

PPVs were similar. A relatively high difference explains why F14.1158H was not detected by several PCRs designed for detecting PPV, which should be considered when designing diagnostic protocols. These phylogenetic results and sequence identities, together with the high guanine and cytosine content and disease characteristics, indicate that F14.1158H represents a novel PPV, designated equine parapoxvirus (EqPPV). The final taxonomic position and the possible differences of human and equine-derived variants (6) will require more data.

Most known PPVs are zoonotic, and any novel virus detected in animals should be treated with concern (6). Thus, considering the tendency of PPVs to cause diseases in humans, EqPPV has a zoonotic potential. It is therefore important to sample humans and other animals in contact with infected horses. It is also critical to establish diagnostic protocols due to low specificity and sensitivity of pan-PPV PCR for EqPPV (Appendix). In terms of veterinary importance, this virus poses a threat for horses that could translate to financial losses for owners. The information provided here will inform development of proper diagnostic tools and also enable establishment of prevention measures.

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## Rickettsial Disease Outbreak, Mexico, 2022

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Beginning in 2022, Nuevo Leon, Mexico, experienced an outbreak of rickettsioses that is still ongoing despite multidisciplinary control efforts. A total of 57 cases have been confirmed, particularly affecting children. We report a high mortality rate among hospitalized persons in Nuevo Leon. Continuing efforts are required to control the outbreak.

**R**ickettsioses are life-threatening vectorborne infections transmitted by several arthropods, such as ticks, lice, fleas, and mites (1,2). Rickettsial diseases are an emerging threat in Mexico, particularly in the northern regions, where previous outbreaks have been reported (3). In 2022, the local epidemiologic surveillance department reported 57 confirmed

and >500 probable rickettsial disease cases in Nuevo Leon, a semiarid state in northeast Mexico. This unprecedented and alarming increase represents the highest number of rickettsial disease cases in a single year in this region, showing significant contrast with 2021, when only 13 confirmed cases were reported. Although surveillance and preventive measures are continuously in place, additional multidisciplinary strategies were established after the outbreak was declared in May 2022.

The Mexican Institute of Epidemiology defines a probable case of rickettsiosis as a patient with fever and  $\geq 2$  compatible clinical and laboratory signs. Technicians at the State Laboratory of Public Health of Nuevo Leon perform real-time PCR targeting the *gltA* gene on all probable cases identified  $< 7$  days after symptom onset. A positive PCR result requires the presence of a well-defined sigmoid curve, where the 3 PCR-reaction phases are distinguished, plus a quantification cycle value  $\leq 38$ . State laboratory staff use an indirect immunofluorescence antibody assay to analyze all samples collected 7–14 days after symptom onset and confirm cases through real-time PCR or, retrospectively, with seroconversion by immunofluorescence

**Table.** Clinical and paraclinical characteristics of patients with rickettsioses during outbreak in Neuvo Leon, Mexico, 2022

Characteristic	Total, n = 57	No. (%) patients		p value†
		Cured, n = 21	Died, n = 36	
Patient age, y				0.106
<4	8	1 (1.7)	7 (12.2)	
4–12	28	12 (21)	16 (28)	
13–18	8	1 (1.7)	7 (12.2)	
>18	13	7 (12.2)	6 (10.5)	
Patient sex				0.768
F	34	12 (21)	22 (38.5)	
M	23	9 (15.7)	14 (24.5)	
Clinical signs‡	n = 48	n = 14	n = 34	
Anemia				<b>0.012</b>
Yes	32	11 (22.9)	21 (43.7)	
No	16	3 (6.2)	13 (27)	
Thrombocytopenia				<b>0.007</b>
Yes	47	13 (27)	34 (70.8)	
No	1	1 (2)	0	
Leukocytosis				<b>0.01</b>
Yes	17	3 (6.2)	14 (29.1)	
No	31	11 (22.9)	20 (41.6)	
Leukopenia				<b>0.014</b>
Yes	4	2 (4.1)	2 (4.1)	
No	44	12 (25)	32 (66.6)	
Treatment with doxycycline				0.074
Yes	52	21 (36.8)	31 (54.3)	
No§	5	0	5 (8.7)	
Time to treatment initiation, h	n = 52	n = 21	n = 31	<b>0.007</b>
$\leq 24$	4	4 (7.6)	0	
>24	48	17 (32.6)	31 (59.6)	

\*n values within columns indicate number of patients in category.

†By  $\chi^2$  test. Bold indicates statistical significance.

‡Anemia: female, hemoglobin  $< 11.6$  g/dL; male, hemoglobin  $< 13.2$  g/dL). Thrombocytopenia: female, platelets  $< 157 \times 10^9/L$ ; male, platelets  $< 135 \times 10^9/L$ .

