Epidemic cholera in Mali: high mortality and multiple routes of transmission in a famine area

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SUMMARY

During the 1984 cholera outbreak in Mali, 1793 cases and 406 deaths were reported, a death-to-case ratio of 23%. In four affected villages, the mean clinical attack rate was 1.5 and 29% of affected persons died. In 66% of cases the illness began more than 48 h after the village outbreak began, when supplies from outside the village were potentially available. Deaths occurred because patients failed to seek care or received only limited rehydration therapy when they did. Case-control studies identified two routes of transmission: drinking water from one well in a village outside the drought area, and eating leftover millet gruel in a drought-affected village. Drought-related scarcity of curdled milk may permit millet gruel to be a vehicle for cholera. Cholera mortality in the Sahel could be greatly reduced by rapid intervention in affected villages, wide distribution of effective rehydration materials, and educating the population to seek treatment quickly.

INTRODUCTION

The seventh pandemic of cholera was first recognized in West Africa in 1970, when the catastrophic extension of that epidemic into drought-stricken sub-Saharan regions was associated with death-to-case ratios (DCRs) of 20–30% (Goodgame & Greenough, 1975). Although some African countries have reported cholera cases each year since 1971, and epidemic cholera has recurred in famine-affected areas of the Sahel, the transmission of cholera in Africa is not well understood. One outbreak was attributed to drinking river water, but it has been suggested that other routes of transmission may also be important (Dodin & Felix, 1972; Sinclair et al. 1982; Mhalu, Mtango & Msangi, 1984; Cliff, Zinkle & Martelli, 1986). In 1984, 19 African countries reported Vibrio cholerae infections, more than at any other time since 1974 (World Health Organization, 1985). We investigated the 1984 epidemic recurrence of cholera in Mali to determine the validity of the reported DCR of more than 20%, the circumstances of cholera-related deaths, and the routes of transmission.

The Republic of Mali has a population of 7.8 million (1984 estimate), living in an area of 1.24 million square kilometres. Much of the land is non-arable desert;
Fig. 1. Location of Mali in Africa and map of Mali indicating the location of the four study villages.
most of the remainder is arid tropical savannah. During the June to October rainy season, the inland delta of the Niger River in the center of the country floods and the millet culture and fishing there are important to the national economy. From 1982 through 1984, the rainfall was subnormal, and extensive crop failures and famine occurred in the areas immediately south of the Sahara desert.

THE EPIDEMIC

An outbreak of cholera-like illness was reported in early July 1984 in Ansongo Cercle, Gao region (Fig. 1). The epidemic spread up the Niger river, reaching Mopti by 22 September. As of 15 November 1984, cases had been reported from five of the seven regions of Mali. The regions most affected by the drought, Tombouctou, Gao, and Mopti, had the highest attack rates, 154, 79, and 42 per 100000 respectively. The reported national DCR was 40% for July and August, 24% in September, 27% in October, and 28% in November (Fig. 2). In 1984, a total of 1793 cases and 406 deaths were reported, a national attack rate of 22.9 per 100000 and a DCR of 23% (Ministry of Public Health & Social Affairs, Republic of Mali, 1986).

Cholera treatment and control efforts were hindered by the lack of hard-surfaced roads and gasoline, the dispersion and mobility of the population, the limited health infrastructure, and slow communication between villages and regional centres. It is common folk-practice in Mali to treat diarrhoea by withholding fluids and food. Rehydration in treatment centres was largely attempted with physiologic saline; oral rehydration salts (ORS) were not widely used. As in the 1970–72 outbreak, control efforts included mass vaccination campaigns and prophylactic antimicrobial treatment of healthy travellers at roadblocks (Imperato, 1974a).

METHODS

Epidemiologic investigations

Four villages with recently reported outbreaks of cholera-like illness were investigated between 16 and 29 November 1984 (Fig. 1). Three village investigations were retrospective; the fourth was conducted during an outbreak of cholera. We defined a case of cholera-like illness as an illness with diarrhoea and vomiting which was seen at a cholera-treatment post, or treated at home by family members who could describe the illness, and which occurred between 1 September and our visit to the village. Cases were identified with the help of the village nurse, village council and village chief; the patient or a close relative was interviewed. In each village, we conducted a case-control study. One matched control per case was chosen in the first three villages, and two matched controls per case in the fourth. Control persons were matched for sex and for age within 5 years, and lived in family compounds that had experienced no recognized cholera-like illness. Data were collected about the sources of water used for drinking, cooking, and washing, recent travel to markets or other villages, visitors to their compound, participation in funerals, and eating dried fish or shellfish. In the third and fourth villages, persons were also asked about eating grain-based foods, particularly those eaten more than 3 h after cooking. In the fourth village, detailed food histories were
obtained for the 3 days preceding the onset of illness in the case patient's or the control's interview. Confidence limits for odds ratios were determined by the method of Thomas & Gart (1977).

