

Factors Contributing to the Emergence of *Escherichia coli* O157 in Africa

Paul Effler,* Margaretha Isaäcson,† Lorraine Arntzen,† Rosemary Heenan,‡
Paul Canter,§ Timothy Barrett,* Lisa Lee,* Clifford Mambo,§ William Levine,*
Akbar Zaidi,* and Patricia M. Griffin*

*Centers for Disease Control and Prevention, Atlanta, Georgia, USA; †South African Institute for Medical Research, Johannesburg, South Africa; ‡GOAL, Dublin, Ireland; and §Ubombo Sugar Limited, Big Bend, Swaziland

In 1992, a large outbreak of bloody diarrhea caused by *Escherichia coli* O157 infections occurred in southern Africa. In Swaziland, 40,912 physician visits for diarrhea in persons ages ≥ 5 years were reported during October through November 1992. This was a sevenfold increase over the same period during 1990-91. The attack rate was 42% among 778 residents we surveyed. Female gender and consuming beef and untreated water were significant risks for illness. *E. coli* O157:NM was recovered from seven affected foci in Swaziland and South Africa; 27 of 31 patient and environmental isolates had indistinguishable pulsed-field gel electrophoresis patterns. Compared with previous years, a fivefold increase in cattle deaths occurred in October 1992. The first heavy rains fell that same month (36 mm), following 3 months of drought. Drought, carriage of *E. coli* O157 by cattle, and heavy rains with contamination of surface water appear to be important factors contributing to this outbreak.

Early in November 1992, physicians arriving for duty at a small hospital on a sugar plantation in Swaziland found >100 persons sprawled on the ground in front of the casualty department. Many had bloody diarrhea, and almost all were suffering severe abdominal pains. The next day the number of patients with the dysenteric illness nearly doubled, yet stool specimens sent to local laboratories did not yield common parasitic or bacterial pathogens, including *Shigella* spp. With the etiologic agent still unknown into the second week of the outbreak, specimens were forwarded to a reference laboratory in South Africa, where a surprising discovery was made: *Escherichia coli* O157 had emerged in Africa (1).

An outbreak of *E. coli* O157 infections was heretofore unheard of in Africa, or for that matter, anywhere in the developing world. *E. coli* O157 had been isolated only once before in southern Africa, from an elderly man undergoing surgery for lower gastrointestinal bleeding in Johannesburg in 1990 (2). We present a comprehensive account of a 1992 regional outbreak in Africa, perhaps the largest *E. coli* O157 outbreak ever reported.

The Kingdom of Swaziland occupies 17,360 km² in southern Africa; 62% of the surface area is pastureland used primarily for cattle. The estimated human population in 1992 was 850,000. The sugar plantation referred to in this report is located in the Lubombo District, a lowland area that shares borders with Mozambique and South Africa (Figure 1). The plantation irrigates its extensive cane fields with water drawn from the nearby Usutu River. Twenty villages dispersed across the plantation housed approximately 5,000

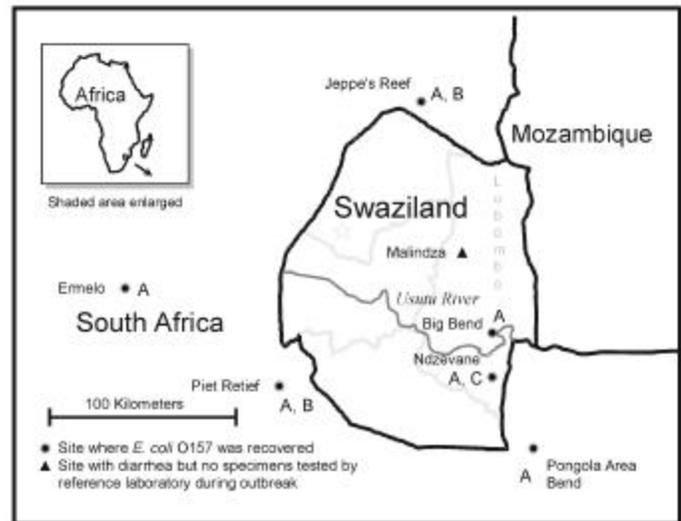


Figure 1. Map of the area affected by an outbreak of diarrheal illness in 1992.^a

^aPulsed-field gel electrophoresis of 31 of the *Escherichia coli* O157:NM isolates from six locations identified three distinct patterns, designated A, B and C; the locations where these isolates were obtained are indicated on the map by the corresponding letter. Not shown on the map is Empangeni, South Africa, located approximately 200 km south of Swaziland border, where *E. coli* O157 was also recovered. The Usutu River is also called the Lusutfu River.

workers and dependents. Standpipes with treated potable water and other pipes carrying untreated surface water were located in most villages. Plantation workers were provided with a weekly ration of beef obtained from local abattoirs.

When the outbreak occurred, two refugee settlements, Ndzevane (population 7,700) and Malindza (population 11,900), were located 19 km and 60 km, respectively, from

Address for correspondence: Paul V. Effler, State of Hawaii Department of Health, 1250 Punchbowl Street, Room 444, Honolulu, Hawaii 96813, USA; fax: 808-586-8347; e-mail: pveffler@mail.health.state.hi.us

Research

the plantation. Refugees and Swazi nationals residing locally received health care at settlement clinics. Jeppe's Reef, Pongola, Empangeni, Piet Retief, and Ermelo are towns and villages in nearby South Africa.

