Epidemic cholera among refugees in Malawi, Africa: treatment and transmission

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SUMMARY

Between 23 August and 15 December 1990 an epidemic of cholera affected Mozambican refugees in Malawi causing 1931 cases (attack rate = 2·4%); 86% of patients had arrived in Malawi < 3 months before illness onset. There were 68 deaths (case-fatality rate = 3·5%); most deaths (63%) occurred within 24 h of hospital admission which may have indicated delayed presentation to health facilities and inadequate early rehydration. Mortality was higher in children < 4 years old and febrile deaths may have been associated with prolonged IV use. Significant risk factors for illness ($P < 0.05$) in two case-control studies included drinking river water (odds ratio [OR] = 3·0); placing hands into stored household drinking water (OR = 6·0); and among those without adequate firewood to reheat food, eating leftover cooked peas (OR = 8·0). Toxigenic *V. cholerae* O1, serotype Inaba, was isolated from patients and stored household water. The rapidity with which newly arrived refugees became infected precluded effective use of a cholera vaccine to prevent cases unless vaccination had occurred immediately upon camp arrival. Improved access to treatment and care of paediatric patients, and increased use of oral rehydration therapy, could decrease mortality. Preventing future cholera outbreaks in Africa will depend on interrupting both waterborne and foodborne transmission of this pathogen.

INTRODUCTION

The seventh pandemic of cholera reached Africa in 1970 [1] and Malawi in 1973. Cholera epidemics are a particular problem in refugees and displaced populations, whose usual patterns of food and water supply have been disrupted. Malawi accepted refugees fleeing armed conflict in Mozambique beginning in

1986. At the end of October 1990, there were approximately 920000 such refugees in Malawi, representing more than 10% of the Malawian population. In Nsanje District in southern Malawi (Fig. 1), almost 300000 Mozambican refugees, living mainly in refugee camps, outnumbered the Malawian population. Nyamithuthu, the largest camp, opened in September 1988 and was originally planned for 50000 persons. A large and unexpected influx of refugees in late 1990 caused the camp population to increase from about 57000 persons on 15 October to about 74000 persons on 15 November. Sanitary facilities and water supplies were not available to
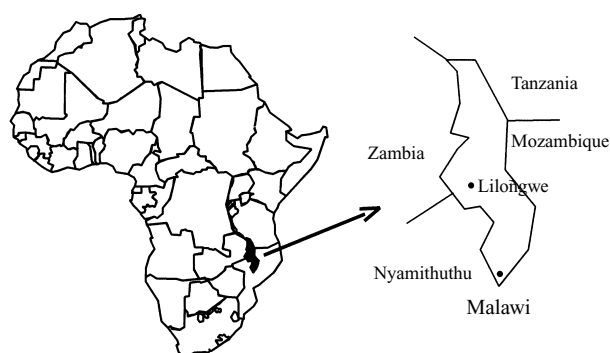
Fig. 1. Malawi, Africa, showing location of Nyamithuthu refugee camp.

accommodate the 1000 new arrivals per day. Beginning in mid-October, new arrivals were placed in a new area of the camp called Nyamithuthu North. Water was supplied from drilled wells, but quantities were inadequate; long waiting lines caused many persons to obtain water from a river several kilometres from the camp. Defecation occurred almost entirely in open fields or at the river.

Between 1988 and 1990, at least nine cholera outbreaks were reported among refugees in Malawi, including three that affected Nyamithuthu. On 23 August 1990, a fourth outbreak of cholera began in Nyamithuthu. A cholera camp was established with observation tents (equipped with oral rehydration facilities) and intravenous (IV) treatment tents. We report an epidemiologic investigation of this cholera outbreak and document the challenges of providing adequate treatment and prevention in these circumstances.

METHODS

A cholera case was defined as diarrhoeal illness in a person admitted to an IV treatment tent at Nyamithuthu Camp between 23 August and 15 December, 1990. We determined clinical and demographic characteristics of a sample of these patients by systematically selecting the chart of every fifth patient admitted between 23 August and the day of the chart review, 17 November 1990. To evaluate the use of IVs, we interviewed and examined all patients in two IV treatment tents at the cholera camp on 12 December 1990. The prevalence of fevers was evaluated in one paediatric tent on 12 December. All available charts of patients who died after admission to the cholera camp between 29 September and 30 November were reviewed. Population figures were based on camp registration records.