**Microbiologic techniques**

*Clinical specimens.* Rectal swabs from ill patients and from control persons in the fourth village were transported in Cary-Blair medium to the National Institute for Public Health Research (INRSP), Bamako, Mali, and cultured within 48 h after collection. The Cary-Blair transport media tubes (without swabs) were then taken to the Pasteur Institute, Paris, where they were incubated with alkaline peptone broth, streaked on thiosulphate-citrate-bile salt-sugar agar (TCBS) and incubated at 37 °C for 24 h. Characteristic oxidase-positive colonies were confirmed with slide agglutination with polyvalent and monovalent antisera.

Environmental samples were obtained in three villages (nos. 1, 2 and 4). River and canals were sampled with Moore swabs left in place for 24 h, transported in alkaline peptone broth for 12–24 h, and plated on TCBS at the INRSP (Barrett et al. 1980). Communal well-water collected from a control household in village no. 4 was sampled by filtering 30 l through a sterile gauze pad, which was then transported in normal saline. Then 5 ml of the normal saline was inoculated 48 h after collection into alkaline-peptone water, incubated at 37 °C for 24 h, and plated on TCBS. Environmental and clinical isolates and eight *Vibrio cholerae* 01 strains isolated from clinical specimens during October at the INRSP were confirmed at the WHO Vibrio Reference Laboratory of the Pasteur Institute, Paris. Antimicrobial sensitivity was determined by the disk diffusion method and the broth microdilution method at Centers for Disease Control (CDC), Atlanta, Georgia (Bauer et al. 1966; National Committee for Clinical Laboratory Standards, 1985).
Food inoculation. A total of 160 g of millet (Pennisetum ssp.) were wet-ground in mortar and pestle, rinsed in dechlorinated tap water, steamed for 20 min, and allowed to cool for 10 min. The steamed millet was then resuspended in 150 ml of dechlorinated tap water, and 0.5 g NaCl was added. The suspension was divided into two equal portions, each of which was brought to 500 ml with either dechlorinated tap water or raw curdled goat’s milk. The goat’s milk was curdled by allowing it to stand at room temperature for 24 h after collection. The Mali epidemic strain (CDC no. 9915–84) of V. cholerae was inoculated into the two gruels at a concentration of $10^8$ organisms per ml, and the inoculated gruels were then incubated at 37 °C for 48 h. Counts of V. cholerae and pH determinations were performed at 0, 6, 18, 24 and 48 h.

RESULTS
Illnesses identified by local authorities were consistent with cholera. Affected individuals in the four villages were moderately to severely ill; few mild diarrhoeal illnesses were recognized during the outbreaks, and such illnesses would not have been reported as cholera. The combined attack rate of cholera-like illness at the four villages was 1.5% (Table 1). The combined DCR was 29%, and did not vary significantly by sex. The median age was 32 years for fatal cases and 23 years for non-fatal cases ($P = 0.32$, Mann–Whitney $U$ test). In villages 1 and 2 for which census data were available, the attack rate was similar for males (1.07%) and females (1.09%). The attack rate varied significantly by age: no cholera-like illness was recognized in infants, while the elderly were at highest risk (Table 2). Family relationships were defined for 57 cases, of which 12 occurred in families that had already had a case. Six of the 12 (10% of the total) had onset more than a day after the onset of illness in the index case.

The duration of the outbreaks in the four villages was short, ranging from 7 to 15 days (Fig. 3). Three of the villages already had a health centre, and in one village (no. 3) an emergency treatment centre was established on day 3 of the outbreak. Limited additional supplies of antimicrobials and small amounts of physiologic saline and oral rehydration salts were available at all four villages by day 3 of the outbreak. Combining the data from the four villages, 9 (36%) of 25 persons with onset of cholera-like illness in the first 48 h of the village outbreak died. Nine (36%) of 25 with onset of illness in days 3–7 of the village outbreak died. The fatality rate dropped to 3 (13%) of 23 cases with onset in the second week of the outbreak.

