

AN APPARENT OUTBREAK OF RICKETTSIAL ILLNESS IN COSTA RICA, 1974^{1,2}

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A focal outbreak of highly fatal disease occurred in eastern Costa Rica in 1974. No rickettsial spotted fevers have previously been reported in Costa Rica. Nevertheless, the available evidence points to an unidentified rickettsial pathogen, probably of the spotted fever group, as the agent responsible for this outbreak.

Introduction

Human rickettsial infections are reported every year throughout Latin America. The majority of those described are cases of murine typhus caused by *Rickettsia typhi*. In addition, well-established foci of epidemic (*R. prowazekii*) typhus exist in the mountains of Bolivia and Guatemala (1, 2), and *R. rickettsii* (Rocky Mountain spotted fever) infections have been reported in various Latin American countries.

In contrast, Panama is the only country along the Central American isthmus that has reported cases of rickettsial spotted fevers (3, 4). Three human cases, unrelated to each other, were documented in 1950-1951; the tick *Amblyomma cajennense* was the presumptive vector (5).

This article deals with an isolated disease outbreak in northeastern Costa Rica which

killed four people living on one farm. Clinical and serologic evidence suggests that the causative agent was a rickettsia, although no agent was actually isolated or identified. Studies of the arthropod fauna in the area of the affected farm revealed heavy tick infestations, suggesting that the infecting organism was a rickettsia belonging to the spotted fever group. Although no previous reports from Costa Rica cite like outbreaks or clinical illnesses as severe as those reported here, an earlier serologic study (6) suggests that other human infections with similar rickettsiae have occurred along Costa Rica's Atlantic coastal zone.

The Outbreak

The outbreak began among residents of a farm in the community of Los Altos de Herediana in Costa Rica's Limón Province (see Figure 1). Individual illnesses had dates of onset ranging from May through July 1974, a period falling within the dry season of this coastal subtropical region. A family of 11 persons lived on the farm; all members were healthy before the epidemic.

On 13 May a boy 17 years old developed fever, chills, arthralgias, and myalgias. His neurological condition subsequently showed progressive deterioration, with stupor and convulsions. On the third day of illness he developed a generalized rash which rapidly

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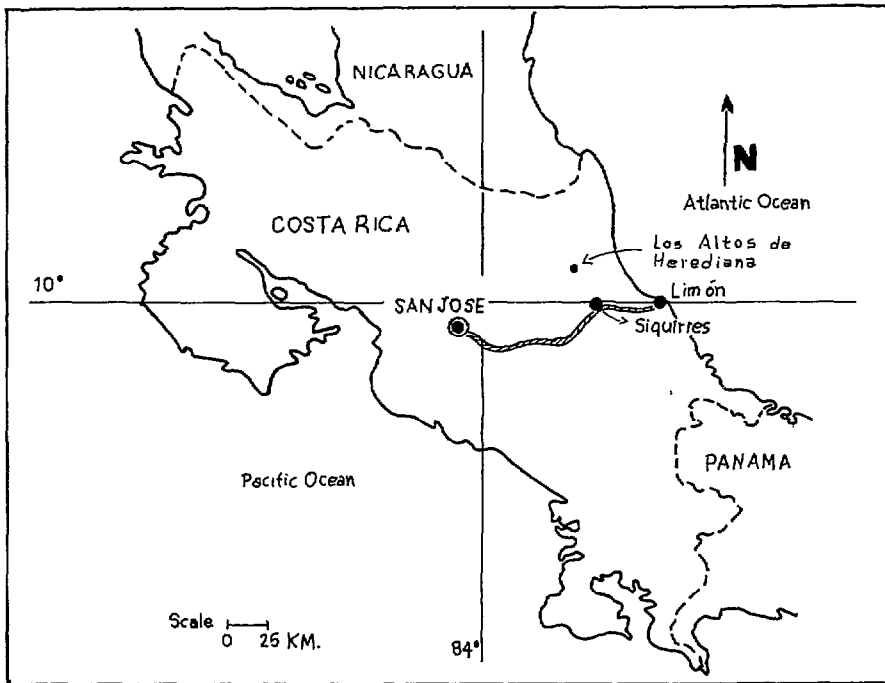
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Figure 1. A map of Costa Rica showing the location of Los Altos de Heredia, where the outbreak occurred.



became purpuric. He was hospitalized on the eighth day in shock, but he died before laboratory data was available to the attending physicians.