Case-control study A

To determine modes of transmission of *V. cholerae* O1 during the outbreak, a matched case-control study was performed between 28 November and 4 December. For this study, we selected patients in the IV treatment tent who were the first ill persons in their families and who lived in the section for new arrivals (Nyamithuthu North). Patients were interviewed in the treatment tent. Controls were selected from registration records and matched by age-group (0–4 years, 5–14 years, ≥ 15 years), sex and date of arrival; patients' names were located in the registration records and names of possible controls were selected by using the names of the nearest non-related persons on the list (who thus would have arrived on the same day) who were in the correct age-group and of the same sex. Controls were interviewed within 2 days after they were matched with a case-patient. Potential controls were excluded if anyone in their households had been ill with diarrhoea since arrival. Information was elicited about exposures to foods, various water sources, and utensils for the week before becoming ill for patients and the week before the interview for controls. The questionnaire format included 'yes', 'no', and 'don't know' responses; 'don't know' responses were excluded in the analysis.

Case-control study B

A second case-control study, contrasting households, was performed between 10 and 14 December to define further modes of cholera transmission. Household information was collected from patients in the IV treatment tent. Control households were selected by going door-to-door in Nyamithuthu North using a cluster survey design. Control households were excluded if any members had been ill since arrival. Exposures to foods and water sources were elicited for the week before a household member became ill for case households and the week before the interview for control households.

Laboratory methods and environmental sampling

Rectal swabs of patients were placed in Cary–Blair medium, held at ambient temperature, and transported to CDC. The swabs were then placed in alkaline peptone broth for 6 h at 37 °C for enrichment before being plated onto thiosulphate–citrate–bile salts–sucrose (TCBS) agar. Colonies typical of *V.*

cholerae on TCBS were subcultured and tested for agglutination with *V. cholerae* O1 polyvalent and monovalent antisera. Representative isolates were biochemically identified and biotyped. Isolates were tested for cholera toxin production by enzyme-linked immunosorbent assay [2].

Three *V. cholerae* O1 isolates (2 patient isolates and 1 water isolate) were tested for susceptibility to ampicillin, chloramphenicol, ciprofloxacin, doxycycline, erythromycin, furazolidone, kanamycin, nalidixic acid, streptomycin, sulphisoxazole, tetracycline, and trimethoprim/sulphamethoxazole as described by the National Committee for Clinical Laboratory Standards [3, 4].

We obtained water and food samples for culture in December by walking in a preset direction from the centre of Nyamithuthu North and collecting samples from every third hut encountered. Water from household water containers was tested for chlorine using standard DPD reagents [5] and cultured with the Spira jar technique [6]; 2 l of water from each of 4–6 water containers was poured through the gauze of each Spira jar. River water was tested with the Spira jar and Moore swab [7] techniques. Food samples were cultured by placing 25–50 g of food pooled from 3–6 samples into 500 ml of alkaline peptone broth. Alkaline peptone broth was incubated for 18 h before being plated on TCBS agar. One to two yellow colonies on each TCBS plate were picked, placed onto heart infusion agar (HIA) slants, and transported to CDC for identification.

Statistical analysis

We used Taylor Series 95% confidence limits for relative risk to compare proportions between groups. The 95% confidence intervals for matched odds ratios reported in case-control study A were calculated using the procedure described by Robins, Greenland and Breslow [8]. In case-control study B we used Cornfield 95% confidence limits for odds ratios for unmatched analysis.

RESULTS

Patients with new cases of diarrhoeal illness were sent to an observation tent at the cholera camp for oral rehydration therapy. Patients with moderate or severe dehydration were admitted from there to the IV treatment tent. Patients were also treated with tetracycline or doxycycline. From 23 August to 15
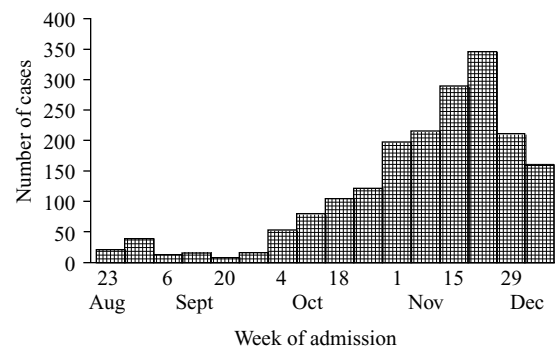