The circumstances of death were determined for 20 of the 21 deaths associated with cholera-like illness in the four villages. Two of the 20 deaths occurred before any health care was available. Five persons died who had not sought available care when cholera was suspected; their illness was treated at home with black-market antimicrobials instead. Of 13 who sought aid from the village nurse, health aid, or cholera treatment post (‘lazaret’), 6 received no rehydration therapy, 6 received intravenous saline alone, and 1 received a single packet of ORS. All 17 of the deaths for which the time of onset and death was known occurred in the first 24 h of illness.

No case patients in the four villages had eaten shellfish or partially dried fish, and cholera-like illness was not associated with travel, recent visitors, or...
Table 1. Population-based incidence and mortality of cholera-like illness in four villages in Mali, 1984

<table>
<thead>
<tr>
<th>Village</th>
<th>Population*</th>
<th>Ethnicity</th>
<th>Cases</th>
<th>Deaths</th>
<th>Attack rate (%)</th>
<th>Death-to-case ratio (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) N’Dogofri</td>
<td>1007</td>
<td>Mixed</td>
<td>24</td>
<td>7</td>
<td>2-4</td>
<td>20</td>
</tr>
<tr>
<td>(2) Sekoro</td>
<td>2138</td>
<td>Bambara/Bozo</td>
<td>14</td>
<td>4</td>
<td>0-7</td>
<td>20</td>
</tr>
<tr>
<td>(3) Niodougou</td>
<td>1000</td>
<td>Songhay</td>
<td>12</td>
<td>5</td>
<td>1-0</td>
<td>42</td>
</tr>
<tr>
<td>(4) Diona</td>
<td>600</td>
<td>Peul</td>
<td>23</td>
<td>5</td>
<td>3-8</td>
<td>22</td>
</tr>
<tr>
<td>Total</td>
<td>4745</td>
<td>—</td>
<td>73</td>
<td>21</td>
<td>1-5</td>
<td>20</td>
</tr>
</tbody>
</table>

* Census data for villages 1 and 2, estimated population for villages 3 and 4.

Table 2. Age-specific incidence and mortality of cholera-like illness in two villages in Mali, 1984

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Population</th>
<th>Cases</th>
<th>Deaths</th>
<th>Attack rate (%)*</th>
<th>Death-to-case ratio (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1</td>
<td>75</td>
<td>0</td>
<td>0</td>
<td>0-0</td>
<td>—</td>
</tr>
<tr>
<td>1-14</td>
<td>1207</td>
<td>16</td>
<td>5</td>
<td>1-3</td>
<td>31</td>
</tr>
<tr>
<td>15-59</td>
<td>1684</td>
<td>16</td>
<td>3</td>
<td>1-0</td>
<td>10</td>
</tr>
<tr>
<td>≥ 60</td>
<td>179</td>
<td>6</td>
<td>3</td>
<td>3-4**</td>
<td>50</td>
</tr>
</tbody>
</table>

* $\chi^2$ for linear trend, age groups $< 1$, 1-59, $\geq 60$ years = 7-52, $P = 0-006$, two-tailed.

Fig. 3. Day of onset of cholera-like illness in four Malian villages, measured from the day of onset of the first case in each village.

participation in funerals. Case-control studies identified specific vehicles in two villages.

N’Dogofri (village no. 1), in Segou Region, a culturally mixed rice-farming village surrounded by irrigation canals, was little affected by the drought. The study was conducted 3 weeks after an outbreak. Patients identified as the index
cases in 13 affected families were matched by age and sex with control persons from neighbouring compounds. Drinking unboiled water from one well (of approximately 50 in the village) was associated with diarrhoeal illness (6/13 cases vs. 0/13 controls: Odds Ratio (OR) = 6/0, \( P = 0.03 \) exact binomial probability, two-tailed). Three of seven secondary cases in affected families also drank water from this well. The well was in sandy soil within 10 m of three pit latrines; the water table was 1 m below the surface. The well had been treated heavily with bleach just before the study, and the entire village had received chemoprophylaxis, so bacteriologic samples were not obtained. Two Moore swabs of the irrigation canal adjacent to the village did not yield \( V. \text{cholerae} \) 01.