Methods

Diarrheal Disease Surveillance

The number of patients with diarrhea at clinics in the affected area was obtained by reviewing outpatient logbooks at Malindza, Ndzevane, and the plantation hospital. National and district figures for reported diarrheal illness by month and year were provided by the Statistics Section of the Ministry of Health, Swaziland. Data on deaths were unavailable.

Rainfall Measurements

Data on rainfall at the Big Bend Experimental Farm, located approximately 1 km from the plantation, were obtained for 1991-92 from the Swaziland National Meteorological Service, Ministry of Transport and Communication. A meteorologic station on the plantation site also provided precipitation figures for October 1992.

Surveillance of Cattle Deaths

Periodic dipping of cattle with insecticides used for the control of ticks was mandatory, and losses were closely monitored in this manner. Figures for cattle deaths from 1988 through 1992 were obtained from the Ministry of Agriculture, Swaziland.

Clinical and Environmental Laboratory Methods

Initial stool specimens were cultured at local laboratories in Swaziland, which did not test for *E. coli* O157. Subsequent specimens were submitted to the South African Institute of Medical Research (SAIMR), which routinely attempted to identify *Vibrio cholerae*, *Salmonella* spp., *Shigella* spp., and *Yersinia enterocolitica* from all specimens; methods for isolating *E. coli* O157 were introduced in response to the outbreak. Human stool specimens and rectal swabs, cattle dung, and food samples were plated on alkaline peptone water, thiosulfate citrate bile salts sucrose (TCBS) agar, blood agar, selenite broth, desoxycholate citrate agar (DCA), and sorbitol/MacConkey agar and were incubated overnight. Water samples were vacuum filtered, and the filters were cut in half and incubated overnight in alkaline peptone water and selenite broth. These waters and broths were then subcultured onto TCBS, blood, and sorbitol/MacConkey agars; the selenite broth was also subcultured onto DCA and *Shigella-Salmonella* agars. Sucrose-fermenting colonies were further investigated biochemically as potential *V. cholerae*, and sorbitol-nonfermenting colonies as potential *E. coli* O157. Final identification was done by serotyping of *V. cholerae* with Wellcome polyvalent (Burroughs Wellcome Co., Research Triangle Park, NC), Inaba and Ogawa agglutinating sera, and of *E. coli* with the Prolex latex agglutination test kit. All other lactose-nonfermenting colonies were further investigated.

A sample of isolates identified as *E. coli* O157 by the Prolex kit underwent confirmatory testing at the Centers for Disease Control and Prevention (CDC), using standard methods (3). Isolates were also examined for the presence of

genes encoding Shiga toxins 1 and 2, and the *uidA* allele specific for *E. coli* O157:H7 by polymerase chain reaction (PCR) (4,5). All isolates were characterized by macrorestriction analysis pulsed-field gel electrophoresis (PFGE) (6). The *fliC* gene from selected isolates was amplified and restriction digested as previously described to determine whether the isolates had the allele characteristic of *E. coli* O157:H7 (7).

Survey Methods

To characterize the diarrhea and identify risk factors for illness during the outbreak, a survey was conducted at the sugar plantation. The survey questionnaire solicited information on demographic characteristics, travel, and food and water consumption in the 2 weeks before the outbreak (October 15 to 31) and diarrheal illness from November 1 to December 31, 1992. All villages that had a village health worker available to assist on the day of the survey were included (16 of the 20 villages). Maps of each village were reviewed, and houses were randomly selected. All persons at home at the time of survey who had lived on the premises since October 1, 1992, were included.

Statistical analyses were conducted by using EpiInfo Version 6.4c. Confidence intervals (CI) for means and proportions were calculated according to the Fleiss-Quadratic method, taking stratified-cluster sampling framework into consideration. An exposure effect was considered to be statistically significant if the 95% CI for the summary risk ratio did not include 1.0.

Results

Surveillance of Cattle Deaths

Reports from Swaziland for the 5 years from 1988 to 1992 indicate that an increase in cattle deaths began in August 1992 (Figure 2). In Lubombo District, 12,685 cattle died in September and October 1992; this represented a sevenfold increase over the monthly average of cattle deaths in Lubombo for the previous 8 months (data not shown).

Rainfall Measurements

The Big Bend Agricultural Experimental Farm reported 1.5 mm of precipitation during the 3 months preceding October 1992 (Figure 2), compared with 40 mm of precipitation for the same period in 1991 (data not shown). Of the 36 mm

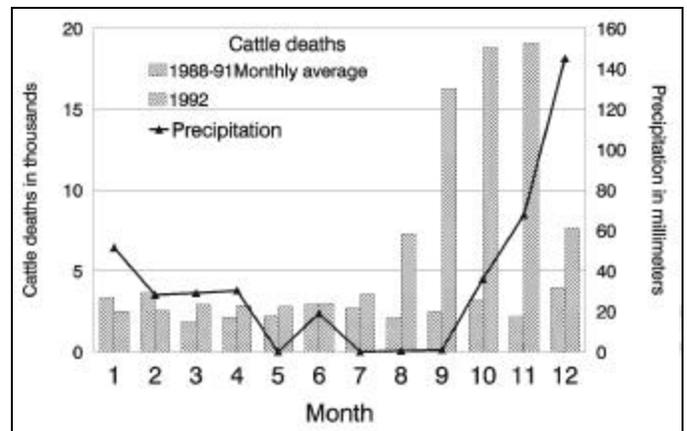


Figure 2. Reported cattle deaths in Swaziland (1988-1992) and monthly precipitation at the Big Bend Agricultural Experimental Farm, Swaziland, 1992.

of rain that fell on Big Bend during October 1992, 27 mm (75%) fell on the 29th and 6 mm (17%) the next day. At the plantation, 34 mm of rain fell on October 29, accounting for 72% of the monthly total.