Fig. 2. Number of cases of diarrhoeal illness for which intravenous rehydration was required, Nyamithuthu refugee camp, Malawi, August–December, 1990.
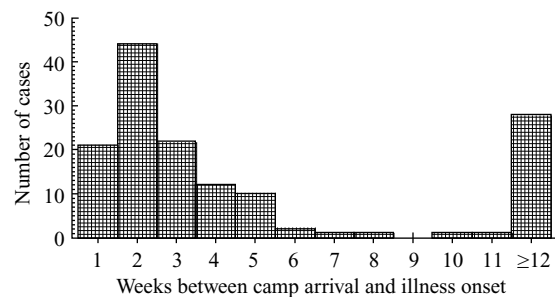

Fig. 3. Number of weeks between camp arrival and illness onset.

December 1990, 1931 (31·6%) of the 6114 persons seen at the observation tent were admitted to the IV treatment tent (Fig. 2). Using camp population figures of 15 December 1990, the attack rate [AR] (of persons requiring IV treatment) for the whole camp was 2·4% (1931/80 519); 68 deaths occurred, a case-fatality rate [CFR] of 3·5% (68/1931).

We reviewed the records of 173 patients admitted to the IV treatment tent. Of these, 55% were female and the mean age was 17 years. Twenty-eight percent were under 6 years of age, and 65% were < 19 years of age. One hundred and twenty-four (84%) of 166 patients for whom such data were available had come to Malawi less than 3 months before onset of illness (FIg. 3). Most became ill soon after arrival; 52% were admitted within 16 days of arriving at the camp.

Of these 173 patients, the mean number of days from admission to the IV treatment tent to discharge was 5·4 days. Patients received a mean of 8·5 l of IV fluid and 45 cups of oral rehydration solution (ORS).

Fifteen of the 19 patients in two IV tents evaluated on 12 December had IV lines in place. Of those 15, 4 had not had diarrhoeal stools in the previous 8 h and 3 others described their stools as being partly formed. Fourteen were able to eat, and only five reported still

having episodes of vomiting. Five had clinical signs of dehydration, but of those, four also had concurrent fever. IVs were rarely changed. Only 2 of the 15 patients with IVs had had their IVs changed since admission. Six had had their IVs for 38 h or more, 3 for 96 h or more.

Among 40 charts reviewed of patients who died, 24 (63%) of 38 (with information available) died < 24 h after admission and 14 (37%) died ⩾ 24 h after admission. The cause of death for persons who died early appeared to be acute dehydration and may have been because of late presentation to the cholera camp or because of inadequate initial rehydration. The cause of death for those who died late appeared to be from complications (infections with fever caused by prolonged use of IVs, etc.). Febrile death was associated with being in the IV tent > 24 h: 9 of the 13 who developed fever died after > 24 h in the IV treatment tent compared with 5 of 25 patients who died without developing fever (relative risk [RR] = 3·9, CI = 1·5–10·2). However, no diagnostic tests were available to determine the cause of febrile episodes. Symptoms were treated with chloroquine and aspirin.

A disproportionate number of children under 4 years of age who were cases died when compared to the overall estimate of the proportion of cases who were children. Twenty-four (60%) of the 40 persons whose deaths were reviewed were children under 4 years of age compared to 29 (17%) of the 173 selected patients who were children (RR = 4·5, CI = 2·6–7·9). Fever was especially common among children. Ten of 15 patients in a paediatric tent that were evaluated had temperatures greater than 38 °C; however, high ambient temperatures may have complicated temperature determination.

Case-control study A

Exposures of 50 case-patients and 50 matched controls were compared. The mean number of household members was similar for cases (4·9) and Controls (4·8). Placing hands into the water in the storage container holding household drinking water during washing or drinking in the previous week was significantly associated with illness (matched odds ratio [mOR] = 6·0, 95% confidence intervals [CI] = 1·3–26·8) (Table 1). Drinking river water tended to be associated with illness, but this was not statistically significant (mOR = 2·2, CI = 0·8–6·3). Eating cooked pigeon peas that had been left out overnight was not significantly associated with illness for all cases

combined. However, among persons who ran out of firewood during the previous week, eating cooked pigeon peas that had been left out overnight was significantly associated with illness (mOR = 8·0, CI = 1·0–64·0, $P < 0.05$ Fisher exact test, 2-tailed). This may have been because without firewood they could not reheat the leftover peas. Factors associated with previous outbreaks among refugees in Malawi including eating dried fish and lack of soap or a cooking pot, and other foods and eating practices were not significantly associated with illness.