On 14 May the boy's father (age 48) and brother (age 16) developed a clinically similar illness. The father was diagnosed as being septic; despite rehydration, penicillin, and heparin therapy he died on the seventh day of his illness. The 16-year-old boy, reportedly having witnessed his brother's illness, refused to be hospitalized. According to his mother he experienced unrelenting fever, delirium, and hemorrhages in the skin before dying on the eighth day of his illness.

The fourth patient from this family, an eight-year-old boy, became ill on 19 May. The similarity of his illness to that of his father and brothers prompted surviving family members to transport him to the

hospital on 23 May, where physicians were aware of the family's three previous deaths. On 27 May results of the father's autopsy became available; these cited "rickettsial bodies" in the spleen. The patient was therefore treated with tetracycline, chloramphenicol, and heparin. Within 48 hours of the initiation of antibiotic treatment his fever subsided and he recovered.

As this account shows, four members of this 11-person family became ill over a span of six days. However, the seven unaffected people (four females, including the mother, and three young males) showed no clinical evidence of similar febrile illness. The surviving family members abandoned the farm in late May.

During the latter part of May and the month of June a 51-year-old caretaker stayed at the farm. His dwelling was an improvised shelter at the periphery of the

bean field. Various members of his family visited him, but only his 14-year-old son (patient 5) remained to work in the field. Neither the father nor the son slept in the main house.

On 26 June patient 5 became ill with symptoms identical to those of the first four cases. The boy was taken to the hospital on the third day of his illness. Because he had a febrile illness with a petechial rash, presumptive therapy for a rickettsial infection was initiated upon admission. On 4 July, as he began to recover, his father (patient 6) became ill. The course of the father's illness was short and malignant. His fever was high and unremitting; despite vigorous therapy he died on the third hospital day of a cardiac-respiratory arrest.

The surviving members of this second family, a 60-year-old woman and a 13-year-old girl, remained healthy.

To sum up, the cases occurred over two time periods. Four males from the first family became ill between 13 and 19 May, and two males from the second family became ill between 26 June and 4 July. Six of the 15 persons in the two families became ill and four of the six died. All of the patients were males. The average time from onset of symptoms to death was 7.5 days. The two survivors (8 and 14 years of age) were the youngest patients; their symptoms abated within 48 hours after the initiation of antibiotic treatment. None of the victims showed evidence of any condition—such as malnutrition or chronic illness—predisposing to an overwhelming infection.

Clinically, the illness was characterized by sudden onset of unremitting fever accompanied by severe myalgias and arthralgias. All five patients for whom hospital records were available developed a macular rash within three days of the onset of fever. This rash became generalized to involve the trunk, and petechiae and ecchymoses later appeared. Each patient had episodes of stupor, confusion, and delirium, and three patients had generalized seizures. Only one

patient had hepatosplenomegaly. Neither pulmonary nor gastrointestinal involvement was prominent.

Only patient 5 was anemic on admission to the hospital. Of the four patients for whom white blood cell counts were available, three had leukopenia (less than 5,000 leukocytes per mm^3). The differential count in three of these four patients revealed an increased number of immature neutrophils. Patients 4, 5, and 6 all had lumbar punctures, but neither examination nor cultures of the spinal fluid revealed evidence of central nervous system infection.

The initial platelet counts for patients 3, 4, 5, and 6 were 100,000 platelets or less per mm^3 (a normal count is 200,000 or more). Two of these patients had prolonged prothrombin times and all of them had decreased fibrinogen levels. These data, combined with the clinical finding of petechiae, clearly suggest disseminated intravascular coagulopathy.

