaths caused by meningitis, whether the cases were further confirmed or not. The CFR was thus estimated as the number of deaths due to meningitis as a proportion of the number of clinically suspected cases.

Laboratory tests

A lumbar puncture was performed on each clinically suspected case (neck stiffness and fever). A latex agglutination test for the identification of meningococcus A antigen or bacterial culture was performed by either the Bioforce or Israeli hospital laboratories to obtain confirmation.

Case management

A single dose of chloramphenicol in oil intramuscular (Moore *et al.* 1990b; Wali *et al.* 1979) was given for the treatment of all suspected and laboratory confirmed cases (3 g in adults and 50–100 mg/kg in children). In both camps, home visitors were trained to recognize the clinical signs of meningitis and held responsible for active case detection and referral to hospitals.

Kibumba vaccination campaign

The target population for the vaccination campaign was defined as all refugees over 6 months of age. The objective was to vaccinate the entire target population (176 000) within one week. The first case was detected on 28 July. Six vaccination posts were set up between 17 and 19 August. The refugees were informed by radio and by 150 home visitors. Each vaccination post was staffed by 30 persons including a team supervisor, staff to reconstitute the lyophilized vaccine and prepare syringes, vaccinators, persons to assist during the injection of children, guards, and clerks to complete the vaccination cards and to collect age-related data. A subcutaneous injection of 0.5 ml meningococcal polysaccharide (A+C) vaccine was administered in the deltoid muscle region. The vaccination campaign took place from 20 to 28 August.

Katale vaccination campaign

The first case was detected on 1 August 1994. Immunization was initially postponed as resources were preferably allocated to other priorities. Further delays followed due to vaccine shortage. Mass vaccination finally took place between 8 and 22 September. The strategy applied was similar to that in Kibumba.
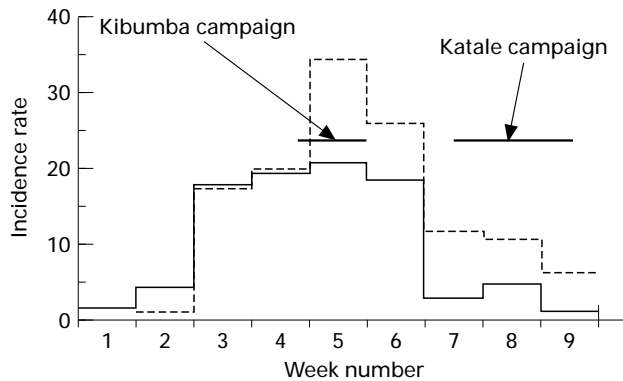
Figure 1 Weekly incidence rates of meningococcal A meningitis, cases per 100 000 per week, Kibumba (solid line) and Katale (dotted line) refugee camps. From 25 July to 25 September 1994.

Operational effectiveness of the Kibumba vaccination campaign

The public health impact of the vaccination campaign was evaluated by estimating its operational effectiveness. This was defined as the number of cases prevented as a proportion of the number of expected cases over a follow-up period of 2 months. In this way, the overall effectiveness of the campaign could be quantitated. Field vaccine efficacy was not measured. We did not examine prevention of cases in the long term, as the main objective of a mass vaccination campaign in the emergency phase of a refugee crisis is to control an ongoing epidemic. We assumed that both camps were comparable, and Katale refugee camp served as a control. We also assumed that the number of cases prevented in Katale during that period was negligible as the vaccination campaign was implemented towards the end of the epidemic curve. Weekly incidence rates (WIR) and attack rates (cumulative incidence rates over the entire epidemic period) were compared. The number of expected cases in Kibumba was estimated from the attack rates observed in Katale. The number of cases prevented in Kibumba was obtained by subtracting the number of observed cases from the number of expected cases. The number of deaths prevented was computed by applying Kibumba CFR to the estimated number of cases avoided. The number of ABM cases prevented by 10 000 doses of vaccine administered was also computed.