Diarrheal Disease Surveillance

The number of visits for diarrhea at the plantation hospital from October 15 through December 5, 1992, is shown in Figure 3. Three days after the heavy rainfall, the number of patients with diarrhea seen at the plantation hospital began to increase rapidly. A total of 2,868 persons were treated for diarrhea in November; 1,884 (66%) of these presented in the first 2 weeks of the outbreak.

When the plantation outbreak occurred, nearby refugee settlements in Swaziland and townships in proximal areas of South Africa were also reporting increases in diarrheal illness. Clinician accounts indicated that patients seen at the refugee settlements in early November had abdominal pain and bloody diarrhea and were frequently locally residing Swazi nationals, not refugees. By the end of the month, however, the clinical picture had shifted to profuse watery diarrhea, characteristic of cholera, initially observed among the refugees. These impressions are supported by data from the refugee settlement clinics (Figure 4). Ndzevane clinic staff routinely recorded whether the patient was a local Swazi resident or refugee. Examining the visits of local residents and refugees separately indicates that there were two waves of diarrheal illness at Ndzevane: the first, predominantly among local residents, peaked in the second week of November; the second, primarily among refugees, peaked in early December 1992. Figures for the Malindza clinic confirm that a large outbreak occurred there as well, also peaking in the second week of November, followed by a second, subtler wave of diarrheal illness that peaked in the latter half of December. The Malindza clinic staff classified cases of diarrhea as dysentery if blood was visible in the stool. Although this diagnosis was usually made infrequently, for the week ending November 4, 1992, 74 (29%) of the 255 diarrheal illnesses treated were recorded as dysentery.

Swaziland's national diarrheal disease surveillance figures for 1990 through 1992 for persons ≥5 years of age are shown in Figure 5. A substantial increase in diarrheal ill-

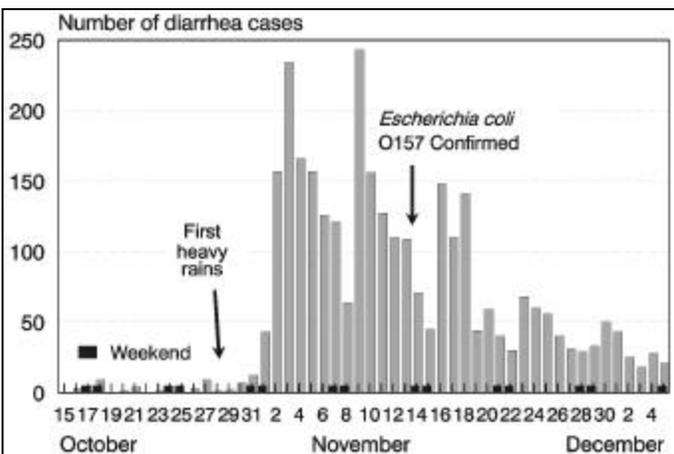


Figure 3. Number of persons with diarrhea visiting a plantation hospital in Lubombo, Swaziland, October 15 through December 5, 1992.^a
^aDate of onset of the first heavy rains (October 29, 1992) established by precipitation data from two sites in Lubombo.

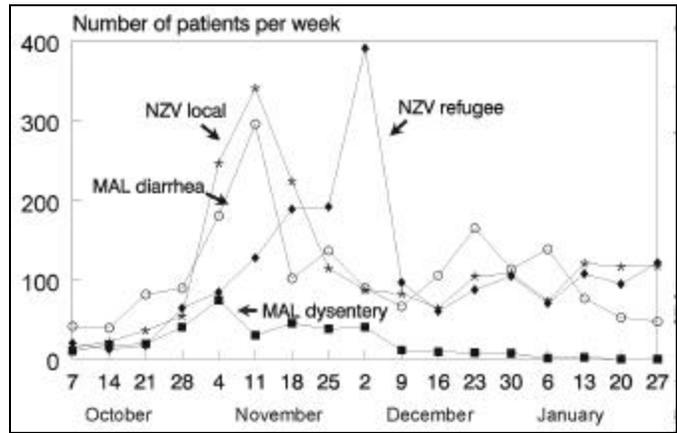


Figure 4. Number of persons with diarrhea visiting the Ndzevane (NZV) and Malindza (MAL) settlement clinics, Lubombo, Swaziland, October 7, 1992, through January 17, 1993. Data were obtained by retrospectively reviewing the clinic logbooks at each site. "NZV local" indicates Swazi nationals residing locally who sought care at the Ndzevane clinic. "NZV refugee" indicates refugees resident in the settlement treated at the clinic. "MAL dysentery" indicates all persons seen at the Malindza clinic with bloody diarrhea. "MAL diarrhea" indicates all persons seen at the Malindza clinic with diarrhea that was not specified as bloody.

ness in Swaziland began in October 1992, and 40,912 consultations for diarrheal illness in persons aged ≥5 years were reported during October and November, representing a sevenfold increase over the mean number of visits for diarrhea reported for the comparable period during 1990 and 1991. This increase was also observed among children <5 years of age, who had 15,312 consultations for acute diarrheal illness reported in November 1992, a figure more than double the monthly average for the preceding 34 months. All areas of Swaziland had increases in reported diarrheal illness in October and November 1992; this increase was most pronounced in Lubombo District (data not shown).