Leukocytosis: leukocytes  $> 9.6 \times 10^9$  cells/L. Leukopenia: leukocytes  $< 3.4 \times 10^9$  cells/L.

§Five patients died before treatment and had their diagnosis confirmed by autopsy.

antibody analysis (4). The data discussed in this report comprise all 57 confirmed cases in 2022.

Compared with results from 2021, the incidence rate of rickettsioses in Nuevo Leon in 2022 rose from 0.2 to 0.9 cases/100,000 inhabitants. Most cases occurred in October ( $n = 14$ ) and December ( $n = 9$ ). The median patient age was 10 years (range 1–61 years); 59.6% of case-patients were female and 40.4% male. The pediatric population ( $\leq 18$  years of age) represented 77% of all cases (Appendix Table, <https://wwwnc.cdc.gov/EID/article/29/9/23-0344-App1.pdf>). Most patients required hospitalization ( $n = 50$ ), and all had a positive history of tick exposure within 2 weeks before symptom onset. More than half of cases (54%) originated in 2 remote municipalities of Nuevo Leon, where most patients had a positive contact history with stray dogs or cats. The most frequent clinical signs were fever (100%), petechial rash (56%), and tachycardia (40%) (Table). Predominant symptoms were headache (75%), abdominal pain (75%), myalgia (74%), and arthralgia (58%). Laboratory findings at hospital admission included anemia in 66% of case-patients, thrombocytopenia in 98% (median platelet count  $25 \times 10^3/\mu\text{L}$ ), leukocytosis in 35%, and leukopenia in 8%.

Of the 57 case-patients, 52 were treated with doxycycline; the remaining 5 died before treatment and had their infections diagnosed through autopsy. The

median time-to-treatment initiation from symptom onset was 4 days, and only 8% of the patients received prompt antibiotic therapy within the first 24 hours of symptom onset. More than half (63%) of the total case-patient population died, and median time from symptom onset to death was 5 days (range 2–17); median length of hospital stay was 1 day (range 0–41). The annual rickettsiosis mortality rate for the region was 0.6 deaths/100,000 inhabitants.

To determine clinical, laboratory, and demographic associations with mortality, we performed  $\chi^2$  testing by using SPSS Statistics software (IBM, <https://www.ibm.com>). We found statistically significant associations with mortality in patients with anemia ( $p = 0.012$ ), thrombocytopenia ( $p = 0.007$ ), leukocytosis ( $p = 0.01$ ), and leukopenia ( $p = 0.014$ ) at hospital admission. Likewise, a time-to-treatment initiation of 24 hours was associated with survival ( $p = 0.007$ ). Among the 57 cases, 4 were confirmed as spotted fever group rickettsiosis because of seroconversion to *Rickettsia rickettsii* antigens, 5 seroconverted to *R. typhi* and were confirmed as typhus group rickettsiosis, and the remaining 48 cases were tested by molecular analysis and were confirmed as simply rickettsiosis (*Rickettsia* sp.)—that is, PCR did not discriminate between spotted fever group and typhus group rickettsiae.

An alarming feature of this ongoing outbreak is its high fatality rate (63%). The most recent outbreaks of rickettsiosis in Mexico reported fatality rates of 40% in Sonora and 29% Baja California (5,6). In northeastern Mexico, the brown dog tick (*Rhipicephalus sanguineus*) is highly prevalent (Figure), posing a high risk for rickettsioses (7). Social determinants of health in hard-to-reach municipalities are thought to contribute to the rise in rickettsial disease cases. The abundance of stray animals, lack of healthcare accessibility, and poor disease knowledge may play a significant role in this outbreak.

To date, the local epidemiologic surveillance department has led various interventions in an attempt to control the outbreak by implementing vector control strategies, educating healthcare personnel of high-risk municipalities, designating community champions against rickettsioses, and raising public awareness through media. Clinicians on the Mexico–United States border should have a high index of suspicion of rickettsiosis among febrile patients and consider early empiric antibiotic treatment to reduce mortality risk.

The work on which this report is based was carried out at the Secretary of Health of Nuevo Leon.



**Figure.** Brown dog ticks collected by the vector control department of Nuevo Leon, Mexico, in a hard-to-reach municipality.