Case-control study B

In the second case-control study, household data were collected from 47 patients in the IV treatment tent and from 245 households in Nyamithuthu North; 108 of the 245 potential control households were then excluded from analysis (leaving 137) because at least one family member had been sick with diarrhoea since arrival in Malawi. The unit of analysis was the household.

Obtaining drinking water from the river in the previous week was significantly associated with illness (odds ratio [OR] = 3·0, CI = 1·4–6·4) (Table 2). This association remained when analysis was limited to households in which someone had visited the river (OR = 16·1, CI = 2·0–351·2). Heating leftover peas was protective (OR = 0·15, CI = 0·02–1·0, $P < 0.05$ Fisher exact test, 2-tailed). Placing hands in the water container (OR = 1·8, CI = 0·6–5·5) was not significantly associated with illness in this analysis.

Laboratory and environmental results

Eight isolates recovered from rectal swabs transported to CDC were identified as toxigenic *V. cholerae* O1 biotype El Tor, serotype Inaba. A pooled sample of water from four household water containers yielded *V. cholerae* O1, serotype Inaba. One of the four households had a child with diarrhoea at the time. Other environmental samples including a pooled sample of 6 household water containers, 3 Moore swabs and 2 Spira jars collected from the river, pooled fish samples from 7 vendors, and pigeon peas pooled from 27 households did not yield *V. cholerae* O1.

Of the three isolates tested for antimicrobial susceptibility, the water isolate and one patient isolate were resistant to chloramphenicol, streptomycin, sulphisoxazole, ampicillin, and trimethorim/ sulphamethoxazole. Both of these resistant isolates

Table 1. *Risk factors for illness, case-control study A*, Nyamithuthu refugee camp, *Malawi, 1990*

| Risk factors | Proportion exposed (%) | | Matched odds ratio | 95% CI |
	Case	Control		
Put hands in water container	19/37 (51)	8/37 (22)	6·0	1·3–26·8
Used separate container to drink or wash	14/50 (28)	19/49 (38)	0·6	0·2–1·5
Shared water container with neighbours	43/49 (88)	37/48 (77)	2·3	0·7–7·3
Went to river	35/50 (70)	30/50 (60)	2·0	0·7–5·9
Drank any river water	33/49 (67)	28/50 (56)	2·2	0·8–6·3
Left peas out overnight	19/46 (41)	14/49 (29)	1·7	0·7–4·4
Ran out of firewood in previous week	31/49 (63)	33/50 (66)	0·7	0·3–2·7
For those who ran out of wood				
Left peas out overnight	16/28 (57)	7/32 (22)	8·0	1·0–64·0
Ate dried fish	37/50 (74)	37/50 (74)	1·0	0·4–2·5
Owned soap	23/50 (46)	24/49 (49)	0·8	0·3–2·2
Owned a cooking pot	21/50 (42)	17/50 (34)	1·7	0·6–4·6

Table 2. *Factors associated with illness, case-control study B*, Nyamithuthu refugee camp, *Malawi, 1990*

| Factors | Proportion exposed (%) | | Odds ratio | 95% CI |
	Case	Control		
Drank river water	22/47 (47)	31/136 (23)	3·0	1·4–6·4
Went to river	23/47 (49)	52/84 (38)	1·6	0·8–3·2
Among persons who went to river				
Drank river water	22/23 (96)	30/52 (58)	16·1	2·0–351·2
Reheated leftover peas	38/42 (91)	129/131 (99)	0·2	0·02–1·0
Put hands in water container	13/20 (65)	64/127 (50)	1·8	0·6–5·5

were sensitive to tetracycline, the principal agent in use at the camp, and to the other antimicrobials tested. The other patient isolate was sensitive to all antimicrobials.

Camp policy was to add chlorine at the wells to individual water containers or to large storage 'bladder tanks' where water was sometimes held before distribution. However, no chlorine (free or total) was detected from seven randomly selected water samples taken from containers filled at three different wells.

DISCUSSION

In 1990 a cholera outbreak caused over 1931 clinically recognized cases and 68 deaths among Mozambican refugees living in a camp in Malawi. The outbreak mainly affected new arrivals who had unexpectedly come to the refugee camp before sanitary facilities were in place. To prevent similar outbreaks whenever possible, latrines and water facilities should be available before refugees arrive because most became ill before facilities could have been built (over half within 16 days of arrival).