Laboratory Results

Clinical Specimens

Specimens submitted to local laboratories in Swaziland during the first 10 days of the outbreak did not yield a pathogen. At SAIMR, four of five rectal swabs collected on November 13, 1992, from patients treated at the plantation hospital yielded *E. coli* O157; no other pathogens were identified. From November 21 to December 3, 1992, 51 stool specimens were collected at the Ndzevane clinic; 7 yielded only *E. coli* O157, 18 yielded only *V. cholerae* El Tor, serotype Ogawa, and 8 yielded both pathogens.

In neighboring areas of South Africa, stool specimens obtained during nearly simultaneous outbreaks of diarrhea also yielded *E. coli* O157, including 3 of 20 specimens received on December 2 and 3, 1992, from Ermelo; 1 of 8 specimens received on December 2, 1992, from Empangeni; and 4 of 40 specimens collected on December 17, 1992, in Piet Retief. None of these stool specimens yielded *V. cholerae*, although nontyphoid *Salmonella* spp. were isolated from two stool specimens from Piet Retief.

Environmental Specimens

Between November 21 and December 4, 1992, *E. coli* O157 was isolated from 16 of 81 water samples from Swazi-

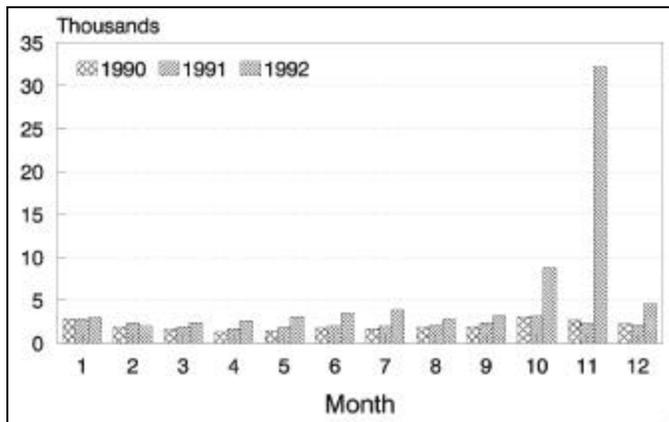


Figure 5. Clinic visits for diarrheal illness among persons ≥ 5 years of age in Swaziland, by month, 1990 through 1992. Data were obtained from Ministry of Health, Government of Swaziland, February 1993.

land and South Africa. Eight of the positive samples came from surface water on the sugar plantation (including the Usutu River), four were obtained from various sites in Ndzevane (including a borehole, a water distribution standpipe, and water stored in the home of a patient), and four were collected near Jeppe's Reef during a diarrhea outbreak (including samples from the Magadu and Sithlangu rivers). *V. cholerae* was not isolated from any water sample.

E. coli O157 was isolated from 3 (20%) of 15 cattle dung specimens collected at the sugar plantation on November 21, and from 3 (11%) of 27 cattle dung specimens collected near Jeppe's Reef on December 4, 1992. A single sample of day-old cooked maize collected December 3, 1992, in the Ndzevane refugee camp also yielded *E. coli* O157, as did two of two sewage specimens received December 2, 1992, from the Pongola area.

Plantation Survey

A total of 778 (92%) of 850 survey questionnaires distributed to residents of the 16 participating villages on the plantation were completed. Four hundred (53%) of the 752 respondents were male. The median age was 26 years.

A total of 327 (42%; 95% CI 38% to 46%) of the 778 plantation residents surveyed reported having diarrheal illness during November or December 1992; 128 (60%) of 212 persons who recalled the time of onset indicated that the illness began in the first 2 weeks of November. Of those ill, 90 (28%) reported bloody diarrhea, 285 (87%) abdominal pain, and 145 (44%) vomiting. The mean duration of illness was 4.2 days (95% CI: 3.6 to 4.8). A total of 257 (79%) of ill persons sought care at the plantation hospital, and 52% indicated they were the first person in their household to have diarrhea. All ages were affected; diarrheal attack rates were 25% to 56% for all age groups when aggregated by 5-year intervals; the attack rate varied widely among villages, from 13% to 75%.

Univariate analyses identified consumption of beef or untreated water in various forms, as well as female gender, as factors significantly associated with diarrheal illness (Table). These associations remained significant even when the case definition was restricted to those who became ill during the first 2 weeks of the outbreak or to those who stated they had been the first ill person in their household.

Defining cases as only bloody diarrhea generally increased the relative risk for each of the dietary exposures. The respondents' job duties on the plantation, a history of travel away from the plantation during the last 2 weeks of October, location of their homestead in Swaziland, and household size were not associated with diarrheal illness.

Stratified analyses were conducted to assess possible confounding or interaction between the exposures identified as significant on univariate analyses. All exposure variables except the consumption of beef not purchased from the butcher remained statistically associated with self-reported diarrheal illness when the variables were stratified by each of the other exposures individually.

Molecular Analysis and PFGE Typing

Thirty-one suspected *E. coli* O157 isolates obtained from clinical and environmental specimens were referred to CDC, and all were confirmed as *E. coli* O157:NM. All isolates had the *uidA* allele specific for *E. coli* O157:H7 and the genes encoding Shiga toxins 1 and 2. All eight isolates characterized by restriction digestion of the PCR-amplified *flxC* gene showed a pattern characteristic of the H7 allele found in *E. coli* O157:H7 isolates. Twenty-seven (87%) of the 31 isolates had indistinguishable PFGE patterns (Pattern A in Figure 1), indicating that the outbreak was largely caused by a single predominant clone. This clone was isolated from various specimens, including human stools, cattle dung, surface water, sewage water, and maize, and was recovered from all six sites where specimens were obtained and tested by PFGE (isolates from a seventh site, Empangeni, were not evaluated by PFGE). Two other PFGE patterns were identified among the four remaining isolates.