Attempts to isolate the causative agent from the patients' blood and spleen in artificial media, embryonated eggs, and guinea pigs produced a pathogen. That pathogen caused testicular necrosis in male guinea pigs and had giemsa-staining characteristics similar to a rickettsia. Unfortunately, this agent was lost in transport before it could be fully identified.

Serology

Sera from patients 3, 4, 5, and 6 were tested for the presence of *Proteus vulgaris* OX-19 febrile agglutinins (see Table 1). Sera taken from these four patients at their initial examinations had negative titers. Two of the patients died before a second serum sample was obtained. However, patients 4 and 5 (the survivors) each developed high OX-19 titers by the second week of their illness, suggesting a recent rickettsial infection.

Table 1. Serologic data obtained with samples from patients 3, 4, 5, and 6 (Costa Rica, 1974).

Patient providing the sample	Days following onset of illness	Reciprocal CF Titer to:					Weil-Felix ^a OX-19
		<i>R. prowazekii</i>	<i>R. typhi</i>	<i>R. canada</i>	<i>R. akari</i>	<i>R. rickettsii</i>	
3	8						Negative
4	5						Negative
"	7						1:320
"	12						1:1,280
"	52	<8	<8	<8	<8	32	
"	83	<8	<8	<8	<8	8	
"	141	<8	<8	<8	<8	<8	
5	5						Negative
"	9	<8	<8	<8	<8	<8	
"	14	<8	64	16	<8	<8	1:1,280
"	42	<8	<8	<8	<8	32	
"	76	<8	<8	<8	16	512	
6	5						Negative
"	7	<8	<8	<8	<8	<8	

^aThe Weil-Felix reaction is the diagnostic agglutination of *Proteus X* bacteria by blood sera from typhus fever cases, apparently due to the presence of a common antigen.

Serum samples from patients 4, 5, and 6 were tested for complement-fixing (CF) antibody with five known rickettsial antigens (7) at the CDC laboratory in Atlanta (Table 1). These antigens were prepared from egg yolk-sacs infected with *R. rickettsii*, *R. akari*, *R. prowazekii*, *R. typhi*, and *R. canada* (8). A CF titer greater than 1:8 is considered positive. A sample taken early in the illness was not available from patient 4; however, about two months after the onset of illness a convalescent serum from patient 4 showed a significant but low-level CF titer to *R. rickettsii*. A third serum specimen obtained nearly five months after his illness had a titer or less than 1:8.

Serum taken from patient 5 two weeks after the onset of illness was CF positive to *R. typhi* antigen (1:64) and *R. canada* antigen (1:16). At weeks 6 and 11 there was a positive complement-fixing *R. rickettsii* titer. The differences in the typhus (*R. typhi*) and spotted fever (*R. rickettsii*) complement-fixing activity are difficult to interpret, since they do not represent a recognized pattern of serologic response or cross-reaction in rickettsial illnesses. Patient

6 had negative CF titers to all the antigens when tested on the seventh day of his illness.

Field Studies

Epidemiologic and Serologic Investigation in Los Altos de Herediana

The field investigation in Los Altos de Herediana began in late August, six weeks after onset of the last case. Each resident of the community was questioned concerning recent febrile illness, visits to a health facility, occupation, contacts with animals, recent visitors, travel, and animal or insect bites experienced during the period April-June 1974. The population of the area was found to be 199 persons. A total of 196 persons were located and interviewed. Serum specimens were obtained from 165 residents (83 per cent of the population) who consented to venipuncture. No instance was discovered of any febrile illness similar to that of the two boys who recovered.

No significant differences were detected between the two affected families and other residents of Los Altos de Herediana with

respect to type of work, travel, or exposure to animals and blood-sucking arthropods. Most residents reported tick, mite, and mosquito bites during the interval of the outbreak.