The case-fatality rate during this epidemic was 3·5%. This rate is lower than that seen in some areas with few health resources [9], but higher than in the epidemic in Latin American [10]. Although case definitions vary, affecting the ability to compare rates from different epidemics, and we only included as cases those with severe enough illness to require IV therapy, many of the deaths in the Malawi camp appear to be preventable. Most deaths occurred within 24 h of arrival and presumably were due to profound dehydration. This may have been because patients were extremely dehydrated on presentation due to transport problems, oral rehydration treatment was suboptimal, or IV therapy was delayed. Staff and ORS were in short supply, and extreme heat exacerbated the situation. Patients appeared reluctant to drink ORS, did not refill empty cups, and at times were unable to keep up with fluid losses without vigorous encouragement. Some patients on main-

tenance ORS following IV treatment needed to have their IVs replaced because they did not consume enough fluid. As problems in ORS therapy became apparent 'ORS officers' were trained and assigned to each cholera tent. ORS officers encouraged oral intake by continuously telling patients to drink and by frequently refilling their ORS cups. Forceful encouragement such as this may be necessary to ensure the adequate intake of ORS in similar settings.

Late mortality was associated with febrile illness. Fevers were common and may have been related to overuse of IVs. More frequent changes of IV sites may decrease the risk of infection. Simple criteria could be used to decide to remove IV lines, such as the ability to eat and drink without vomiting in the preceding 6 h and an adequate urine output. Some fevers may also have been caused by other infections, including malaria. The elevated temperatures observed may also have been the result of high ambient temperatures. In the future, performing simple laboratory tests, such as malaria smears and blood cultures, would help determine the source of fevers and guide appropriate therapy.

Mortality was higher in children than in older patients. Care of paediatric patients was more difficult than adults because fluid management was more complex, many children presented with malnutrition and chronic disease, and fevers were common. Paediatric tents were established in December, allowing specially trained staff to focus resources on these cases and to concentrate on accurate fluid management.

It appears that cholera was transmitted by both water and food at the camp. It is likely that well water was initially clean because it was from deep sources and coliform bacteria had not been found during routine monitoring. Water probably became contaminated with *V. cholerae* O1 during collection and storage in the house when persons dipped their hands into the water. Placing one's hands into the water in the storage container holding household drinking water was associated with illness in the first case-control study, and *V. cholerae* O1 was isolated from water from household drinking containers. Educators had told refugees to wash their hands after defecation. However, no running water was available for this purpose and few households had separate wash water containers. Refugees reported washing their hands by placing them in the water of the household drinking water containers; an efficient means of spreading the infection from one infected family member to others.

Infection with *V. cholerae* O1 has also been associated with contamination of home water storage containers in Calcutta [11] and subsequent to this investigation, in Peru [10]. In Peru, water from storage containers was shown to have higher coliform counts than tap water, indicating additional contamination after collection. In Calcutta, cholera households that were given water containers with narrow necks were less likely to have intrafamilial spread of cholera than were households using water containers with wide mouths. Presumably, the narrow necks prevented the water from contamination by hands [12]. Because of critical water shortages, the Malawi camp's water rations had not been increased over baseline levels to provide for increased washing needs during the epidemic. Increasing water rations and providing running water during cholera outbreaks in refugee camps may reduce contamination of stored drinking water during washing. Providing storage vessels that protect water from contamination may also be a useful control strategy.

Continuous in-line chlorination at the well is likely to be more effective than intermittent chlorination as was done at the camp. However, chlorine added centrally may not be sufficient to protect against contamination during home storage. A programme of home chlorination of water during storage may decrease illness. Routine measurements of chlorine levels are a necessary component of any chlorination policy.

Drinking river water was associated with illness in the second case-control study. River water can become contaminated with *V. cholerae* O1 when persons defecate during washing or when collecting water. Providing adequate supplies of well water would decrease the need for persons to get water from other unsafe sources, such as a river.