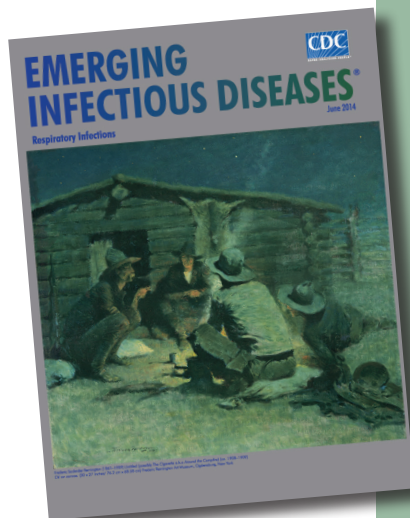
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# etymologia revisited

## Zika [zēkə] Virus

Zika virus is a mosquito-borne positive-sense, single-stranded RNA virus in the family *Flaviviridae*, genus *Flavivirus* that causes a mild, acute febrile illness similar to dengue. In 1947, scientists researching yellow fever placed a rhesus macaque in a cage in the Zika Forest (*zika* meaning “overgrown” in the Luganda language), near the East African Virus Research Institute in Entebbe, Uganda. A fever developed in the monkey, and researchers isolated from its serum a transmissible agent that was first described as Zika virus in 1952. It was subsequently isolated from a human in Nigeria in 1954. From its discovery until 2007, confirmed cases of Zika virus infection from Africa and Southeast Asia were rare. In 2007, however, a major epidemic occurred in Yap Island, Micronesia. More recently, epidemics have occurred in Polynesia, Easter Island, the Cook Islands, and New Caledonia.

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# Rickettsial Disease Outbreak, Mexico, 2022

## Appendix

**Appendix Table.** Demographic, clinical, and paraclinical characteristics of confirmed cases of rickettsiosis in Nuevo Leon, 2022.

Case	Age (y)	Sex	Main clinical signs									Sample	Test (PCR <sup>†</sup> or IFA)	IFA titers (IgG)		Bacteria	Final Outcome
			Fever	Headache	Myalgia	Arthralgia	Rash	Nausea	Vomiting	Abdominal pain	Tachycardia			Acute	Convalescence		
1	61	F	*	*	*	*	Pet	*	*	*		Serum	IFA	1:64	1:32,768	<i>R. rickettsii</i>	Cured
2	15	F	*	*	*	*	Pet/Pu	*	*	*	*	Whole blood	PCR			<i>R. species</i>	Death
3	37	F	*	*	*	*	Pet/Pu				*	Whole blood	PCR			<i>R. species</i>	Death
4	25	M	*	*	*				*	*		Spleen biopsy	PCR			<i>R. species</i>	Death
5	10	F	*	*	*	*				*		Whole blood	PCR			<i>R. species</i>	Death
6	8	M	*	*	*	*	Pet	*	*	*	*	Whole blood	PCR			<i>R. species</i>	Death
7	9	F	*	*	*	*			*	*		Spleen biopsy	PCR			<i>R. species</i>	Death
8	40	M	*		*	*	Mac/Pet	*	*			Serum	IFA	1:2,048	1:8,192	<i>R. typhi</i>	Cured
9	11	F	*	*	*	*						Serum	IFA	<1:64	1:2,048	<i>R. typhi</i>	Cured
10	6	F	*	*	*	*	Mac					Serum	IFA	1:512	1:8,192	<i>R. typhi</i>	Cured
11	56	F	*	*	*	*		*	*	*		Serum	IFA	1:4,096	1:32,768	<i>R. typhi</i>	Cured
12	13	M	*	*	*			*	*	*		Serum	IFA	1:64	1:16,384	<i>R. typhi</i>	Cured
13	9	M	*		*	*	Mac	*	*			Whole blood	PCR			<i>R. species</i>	Death
14	10	F	*				Pet	*	*	*	*	Whole blood	PCR			<i>R. species</i>	Death
15	5	M	*	*			Pet			*		Whole blood	PCR			<i>R. species</i>	Death
16	7	F	*	*			Mac/Pet			*		Whole blood	PCR			<i>R. species</i>	Cured
17	10	M	*	*	*			*		*		Whole blood	PCR			<i>R. species</i>	Cured
18	46	M	*	*						*		Whole blood	PCR			<i>R. species</i>	Cured
19	37	M	*		*	*	Mac/Pet				*	Whole blood	PCR			<i>R. species</i>	Death
20	3	M	*				Mac/Pet			*	*	Whole blood	PCR			<i>R. species</i>	Death
21	13	F	*	*	*	*	Pu	*	*	*	*	Whole blood	PCR			<i>R. species</i>	Death
22	17	F	*	*				*	*	*		Whole blood	PCR			<i>R. species</i>	Death
23	6	M	*	*						*		Whole blood	PCR			<i>R. species</i>	Cured
24	7	F	*				Mac					Whole blood	PCR			<i>R. species</i>	Cured
25	23	F	*	*	*	*	Mac/Pet					Whole blood	PCR			<i>R. species</i>	Cured
26	2	F	*				Mac/Pu/Pet		*	*	*	Whole blood	PCR			<i>R. species</i>	Death
27	6	M	*		*	*	Mac/Pet	*		*	*	Whole blood	PCR			<i>R. species</i>	Death
28	12	F	*	*	*	*			*	*	*	Whole blood	PCR			<i>R. species</i>	Death