On the other hand, differing workplaces distinguished clearly between persons who became ill and those who remained well. In April, the father (patient 3) had begun preparing the bean field for planting. This field had not been cultivated since the previous year. The bean field measured approximately 200 by 300 meters and adjoined a sugarcane field of approximately equal dimensions. The two older boys (patients 1 and 2) had worked in the bean field with their father until they became ill. The youngest boy (patient 4) had brought meals to the field and had remained there for long periods every day. Due to other obligations, the females in the family rarely visited this field, another male (age 10) was in school during the April-May period, and the two youngest males were not yet able to help with field work. Patients 5 and 6 (of the second family) had begun working in the bean field in May and had continued to do so after the survivors of the original family abandoned the area.

No other persons were known to have worked in the area of the bean field during the two months preceding the outbreak. In the three months following the outbreak this area was unattended, and at the time of the investigation it was overgrown with dense vegetation.

None of the unaffected family members had detectable CF antibodies to the five rickettsial antigens tested. CF tests of sera from the other 165 community residents revealed only one adult male with a 1:8 CF titer to *R. rickettsii* and *R. akari* antigens. He had no history of recent febrile illness, nor had he any interaction with the victims or the farm on which the illnesses occurred.

Rickettsial Illnesses in Eastern Costa Rica

To construct a profile of rickettsial

illnesses in the Atlantic zone of Costa Rica, records at health posts, hospitals, and the Ministry of Health were reviewed for the period 1968-1973. Cases were selected from among those illnesses diagnosed as rickettsioses by the attending physicians. For this purpose a case was defined as a febrile illness lasting at least five days that was not explained by another documented illness and that was accompanied by a Weil-Felix OX-19 titer of at least 1:40 at any point in the illness. All health posts and hospitals in Limón and Cartago provinces were surveyed, along with the health facilities in the Capital of San José which received patients from this eastern area.

For all histories that met the case definition, information was recorded concerning the duration of illness, the outcome, and the presence of dermatitis, myalgia, arthralgia, and central nervous system involvement.

All discharge diagnoses at eight hospitals (the total number of discharges averaging 108,000 per year) were reviewed for 6.5 years. Over this interval 14 persons (excluding the five hospitalized in this outbreak) were found who met the case criteria.

While a single hospital reported 10 (71%) of these 14 cases, there was no clustering by place of residence, and none came from Los Altos de Heredia. Of the 14 patients, 12 (86%) lived and worked in an urban area. Nine patients (65%) were males. Four of the patients were less than 15 years old, seven were between the ages of 15 and 30, and three were over 30.

A striking aspect of the clinical illnesses in these 14 individuals was that all were relatively mild. There were no deaths. Only three persons were known to have had a rash during their illness; none of the patients had extensive laboratory studies. All patients were treated with either tetracycline or chloramphenicol, but this was not begun until the second week of illness. All 14 patients had been diagnosed in the hospital as having either murine typhus or "non-specific rickettsiosis."

Field Study of Ticks and Rickettsial Agents

For 10 consecutive days in October, a field team working in Los Altos de Heredia collected ticks which might harbor or transmit rickettsiae. All ticks collected for rickettsial isolation were frozen at -70°C in beef-heart suspension. The livestock remaining on the farm where the outbreak occurred—as well as horses, cattle, and dogs from other residences in Los Altos de Heredia—were examined for ticks. A total of 35 small animals were trapped alive on the farm and likewise examined for ticks. In all, a total of 31 lots of adult ticks were collected from animals in the study area. These ticks were identified as belonging to four different species, all common to eastern Costa Rica. Cattle and horses were invariably tick-infested, but ticks were only found on two of the small wild animal species examined (see Table 2).

In order to detect tick larvae and nymphs in vegetation, strips of cloth were dragged along paths frequented by people and animals at the farm. There was a striking localization of larvae and small nymphs in this vegetation. On four separate days, focal nests of *Amblyomma sp.* and *Boophilus microplus* larvae were captured in the cane field adjacent to the bean field. These

nests—dense concentrations of approximately 1,000 larvae—were routinely encountered on five-minute sweeps through the field. Dragging operations in all other areas of the farm failed to produce anything more than an occasional larva, even though dragging in these zones was performed under identical weather conditions.