Discussion

This report provides comprehensive data on the first outbreak of *E. coli* O157 infections from the developing world. Drought, carriage of *E. coli* O157 by cattle, and contamination of surface water appear to have been important contributing factors. Given the extent of the outbreak, the multiple modes of transmission, and the likely recurrence of predisposing factors, the emergence of *E. coli* O157 has major implications for diarrheal disease control strategies in Africa.

Although the simultaneous occurrence of cholera in some areas where *E. coli* O157 infections were detected makes it difficult to definitively determine the magnitude of the *E. coli* O157 outbreak, national disease surveillance figures for Swaziland leave little doubt that a massive outbreak of diarrheal illness occurred there in 1992, and several lines of evidence suggest *E. coli* O157 played a major role.

First, the clinical presentation of illnesses at the plantation and of the initial patients at the refugee settlements is consistent with *E. coli* O157 infection. Symptomatic cholera infection almost always manifests as profuse watery diarrhea. Severe abdominal pain and bloody stools are very uncharacteristic for cholera but are the hallmark of hemorrhagic colitis caused by *E. coli* O157 (8-10). *E. coli* O157 can also present as nonbloody diarrhea (11,12). In a household survey performed during a waterborne outbreak of *E. coli* O157 infections in the United States, bloody stools were reported by only 35% of those with diarrhea (13). This figure is similar to the proportion of ill persons reporting bloody

Research

Table. Risk factors for diarrheal illness among sugar cane plantation residents during an outbreak of *Escherichia coli* O157 infections in Swaziland, 1992^a

Risk or exposure	Respondents with risk or exposure			Respondents without risk or exposure				
	Total	No. with diarrhea ^a (%)	No. with bloody diarrhea (%)	Total	No. with diarrhea* (%)	No. with bloody diarrhea (%)	RR for diarrhea (95% CI)	RR for bloody diarrhea (95% CI)
Untreated water consumption								
From a standpipe	270	152 (56)	49 (18)	467	157 (34)	36 (8)	1.7 (1.4-2.0)	2.4 (1.5-3.7)
Stream or river	391	204 (52)	65 (17)	354	113 (32)	22 (6)	1.6 (1.3-2.0)	2.7 (1.7-4.3)
Irrigation trench	250	139 (56)	50 (20)	507	178 (35)	38 (7)	1.6 (1.3-1.9)	2.2 (1.8-4.1)
On fruits and vegetables	182	102 (56)	36 (20)	533	199 (37)	49 (9)	1.5 (1.2-1.8)	2.2 (1.3-3.4)
Beef consumption								
In the weekly ration	707	311 (44)	87 (12)	63	14 (22)	3 (5)	2.0 (1.2-3.3)	2.6 (0.8-8.2)
From a cow found dead	180	106 (59)	31 (17)	476	172 (36)	47 (10)	1.6 (1.3-2.0)	1.7 (1.2-2.7)
Not purchased from a butcher	488	226 (46)	67 (14)	255	89 (35)	20 (8)	1.3 (1.1-1.7)	1.8 (1.1-2.9)
Female gender	352	173 (49)	48 (14)	400	143 (36)	41 (10)	1.4 (1.2-1.7)	1.3 (0.9-2.0)

^a Total responses for any given risk factor or exposure may vary slightly and may not equal the total number of survey participants because indeterminate responses to any exposure question (e.g. "Don't remember" or missing value) were not included in the analyses. RR = relative risk; 95% CI = 95% confidence interval.

stools in the plantation survey (28%) and to that observed among the patients seen initially at the Malindza clinic (29%). It seems reasonable, therefore, to infer that some of the cases of nonbloody diarrhea, which were temporally and geographically associated with cases of bloody diarrhea caused by *E. coli* O157, represent milder manifestations of illness caused by this pathogen.

Second, medical personnel clearly recalled that there were two waves of diarrhea, dysentery followed by watery diarrhea, with each surge initially affecting different populations. (Although the term dysentery technically refers to the presence of blood and pus in stools, it is used here to mean nonwatery diarrhea, which may be bloody, accompanied by severe abdominal pain.) In a report filed November 27, 1992, following an assessment of the situation at Ndzevane, the World Health Organization (WHO) representative in Swaziland documented this impression, stating "the type of diarrhea [seen at Ndzevane among the refugees] appeared to be different from that noticed in the neighboring areas," i.e., among the Swazi nationals residing outside the camp (14). Although we suspect that cholera was the likely cause of much of the diarrhea during the second wave of illnesses at the refugee camps, we do not believe the initial dysentery outbreak among the local Swazi population can be attributed to this pathogen.

Third, *E. coli* O157 was isolated from specimens collected from seven different diarrhea-affected foci that spanned a distance of several hundred kilometers. The actual area involved may have been even greater because in the months immediately following this outbreak, investigators in Malawi and Angola reported outbreaks of diarrheal illness in which nucleic acid amplification tests of stool specimens suggested *E. coli* O157 as the cause (15,16).

Estimates of the magnitude of the *E. coli* O157 outbreak ultimately depend on how one apportions the 64,699 consultations for diarrhea (all ages) in Swaziland during October and November 1992, after counterbalancing the identification of cholera in late November with widespread reports of dysentery in the local population and confirmation of *E. coli* O157 over an extended area. Even if *E. coli* O157 accounted for only a small proportion of visits, this would represent thousands, perhaps tens of thousands, of infections and one of the largest outbreaks of this agent in history.