Case	Age (y)	Sex	Main clinical signs									Sample	Test (PCR <sup>†</sup> or IFA)	IFA titers (IgG)		Bacteria	Final Outcome
			Fever	Headache	Myalgia	Arthralgia	Rash	Nausea	Vomiting	Abdominal pain	Tachycardia			Acute	Convalescence		
29	14	M	*	*	*	*	Mac/Pu/Pet	*	*	*		Whole blood	PCR			<i>R. species</i>	Death
30	3	F	*	*	*	*		*		*	*	Whole blood	PCR			<i>R. species</i>	Death
31	12	F	*	*	*	*	Mac/Pet			*		Whole blood	PCR			<i>R. species</i>	Death
32	4	F	*	*	*	*	Pet			*		Whole blood	PCR			<i>R. species</i>	Cured
33	3	F	*	*	*	*	Mac/Pet	*	*	*		Whole blood	PCR			<i>R. species</i>	Cured
34	5	M	*	*			Mac/Pu/Pet				*	Whole blood	PCR			<i>R. species</i>	Cured
35	61	F	*	*	*	*	Mac	*	*	*		Whole blood	PCR			<i>R. species</i>	Death
36	1	M	*				Pet	*	*	*	*	Whole blood	PCR			<i>R. species</i>	Death
37	16	M	*	*	*	*	Mac/Pet/Pu	*	*	*	*	Whole blood	PCR			<i>R. species</i>	Death
38	8	F	*		*	*	Mac/Pet/Pu			*	*	Whole blood	PCR			<i>R. species</i>	Cured
39	3	M	*		*		Pet	*	*	*		Whole blood	PCR			<i>R. species</i>	Death
40	18	F	*	*	*	*					*	Whole blood	PCR			<i>R. species</i>	Death
41	7	F	*	*	*		Mac/Pet		*	*	*	Whole blood	PCR			<i>R. species</i>	Death
42	5	F	*				Mac/Pet			*	*	Serum	IFA	<1:64	1:32,768	<i>R. rickettsii</i>	Cured
43	10	F	*	*			Mac/Pu	*	*	*	*	Whole blood	PCR			<i>R. species</i>	Death
44	31	F	*	*					*	*	*	Whole blood	PCR			<i>R. species</i>	Death
45	6	M	*	*	*	*	Mac/Pet	*	*	*	*	Whole blood	PCR			<i>R. species</i>	Death
46	3	F	*		*	*	Mac/Pet			*	*	Whole blood	PCR			<i>R. species</i>	Death
47	50	F	*	*	*	*			*	*	*	Whole blood	IFA	1:64	1:256	<i>R. rickettsii</i>	Cured
48	37	M	*	*	*	*			*	*	*	Serum	IFA	1:64	1:256	<i>R. rickettsii</i>	Cured
49	12	M	*	*	*		Pet	*	*	*		Whole blood	PCR			<i>R. species</i>	Death
50	8	M	*	*	*		Pet	*	*	*	*	Whole blood	PCR			<i>R. species</i>	Death
51	1	F	*				Pet	*	*	*	*	Whole blood	PCR			<i>R. species</i>	Death
52	7	M	*	*	*	*	Mac	*	*		*	Whole blood	PCR			<i>R. species</i>	Cured
53	41	F	*	*	*	*	Mac/Pet		*	*	*	Whole blood	PCR			<i>R. species</i>	Death
54	13	F	*	*	*		Mac/Pet/Pu				*	Whole blood	PCR			<i>R. species</i>	Death
55	10	M	*	*	*	*		*		*		Whole blood	PCR			<i>R. species</i>	Cured
56	8	F	*	*	*	*	Mac		*	*	*	Whole blood	PCR			<i>R. species</i>	Death
57	7	F	*	*	*	*	Mac/Pet	*	*	*	*	Whole blood	PCR			<i>R. species</i>	Death

<sup>†</sup>Whole genome sequence (WGS) was performed on all patients with a positive RT-PCR.

\* = present; blank = absent; Mac = macular; Pu = purpuric; Pet = petechial; PCR = polymerase chain reaction; IFA = immunofluorescence assay; IgG = immunoglobulin G