Diona (village no. 4), a Peul village in Mopti region, was investigated during an outbreak of cholera. Although November is the usual season of plenty, the village was afflicted by severe drought, and many villagers were eating leaves and seeds of wild shrubs; food consumption histories were exceptionally clear. A survey of water sources of 33 families attending a nutrition supplementation clinic operated by a relief agency showed no association between cholera-like illness in the family and the particular well used for the family’s drinking water. The patient identified as the index case from the nine most recently affected families and two age- and sex-matched controls per case were interviewed. Illness was not associated with using water from any particular one of the village’s five wells. Seven of 9 case patients but only 1 of 18 matched controls per case had eaten leftover millet gruel in the 3 days before onset of illness of the case or interview of the control (OR = 13/0, lower 95% confidence limit = 3-28, Mantel Haenzel \( \chi^2 = 9.4; P = 0.02 \), two-tailed). Culture of Cary–Blair medium which had contained rectal swabs detected \( V. \text{cholerae} \) 01 in samples obtained from 3 of 4 patients cultured before antimicrobial therapy, and in samples from 6 of 18 control persons. After excluding the culture-positive individuals from the control group, the association between illness and leftover millet-gruel remained (OR = 5.7/0, lower 95% confidence limit = 2.2, Pike–Morrow \( \chi^2 = 6.02; P = 0.014 \), two-tailed). Bleach had recently been added to village wells and they were not cultured. One culture of leftover gruel did not yield vibrios. Household water which had been collected from the largest village well before bleaching and stored for approximately an hour in a control household yielded \( V. \text{cholerae} \) 01. All clinical and environmental isolates were \( V. \text{cholerae} \) 01, biotype El Tor, serotype Ogawa, were toxigenic, and sensitive to tetracycline, sulfamethoxazole, and chloramphenicol by disk diffusion. Mean inhibitory concentrations were determined for ten strains: MICs were < 8 \( \mu g/ml \) to sulfisoxazole and < 2 \( \mu g/ml \) to sulfamethoxazole.

The epidemic strain of \( V. \text{cholerae} \) did not survive 6 h in millet gruel prepared

### Table 3. Survival of \( V. \text{cholerae} \) in millet gruel

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>( \text{pH} ) With curdled goat’s milk</th>
<th>( \times 10^{-3} ) Count</th>
<th>( \text{pH} ) Without curdled goat’s milk</th>
<th>( \times 10^{-3} ) Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>5.00</td>
<td>5.5 x</td>
<td>0.34</td>
<td>2.4 x</td>
</tr>
<tr>
<td>6</td>
<td>4.05</td>
<td>0.0</td>
<td>4.00</td>
<td>3.1 x</td>
</tr>
<tr>
<td>18</td>
<td>4.55</td>
<td>0.0</td>
<td>5.50</td>
<td>1.1 x</td>
</tr>
<tr>
<td>24</td>
<td>4.49</td>
<td>0.0</td>
<td>4.99</td>
<td>1.0 x</td>
</tr>
<tr>
<td>48</td>
<td>4.03</td>
<td>0.0</td>
<td>4.37</td>
<td>0.0</td>
</tr>
</tbody>
</table>
in the laboratory with curdled goat's milk (Table 3). Vibrios survived more than 24 h in gruel prepared without goats milk, which had a higher pH. *V. cholerae* counts did not increase appreciably in either gruel.

**DISCUSSION**

The high case-fatality rates in the affected villages confirmed the accuracy of the sustained high national ratio of reported deaths to cases. The national figure could have been inflated by non-reporting of mild illnesses, selective reporting of fatal cases, misdiagnosis of non-cholera diarrhoea, or misattribution to cholera of deaths due to other causes. These biases may possibly explain the extraordinarily high DCRs reported at the outset of the epidemic, but the national DCR of 23% for 1984 is not likely to overestimate the actual case-fatality rate for clinical cholera. Even this high DCR is an improvement over the 1970-2 cholera DCR of 38%, though the improvement may reflect better surveillance as well as better survival. The epidemic recurred in Mali in 1985, when 3805 cases and 836 deaths were reported (DCR = 22%), and in 1986, when 1062 cases and 66 deaths were reported between 1 January and 15 May (DCR = 6%). The recent decrease followed improvements in communication and surveillance, increased efforts to make oral rehydration more widely available, and the organization of a national diarrhoeal disease control program (Ministry of Public Health and Social Affairs, Republic of Mali, 1985). The cholera DCRs of 1-5% reported from Nigeria, Togo and Tanzania appear to be realistic goals even among remote and dispersed populations (Lewis *et al.* 1972; Bockemuehl & Schroeter, 1975; Mandara & Mhalu, 1980).