Understanding the complex interaction of environmental and behavioral factors that enabled *E. coli* O157 to emerge so intensely in Africa is important for future diarrheal disease control efforts. Cattle are the major reservoir of *E. coli* O157 and shed this organism more frequently when stressed (17). This region had been experiencing several years of drought, a situation that worsened from July to Sep-

Research

tember 1992. As the drought continued, cattle began to graze close to the remaining sources of surface water and vegetation. The marked increase in cattle deaths beginning in August 1992 indicates that available pastures and water sources were often insufficient.

Although the number of cattle decreased, demand for beef apparently did not. Nearly one quarter of persons surveyed on the plantation indicated that they had eaten beef from cattle known to have been found dead. Commercial beef slaughter and distribution practices were also affected by the shortage of cattle. Earlier in the year, cattle imports from South Africa to Swaziland were banned, a decision said to be supported by some ranchers because it enabled them to sell off dying animals (18). A senior health inspector noted that a single large abattoir was supplying meat to many butchers in the country since the drought and that "preventive health is not taken as a matter of priority by the look of things" at the abattoir (19). Plantation staff also indicated, for the first time in their memory, that just before the outbreak some of the weekly beef rations were spoiled. Although adequate cooking temperatures will kill *E. coli* O157, much of this beef would have been grilled, leaving the possibility that portions remained undercooked.

How *E. coli* O157 originally found its way to cattle in southern Africa is not known, but once there it is not difficult to speculate on how it spread. Recovery of *E. coli* O157 from surface water in Swaziland and South Africa plausibly explains how this pathogen might be rapidly dispersed over vast stretches of land. According to local residents and our own observations, during the drought, cattle often frequented the trickling streambeds, defecating and dying there (Figure 6). With the onset of heavy rains, water contaminated with cattle feces (and presumably *E. coli* O157) would have become readily available to both livestock and residents in villages downstream. Such a scenario is consistent with the epidemic curve from the sugar plantation outbreak; *E. coli* O157 has a median incubation period of 3 to 4 days, and the outbreak exploded 3 days after the first heavy rains in 4 months (10). PFGE results indicate that a single clone was responsible for much of the outbreak, suggesting that either there was an exceptionally narrow range of diversity among *E. coli* O157 isolates in south African cattle or that a single clone was able to expeditiously spread over large distances, perhaps via surface waterways revitalized by heavy rains.

By early 1993 we no longer detected *E. coli* O157 in patient stools or environmental specimens obtained from the affected area, intimating that the outbreak had ended almost as abruptly as it started. Since that time, however, two other outbreaks of dysentery have been attributed to *E. coli* O157 elsewhere in Africa, the first in Central African Republic in 1996, and the second in Cameroon beginning in 1997 (20,21). Both these reports have some constraints, however; in the Central African Republic, *E. coli* O157 was not isolated at the outbreak site but only implicated from molecular tests. In the Cameroon outbreak, *E. coli* O157 and *Shigella* were each isolated in about half of the specimens tested.

Although reported outbreaks of *E. coli* O157 in Africa have been few to date, available information indicates that the pathogen has wide geographic distribution. Since the 1992 outbreak, culture-proven *E. coli* O157 diarrheal illness

has been reported from multiple locations, including Kenya, Nigeria, Côte d'Ivoire, and Central Africa Republic (22-25). In Egypt, 6 (5%) of 125 meat specimens obtained from slaughterhouses yielded *E. coli* O157 (26). Because *E. coli* O157 is not detected by the usual methods used to isolate and identify traditional enteric bacterial pathogens and microbiology laboratories in many countries in Africa do not routinely test for this pathogen, *E. coli* O157 infections may go unrecognized (27,28). Reports on African dysentery outbreaks attributed to *Shigella* sometimes indicate that specimens were not tested until several months into the outbreak or do not describe laboratory methods that are suitable for detecting *E. coli* O157 (29,30). This is unfortunate because the spectrum of clinical illness resulting from *Shigella* infection overlaps considerably with that of *E. coli* O157 and mixed outbreaks have been reported (20).

WHO has stated that *Shigella dysenteriae* type 1 "is the only cause of large-scale, regional outbreaks of dysentery" (emphasis WHO), but data presented here suggest that this assertion may be too restrictive (27). We are concerned that if another large outbreak of severe bloody diarrhea caused by *E. coli* O157 occurred today in Africa, it might be assumed to be due to *Shigella* spp. and *E. coli* O157 would not be sought.

Determining the extent to which *E. coli* O157 is responsible for dysentery in Africa is of more than academic con-



Figure 6. Cattle grazing in a trickling stream bed, Lubombo, Swaziland, 1992. The nearly ubiquitous hoof prints, visible in the foreground, indicate cattle often frequented the stream beds. Photo credit: Paul Effler.

cern because syndromic management protocols for dysentery in areas where the etiologic agent cannot be readily confirmed often include empiric treatment with antibiotics. Antibiotics have not been clearly shown to ameliorate *E. coli* O157 infection, and recent data indicate that treating these infections with antibiotics may predispose the patient to developing serious complications, including hemolytic uremic syndrome (HUS) (10,31). HUS is estimated to occur in 8% of children and an unknown proportion of adults with *E. coli* O157 and, without dialysis, can be fatal (10).