Larvae and adult ticks from most lots have been processed for rickettsia at the CDC laboratories. Hemolymph testing of six ticks from each of 26 lots, using the Burgdorfer technique (9), was negative for rickettsiae. Rickettsial isolation was also attempted using the guinea pig and yolk sac methods known to be successful in a high percentage of cases of Rocky Mountain spotted fever. It is clear that ordinary strains of *R. rickettsii* are not present.

Discussion

The clinical illness in these six individuals and the serologic results obtained from the two survivors strongly suggest that the outbreak was due to a rickettsia of the spotted fever group. Whether the agent was *R. rickettsii* or a closely related species has not been determined.

Epidemiologically, this seems to have been a "common source" outbreak, despite the fact that it appears bimodal when one considers the time interval between the onsets of illness. The theory that transmission only occurred in a single area is strengthened by the fact that all six cases could be associated with the cane field where larval ticks were later detected.

Clustering of cases of spotted fever rickettsioses, suggesting a common contact, has been reported previously, even though most cases have tended to occur sporadically. Reports of São Paulo fever (10) and Tobia fever (11) have documented the occurrence of clusters of simultaneous spotted fever cases in multiple families. In general, the epidemiology of human spotted fever infections appears to depend largely

Table 2. Ticks collected at Los Altos de Heredia, Costa Rica, in October 1974.

Tick species	No. of lots ^a collected	Sources
<i>Amblyomma oblongoguttatum</i>	4	Horses
	1	Cow
<i>Haemaphysalis leporispalustris</i>	2	<i>Silvilagus brazilensis</i>
	2	<i>Didelphis marsupialis</i>
<i>Boophilus microplus</i>	10	Cows
	1	Horse
<i>Anocentor nitens</i>	10	Horses
	1	Cow

^a A lot is comprised of the ticks of one species found on one animal.

upon the spatial distribution of the infected vector.

The forementioned six-year review of hospital records indicates that the 14 patients from eastern Costa Rica with illnesses defined as rickettsioses all presented pictures different from that noted in the current outbreak. These 14 persons had an illness clinically consistent with murine typhus, a sporadic disease whose presence has been recognized in Costa Rica for many years.

A serologic survey of rickettsial antibodies in Central America by Peacock, et al. (6) previously indicated that undescribed rickettsial species might exist in Costa Rica. The authors examined 507 sera from Costa Rica and found CF and microagglutination (MA) titers suggesting *R. akari* (rickettsial pox) infections in subjects from Limón Province. While there were 13 positive CF reactors to *R. rickettsii*, these sera were negative by MA. The investigators also found a small number of cross-reactions using *R. canada*, *R. rickettsii*, and *R. akari*

antigens; they concluded that this was suggestive serologic evidence for an unknown rickettsial strain (or strains) of the spotted fever group. While the clinical history of the subjects was not investigated, the serologic findings do indeed suggest that there are as yet unidentified rickettsiae transmitted in the area of Costa Rica's Atlantic Coast.

The recent epidemic strengthens the evidence that "spotted fever" group rickettsiosis is transmitted in Costa Rica. To confirm the identity of the agent involved in the transmission, however, will require close clinical attention in order to collect blood and tissue specimens suitable for rickettsial isolation in the event of similar future cases. The focal nature of the disease and the rickettsial CF seropositivity detected in subjects from Los Altos de Heredia indicates that surveillance for febrile hemorrhagic illness should be concentrated at the level of rural health units.

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SUMMARY

A focal outbreak of a highly fatal infection, believed to be rickettsial in origin, occurred in eastern Costa Rica during the months of May, June, and July 1974. The symptoms consisted of fever, a petechial or ecchymotic dermatitis, and central nervous system disorders. An investigation revealed that the illness was limited to inhabitants of a single farm, and more specifically to persons who worked at planting a bean field on that farm. A cane field adjacent to the bean field, unlike surrounding areas of the farm, was

later found to be infested with two species of ticks.

A review of records at health facilities serving residents of eastern Costa Rica revealed that the illness was unlike other rickettsioses reported there over the past six years.

The data available support previous reports that undescribed rickettsial pathogens, probably of the spotted fever group, are transmitted in the region of Costa Rica's Atlantic Coast.

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