Results

Epidemics

The meningitis epidemics started in both camps simultaneously (Figure 1). Prevaccination attack rates were similar (Table 1) confirming the comparable status of both camps. One hundred and sixty-two cases were observed between 28 July and 25 September in Kibumba, and 137 between 1 August and 25 September in Katale, yielding attack rates of 94.2 per 100 000 (60 days) and 133.7 per 100 000 (56 days) respectively. Meningococcus serogroup A was responsible for all confirmed cases. The proportion of confirmed cases amongst all cerebrospinal fluid samples submitted to the Bioforce laboratory was 57% for Kibumba between 1 August and 11 September (141 positive cerebrospinal fluids out of 247 submitted) and 59% for Katale during the same period (48 positives out of 82). The epidemic alert threshold set for Goma camps was crossed during the week of 8 August in both camps (Table 2). The WIR at that time was 17.8 per 100 000 per week in Kibumba and 17.5 per 100 000 per week in Katale. The threshold recommended by Moore *et al.* (1990b) was crossed the following week. Between 15 August and 4 September, the CFR was estimated to be 8% (14 deaths in 182 clinically suspected cases) in Kibumba. In Katale the corresponding computation yielded a CFR of 3% (8 deaths in 232 cases) during the entire epidemic period.

Table 2 Number of new cases per week and weekly incidence rates of meningococcal A meningitis in Kibumba and Katale refugee camps, 25 July–25 September 1994

Period	Number of new cases per week		Population figure (1000s)		Weekly incidence rate (per 100 000 population per week)	
	Kibumba	Katale	Kibumba	Katale	Kibumba	Katale
25–31 July (week 1)	3	—	180	80	1.7	—
1–7 Aug. (week 2)	8	1	180	80	4.4	1.3
8–14 Aug. (week 3)	32	14	180	80	17.8	17.5
15–21 Aug. (week 4)	35	22	180	110	19.4	20.0
22–28 Aug. (week 5)	37	38	180	110	20.6	34.5
29 Aug.–4 Sept. (week 6)	32	29	172	110	18.6	26.4
5–11 Sept. (week 7)	5	13	166	110	3.0	11.8
12–18 Sept. (week 8)	8	12	160	110	5.0	10.9
19–25 Sept. (week 9)	2	8	150	110	1.3	7.3

Vaccination campaigns

From 20 to 28 August, one week after crossing the threshold, 121 588 doses were administered in Kibumba covering 75.9% of the camp population according to a survey carried out on 30 August (95% CI 71.8–80.0%) (MSF-Belgium and Epicentre, unpublished observations). In Katale, 112 354 doses of vaccine were administered between 8 and 22 September.

Operational effectiveness of the Kibumba vaccination campaign

The attack rate in Kibumba was 39.5 per 100 000 less than that of Katale over approximately 2 months (95% CI 12.8–66.2 per 100 000) (P=0.002). In Kibumba, 68 cases, representing 29.6% of 230 expected cases, may have been prevented. Thus, 10 000 doses of vaccine administered may have prevented 5.6 cases, and the Kibumba vaccination campaign may have avoided 5 deaths. The estimated operational effectiveness was confirmed using an independent method of estimation based on work by Pinner *et al.* (1992) (data not shown).

Discussion

Attack rates recorded in this study, 94 and 134 per 100 000 in Kibumba and Katale respectively over 2 months, resemble those found in other refugee camp outbreaks. In Khmer refugee camps attack rates of 130 per 100 000 over 4 months and of 80 per 100 000 over 3 months were observed in 1980 (Moore *et al.* 1990b). A meningitis epidemic in endemic areas is defined as an annual incidence rate of at least 100 per 100 000 population (Moore *et al.* 1992). The Kibumba CFR (8%) is comparable to or lower than that found during other epidemics in refugee camps: 28% in Thailand in 1980 (Moore *et al.* 1990b) and 12.8% in Sudan in 1988 (Boelaert 1988, unpublished observations). In developing countries, CFR between 3.5 and 34% are described during meningococcal meningitis epidemics (Binkin & Band 1982; Bosmans *et al.* 1980; Cochi *et al.* 1987; Moore 1992; Peltola 1983; Tikhomirov 1987). In comparing CFR and attack rates, case definitions should be taken into account. Only bacteriologically confirmed cases were considered in Goma camps.