The short duration of outbreaks in individual villages means that interventions must be swift if they are to be effective. Most cases and virtually all deaths occurred in the first week of the outbreak in each village. However, less than half of the fatal cases had onset within the first 48 h. A mobile team fully equipped with oral and intravenous rehydration materials, and stationed within a 24-hour drive of the village could potentially prevent many deaths. Any delay in communication would limit the effectiveness of such teams. During the first 24-48 h of a village outbreak, only supplies routinely stocked at the village level were available, and reduction of early mortality would require stocking threatened villages with rehydration materials in advance. Some deaths in the affected villages occurred because villagers did not go to the village treatment posts. Further education of local health workers and village authorities about effective cholera treatment may also reduce mortality.

Reported cases were severe, clinically typical cholera-like illnesses, and many infections went unreported. The point prevalence rate for asymptomatic carriage in village no. 4 was 33%, a minimum estimate of the incidence of unrecognized infection in the affected villages. Given the 1-5% attack rate, the proportion of infected persons who had typical clinical cholera can be roughly estimated as 1-5/33 or 4%, comparable to the figure of 7% reported in Asian groups (Gangarosa & Mosley, 1974). The utility of chemoprophylaxis of an entire small village in an outbreak has not been established, but chemoprophylaxis in the immediate household of a case has been useful in other cholera epidemics (McCormack *et al.*
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1968) and could perhaps have prevented up to 10% of cases in the affected villages in Mali. Not everyone in the village is at the same risk, and a selective strategy is less likely to produce resistant strains than is mass chemoprophylaxis. The potential benefit of chemoprophylaxis may increase with age. As in other cholera epidemics, clinical cholera was rare in infants, who are likely to be protected by breastfeeding; the highest attack rates were seen among the elderly, perhaps because of a drop in gastric acidity with age (Sack et al. 1972; Gunn et al. 1979).

Both foodborne and waterborne routes of transmission were identified. In one village with ample supplies of food and water, cholera-like illness was associated with using water from a particular well. In a second drought-stricken village, with adequate water for drinking but very limited food, cholera was strongly associated with eating millet gruel left at ambient temperatures for more than 3 h without reheating. This gruel, a staple of the Sahel diet, is a previously unrecognized vehicle of cholera transmission. It is generally prepared once a day, is eaten communally without reheating, and may be held at ambient temperature for many hours. This gruel is usually acidified by the addition of curdled goat's milk, and thus might seem an unlikely vehicle. We did not observe the preparation of millet gruel in the affected village, and do not know whether or not curdled goat's milk was used. However, we suspect that such milk was in scant supply, because goat's milk is only seasonally available after the rains and would be particularly scarce after a prolonged drought (Swift, 1981; Imperato, 1974b). We hypothesize that without curdled goat's milk, millet gruel may support vibrio growth at ambient temperature, as do other moist grains (Kolvin & Roberts, 1982; Johnston et al. 1983; Holmberg et al. 1984). We found that vibrio survival in gruel was prolonged in the absence of milk. Although we did not observe vibrio growth in our laboratory gruel, gruel in Mali may differ from our gruel in the alkalinity and mineral content of the water, and may indeed support the growth of vibrio. Vibrio growth may depend on the specific type of millet, as it does on the specific type of rice in Bangladesh (Benenson, Ahmad & Oseasohn, 1965). The cuisines of Africa include a variety of grains, including some fermented or malted grains (Cameron & Hofvander, 1976; Leung, Busson & Jardin, 1968). Further study of the role of these grains in promoting or preventing cholera transmission in Africa is needed, particularly with regard to seasonal or drought-related changes in their preparation.

Cholera epidemics have attended major droughts with unexplained regularity. Rogers (1957) used the failure of the monsoon rains in India to predict the appearance of epidemic cholera the following year. Severe cholera epidemics occurred in Sahelian countries affected by the drought in the early 1970s and again in the 1984 drought. One explanation of this association may be the crowding of refugees around limited water supplies; another may be that starvation decreases host defences. A more specific explanation may be that foods prepared during a drought are more likely to transmit infection than are foods prepared in times of plenty. Acidic condiments such as tamarind, vinegar, lemon or sour milk may be lacking. The alkalinity and mineral content of water used to prepare the food may increase. Famine foods may be cooked less often because of lack of fuel, may be diluted with additional water, and may be held longer after cooking, allowing more time for bacterial multiplication (Den Hartog, 1981; Fleurat, 1986).
Reducing cholera mortality with rapid and effective rehydration remains a challenge in the remote and dispersed populations of the Sahel. The high DCR of epidemic cholera may be lowered by efforts to provide rapid communications, the swift provision of aid to affected villages, wide distribution and use of oral rehydration materials, and by educating the public to seek treatment early. Efforts to control the epidemic may be complicated by multiple routes of transmission, and the safety of available foods should be addressed as well as that of water supplies.

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