Foodborne transmission may also have occurred. Illness was associated with eating leftover cooked pigeon peas among those who lacked firewood in the first case-control study, and reheating leftover cooked peas was protective against cholera in the second case-control study. In this investigation, cultures of foodstuffs did not yield *V. cholerae* O1; however, these samples were from randomly selected households, not specifically from households of persons with concurrent illness. We assume that the likelihood of culturing this organism from random households at a single point in time is low. *V. cholera* O1 grows readily in a variety of cooked foods [13]. Eating leftover rice and peanut sauce was associated with

transmission of cholera in Guinea [14], as was eating leftover millet gruel in Mali [9]. The risk of cholera may be less if persons are encouraged to cook only enough food for one meal and discouraged from eating unreheated moist grains that have been kept at ambient temperature overnight after cooking. However, many areas of Africa, including southern Malawi, face critical fuel wood shortages, and cooking all meals may be impossible. Building fuel-efficient stoves could decrease the quantity of fuel needed. Mixing foods with acidifiers such as tomatoes or fermented products to inhibit vibrio growth may decrease the risk of infection from eating leftover cooked foods.

Epidemiologic investigations conducted during previous outbreaks among Mozambican refugees in Malawi have identified a variety of possible risk factors. Lack of cooking pots, soap, and water containers was associated with an increased risk of cholera in one outbreak (Tangani Camp, 1988: [15]). Other investigators found that drinking from shallow wells (Mankhokwe Camp, 1988: [16]); contact with the ORS tent and latrines (Mkwayi Camp, 1989: S. Manoncourt, Epicentre, Paris, unpublished data); and drinking water taken from the swamp or river and new arrival status were associated with illness (Chifunga Camp, 1990 [17]. These studies did not specifically match patients and controls for date of arrival. Because refugees often arrive with few material possessions, and because new arrivals may be assigned to areas with the fewest resources, it may not have been possible to show whether the lack of cooking pots, soap, and water containers simply indicated new arrival status or were themselves factors associated with illness. Higher attack rates in new arrivals could be related to exposures within the camp that are more prevalent among new arrivals (such as having to drink river water because of distance from established wells) or lack of immunity at the time of arrival.

In previous outbreaks in Asia, approximately 75% of persons infected with *V. cholerae* O1 El Tor remained asymptomatic whereas only 2% had illness severe enough to require hospitalization [18]. By 15 December 1990 in Nyamithuthu, 2·4% of the entire population of the camp had been hospitalized. This suggests that the epidemic ended when most of the new arrivals had been infected and the pool of the most susceptible individuals was exhausted. It is likely that many controls in the case-control study were also subclinically infected with *V. cholerae* O1. Thus, the

case-control studies, which categorized cases and controls based on clinical symptoms alone, may have identified risk factors for severe cholera *vs.* asymptomatic infection, rather than risk factors for *V. cholerae* O1 infection *per se* and may have underestimated differences in risk exposures between infected and uninfected refugees.

Cholera vaccination is not a recommended measure for control of cholera in epidemic settings because resources used to vaccinate would be diverted from life-saving measures such as provision of clean water, sanitation and establishment of effective rehydration facilities [19]. In July and August 1994 when massive cholera and dysentery epidemics caused 50 000 deaths among 700 000 Rwandan refugees in Zaïre [20] the policy of not administering cholera vaccine was questioned [21]. In Zaïre the cholera epidemic peaked within 2 weeks and subsided within 4 weeks of refugee arrival; since it would have taken many weeks to administer vaccine and for the vaccine to confer immunity, a programme to vaccinate would not have altered the course of this epidemic and would have diverted efforts of aid agencies [22]. In Malawi, the cholera epidemic lasted several months; this may give the impression that a vaccination programme could have been launched in time to prevent cholera cases. However, most persons became ill soon after arrival before vaccination programmes could be completed and immunity conferred. Therefore, since transmission within refugee camps can occur so quickly, for a cholera vaccine to be effective administration of vaccine would have to be swift, preferably immediately upon camp arrival.

During outbreaks of cholera in refugee camps, case-fatality rates could be decreased with improved transportation and health education so that patients present to treatment facilities less dehydrated. Use of 'ORS officers', stressing the administration of ORS in addition to IV therapy, removing or replacing IV lines quickly, and focusing attention on care of children may also decrease mortality. Several prevention measures may decrease transmission of cholera including providing new arrivals with adequate water supplies and latrines before being settled. Use of water containers with narrow mouths, proper use of 'in line' chlorination at the wells, in addition to chlorination in the home, will decrease water contamination. Water supplies should be increased when outbreaks of diarrhoeal illnesses occur. Since epidemics among new arrivals occur swiftly, cholera vaccination programmes would be unlikely to effect the epidemic

unless vaccine were administered immediately upon camp arrival. Continued efforts to improve *V. cholerae* O1 case management and to understand the varied modes of transmission of *V. cholerae* O1 will affect future cholera control measures among refugees and the general population throughout Africa.

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