In Katale, the epidemic lasted for 2 months and its incidence peak arose within 3 weeks from case 1. Epidemics described in the meningitis belt usually last for several months (Greenwood 1984) with a peak within the first 12 weeks (Moore *et al.* 1990b). Several causes may be hypothesized to explain why the peak in Katale was early. Shorter dynamics have been reported at village scale where outbreaks have lasted for 4–8 weeks (Greenwood 1987). Epidemiological data analysis at the aggregate level of a country reveals longer duration than that seen in discrete populations. Secondly, overcrowding and poor sanitary conditions favour the spread of meningococcus (Greenwood 1984; Peltola 1983;

Schwartz *et al.* 1989). Thirdly, some refugees may not have been susceptible due to previous vaccination although to our knowledge no mass vaccination campaign was carried out in Rwanda during the preceding 3 years. Fourthly, perhaps the early peak was due to the intensification of rainfall in early August. Indeed, spontaneous drops in incidence rates are common at the onset of the rainy season in the meningitis belt (Greenwood *et al.* 1984). However, epidemics in the central African lake region do not seem to corroborate this seasonal pattern (Cadoz 1984; Greenwood *et al.* 1984). Epidemics starting or continuing during the rainy season were described in Rwanda and Burundi (Bosmans *et al.* 1980; Vimont-Vicary & Rogerie 1983; A. Sasse & F. Varaine 1992, unpublished observations). We may therefore assume that low proportions of susceptibles or intensification of rainfall are not valid explanations of an early peak. It seems that the rapid transmission of the epidemic in Katale is due to reproducible conditions inherent in refugee camps: they should be considered as discrete populations, with a higher meningococcus transmissibility.

The Kibumba vaccination campaign was carried out according to recommendations by Moore *et al.* (1990b). Obtaining a coverage of 75.9% in less than 8 days would have been almost impossible. Results show that an estimated 30% of expected cases may have been prevented over 2 months (5.6 cases avoided by 10 000 doses of vaccine administered). The low operational effectiveness obtained by the Kibumba campaign may be attributed to the combined effects of fast transmission and lack of early predictors for the epidemic. Moreover, vaccine field efficacy may have been considerably lower than expected in this severely malnourished population (Moore 1992).

Discussions about public health strategies in refugee camps must consider competing health problems and the phase in which a camp is evolving. The 68 cases of meningitis and 5 deaths possibly prevented by the mass campaign in Kibumba need to be compared to approximately 5400 preventable deaths from diarrhoeal diseases (MSF-Belgium 1994, unpublished observations) that occurred during the same 2 months.

A sudden decrease in incidence subsequent to the vaccination campaign was indeed observed in Kibumba. Some previous reports attributed such immediate decreases to preceding mass vaccination campaigns (Binkin & Band 1982; Cochi *et al.* 1987; Spiegel *et al.* 1993). But our data show that a synchronous decline in incidence occurred in Katale independently of any vaccination. This suggests that the Kibumba campaign might not have been the only factor responsible for the declining incidence rate in this camp.

On the basis of these observations we conclude that the current recommendations for meningitis A epidemic control in refugee camps merit reconsideration. Firstly, is the 'Burkina Faso threshold' valid in a refugee camp? Moore *et al.* (1992) concluded that it may not be applicable in other settings. To improve the potential benefits of mass vaccination campaigns, thresholds allowing for earlier action are needed. A more sensitive threshold might still have a sufficiently high positive predictive value, as the probability for a meningococcal epidemic is higher in a camp due to household crowding (Moore 1992; Reingold *et al.* 1985; Schwartz 1989; Moore *et al.* 1990a), poor health status (Peltola 1983), low nutritional status (Moore 1992), poor living conditions (Peltola 1983) and mass migration of populations (Moore 1992; Schwartz 1989). Other predictive factors should also be considered, such as the presence of an epidemic in a neighbouring area and the clonal type (Moore *et al.* 1989; Moore 1990a; Schwartz *et al.* 1989). Secondly, is it justified to allow for 4–8 weeks from case 1 for completion of a mass vaccination campaign, as the current recommendation holds (Moore *et al.* 1990b)? Would that not be too late to provide protective levels of antibodies for the ongoing epidemic? Special attention should be paid to the promptness of the intervention and the coverage to be achieved.

However, the appropriateness of a mass vaccination campaign in the emergency phase with high overall mortality should be questioned. An alternative strategy under conditions with serious competing mortality risks might be active case detection and early treatment. In untreated meningococcal disease CFR can reach 50% (Galazka 1982) or more during epidemics (Peltola 1983; Galazka 1982), whereas early treatment can reduce CFR to less than 10% (Galazka 1982; Cadoz 1984). Such a strategy also prevents deaths from other causes.

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More research is needed to assess the operational effectiveness of alternative strategies such as a joint measles and meningitis vaccination upon arrival of refugees in a camp. In the long term, a vaccine conferring longer lasting immunity as part of routine childhood immunization programmes would be the best answer to some of the questions raised.

Acknowledgements

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