More work is needed to better define the incidence of *E. coli* O157-associated dysentery in Africa so that optimal recommendations for empiric antibiotic therapy can be provided. At present, we recommend that in outbreaks of dysentery in Africa, stools from ill patients be tested for *E. coli* O157 in addition to *Shigella* spp. If the etiologic agent is not identified, consideration should be given to examining stools for other Shiga toxin-producing *E. coli*. Regional studies of *E. coli* O157 carriage rates among livestock in various parts of Africa might also be useful in assessing the potential for future outbreaks.

In this investigation, *E. coli* O157 was recovered from multiple water sources, including a borehole, a standpipe, and water stored in the home. Thus, ensuring the purity of potable water through practical, low-cost strategies might have reduced the risk for infection (32-34).

Several limitations of this investigation should be noted. First, the survey at the plantation did not adjust the period of exposure inquired about to account for differences in date of illness onset for each patient. Instead we asked all persons, both ill and well, about exposures during the 2 weeks preceding the outbreak.

Second, with conditional logistic regression analyses we were unable to identify significant independent predictors of illness among the risk exposures reported by the plantation residents. Many household clusters had at least one indeterminate response to an exposure question (e.g., replied, "Don't remember" or no response) and therefore the entire cluster had to be excluded from such analyses, resulting in conditional regression models that were unstable.

A third limitation is our inability to assess the impact of the *E. coli* O157 outbreak on human deaths. While visiting area hospitals, we heard anecdotal accounts of patients who became edematous and died without known cause. We suspect that these cases represented end-stage manifestations of HUS, but quantifiable data were not available.

Despite widespread recognition of the importance of environmental factors in facilitating the emergence of infectious agents, the information available in the scientific literature remains relatively limited (35-38). This manuscript combines environmental and veterinary data together with disease incidence, environmental testing, and microbial "fingerprinting" to develop one of the more complete examples currently available. The data presented suggest that carriage of *E. coli* O157 by cattle, cattle deaths secondary to drought, and heavy rains that resulted in contamination of surface water were important factors contributing to the emergence of *E. coli* O157 in Africa. Given that drought and heavy rains will likely recur in Africa, the possibility that *E. coli* O157 will once again emerge to cause a major regional outbreak cannot be excluded. Clinicians need to be aware of

this so that delayed diagnosis and inappropriate treatment resulting in loss of lives can be avoided.

Acknowledgments

The authors thank Serge Male and the United Nations High Commission for Refugees for their support in conducting this investigation. The authors also thank Lynne McIntyre and April Bogard for their valuable editorial assistance.

Dr. Effler is State Epidemiologist for the Hawaii Department of Health. His current responsibilities encompass disease surveillance and outbreak control, oversight of the state's immunization program, and bioterrorism preparedness.

References

1. Isaäcson M, Canter PH, Effler P, Arntzen L, Bomans P, Heenan R. Haemorrhagic colitis epidemic in Africa. *Lancet* 1993;341:961.
2. Browning NG, Botha JR, Sacho H, Moore PJ. *Escherichia coli* O157:H7 haemorrhagic colitis: report of the first South African case. *S Afr Med J* 1990;28:28-9.
3. Ewing WH. *Edwards and Ewing's identification of enterobacteriaceae*. 4th ed. New York: Elsevier Science Publishing Co. Inc.; 1986.
4. Olsvik O, Rimstead E, Hornes E, Strockbine N, Wasteson Y, Lund A, et al. A nested PCR followed by magnetic separation of amplified fragments for detection of *Escherichia coli* Shiga-like toxin genes. *Mol Cell Probes* 1991;5:429-35.
5. Cebula TA, Payne WL, Feng P. Simultaneous identification of strains of *Escherichia coli* O157:H7 and their Shiga-like toxin type by mismatch amplification mutation assay-multiplex PCR. *J Clin Microbiol* 1995;33:248-50.
6. Barrett TJ, Lior H, Green JH, Khakhria R, Wells JG, Bell BP, et al. Laboratory investigation of a multistate food-borne outbreak of *Escherichia coli* O157:H7 by using pulsed-field gel electrophoresis and phage typing. *J Clin Microbiol* 1994;32:3013-7.
7. Fields PI, Blom K, Hughes HJ, Helsen LO, Feng P, Swaminathan B. Molecular characterization of the gene encoding H antigen in *Escherichia coli* and development of a PCR-restriction fragment length polymorphism test for identification of *E. coli* O157:H7 and O157:NM. *J Clin Microbiol* 1997;35:1066-70.
8. Boyce TG, Swerdlow DL, Griffin PM. *Escherichia coli* O157:H7 and the hemolytic-uremic syndrome. *N Engl J Med* 1995;333:364-6.
9. Griffin PM, Ostroff SM, Tauxe RV, Greene KD, Wells JG, Lewis JH, et al. Illnesses associated with *Escherichia coli* O157:H7 infections: a broad clinical spectrum. *Ann Intern Med* 1988;109:705-12.
10. Mead PS, Griffin PM. *Escherichia coli* O157:H7. *Lancet* 1998;352:1207-12.
11. Griffin PM, Tauxe RV. The epidemiology of infections caused by *Escherichia coli* O157:H7, other enterohemorrhagic *E. coli* and the associated hemolytic uremic syndrome. *Epidemiol Rev* 1991;13:60-91.
12. Rodrigue DC, Mast EE, Greene KD, Davis JP, Hutchinson MA, Wells JG, et al. A university outbreak of *Escherichia coli* O157:H7 infections associated with roast beef and an unusually benign clinical course. *J Infect Dis* 1995;172:1122-5.
13. Swerdlow DL, Woodruff BA, Brady RC, Griffin PM, Tippen S, Donnell JD, et al. A waterborne outbreak in Missouri of *Escherichia coli* O157:H7 associated with bloody diarrhea and death. *Ann Intern Med* 1992;117:812-9.
14. Mwambazi WC. Internal report. Swaziland: World Health Organization; 27 Nov 1992.
15. Paquet C, Perea W, Grimont F, Collin M, Guillod M. Aetiology of haemorrhagic colitis epidemic in Africa. *Lancet* 1993;342:175.
16. Calundungo R, Maddau G, Rappelli P, Cappuccinelli P, Leite F, et al. *Escherichia coli* and enteritis in Angola. *Lancet* 1994;344:538-9.
17. Armstrong GL, Hollingsworth J, Morris JGG. Emerging food-borne pathogens: *Escherichia coli* O157:H7 as a model of entry of a new pathogen into the food supply of the developed world. *Epidemiol Rev* 1996;18:29-51.

Research

18. Mkwanazi B. Butcherries threaten closure. *The Times of Swaziland*. Aug 13, 1992.
19. Memorandum from the Senior Health Inspector, Ministry of Health, Government of Swaziland to the Principal Secretary, Ministry of Interior, RE: Control of diarrhoeal outbreak; 28 Nov 1992.
20. Cunin P, Tedjouka E, Germani Y, Ncharre C, Bercion R, Morvan J, et al. An epidemic of bloody diarrhea: *Escherichia coli* O157 emerging in Cameroon? *Emerg Infect Dis* 1999;5:285-90.
21. Germani Y, Soro B, Vohito M, Morel O, Morvan J. Enterohaemorrhagic *Escherichia coli* in Central African Republic. *Lancet* 1997;349:1670.
22. Sang WK, Saidi SM, Yamamoto H, Ezaki T, Iida T, Yoh M, et al. Haemorrhagic colitis due to *Escherichia coli* O157:H7 in Kenya. *J Trop Pediatr* 1996;42:118-9.
23. Akinyemi KO, Oyefolu AO, Opere B, Otunba-Payne VA, Oworu AO. *Escherichia coli* in patients with acute gastroenteritis in Lagos, Nigeria. *East Afr Med J* 1998;75:512-5.
24. Dadie A, Karou T, Adom N, Kette A, Dosso M. Isolation of enteric pathogenic agents in Côte d'Ivoire: *Escherichia coli* O157:H7 and enteroaggregative *E. coli*. *Bull Soc Pathol Exot* 2000;93:95-6.
25. Germani Y, Minssart P, Vohito M, Yassibanda S, Glaziou P, Hocquet D, et al. Etiologies of acute, persistent, and dysenteric diarrheas in adults in Bangui, Central African Republic, in relation to human immunodeficiency virus serostatus. *Am J Trop Med Hyg* 1998;59:1008-14.
26. Abdul-Raouf UM, Ammar MS, Beuchat LR. Isolation of *Escherichia coli* O157:H7 from some Egyptian foods. *Int J Food Microbiol* 1996;29:423-6.
27. World Health Organization. Guidelines for the control of epidemics due to *Shigella dysenteriae* type 1 (WHO/CDR/95.4). Geneva: The Organization; 1995. p. 1,47.
28. Wittenberg DF. Emerging and re-emerging diseases—epidemic enterohaemorrhagic infections 100 years after Shiga. *S Afr Med J* 1999;89:750-2.
29. Aragon M, Barreto A, Chambule J, Noya A, Tallarico M. Shigellosis in Mozambique: the 1993 outbreak rehabilitation—a follow-up study. *Trop Doct* 1995;25:159-62.
30. Malakooti MA, Alaii J, Shanks GD, Phillips-Howard PA. Epidemic dysentery in western Kenya. *Trans R Soc Trop Med Hyg* 1997;91:541-3.
31. Wong CS, Jelacic S, Habeeb RL, Watkins SL, Tarr PI. The risk of the hemolytic-uremic syndrome after antibiotic treatment of *Escherichia coli* O157:H7 infections. *N Engl J Med* 2000;342:1930-6.
32. Mintz ED, Reiff FM, Tauxe RV. Safe water treatment and storage in the home: a practical new strategy to prevent water-borne disease. *JAMA* 1995;273:948-53.
33. Reiff F, Roses M, Venczel L, Quick R, Witt V. Low cost safe water for the world: a practical interim solution. *Health Policy* 1996;17:389-408.
34. Quick RE, Venczel LV, Mintz ED, Soletto L, Aparicio J, Gironaz M, et al. Diarrhoea prevention in Bolivia through point-of-use water treatment and safe storage: a promising new strategy. *Epidemiol Infect* 1999;122:83-90.
35. Morse SS. Factors in the emergence of infectious diseases. *Emerg Infect Dis* 1995;1:7-15.
36. Colwell R, Epstein P, Gubler D, Hall M, Reiter P, Shukla J, et al. Global climate change and infectious diseases. *Emerg Infect Dis* 1998;4:451-2.
37. Engelthaler DM, Mosley DG, Cheek JE, Levy CE, Komatsu KK, Ettestad P, et al. Climatic and environmental patterns associated with hantavirus pulmonary syndrome, Four Corners region, United States. *Emerg Infect Dis* 1999;5:87-94.
38. Feldbaum H. Forging new perspectives on disease surveillance. *Emerg Infect Dis* 1998;4:337-8.