

Of the acutely ill patients who had positive mIFA results, 67% had pathognomonic eschars, confirming the clinical diagnostic value in this sign of systemic infection. Thrombocytopenia as a sign of scrub typhus could be useful but is a less specific diagnostic indicator (9). There was only a 75% agreement between the rapid test kit and the precise mIFA, but RDTs were shown to be more useful in early detection (10).

The deaths of 2 children in this outbreak could have been prevented if the public had greater awareness of the signs and symptoms of scrub typhus. Lapses of 7–10 days from symptom onset to initial medical consultation and >1 month until the outbreak was investigated demonstrate the importance of training school health coordinators to identify and report incidences of abnormal medical findings to public health agencies, especially in remote, hard-to-reach areas. Parents delayed seeking medical advice, and in some cases, school staff had to persuade them to take their children for medical evaluation. Rapid medical care during illnesses should be encouraged through better community education.

Despite inadequate identification and reporting, there is increasing evidence of endemic scrub typhus in Bhutan. Outbreaks may be common but unrecognized, and past outbreaks may have been missed. Scrub typhus warrants a dedicated public health program or incorporation into the existing vectorborne disease control program in this country.

Acknowledgments

We thank the Wangduephodrang district health administration, Singye Namgyal Primary School authorities, students and their families, and the local community. We thank Chelsea Nguyen, Mythili Tadepalli, Gemma Vincent, and Hazizul Hussain-Yusef for laboratory support.

Dr. Tshokey is a clinical microbiologist in the Jigme Dorji Wangchuck National Referral Hospital, Thimphu, Bhutan. He is currently pursuing a PhD at the University of Newcastle, Australia, and undertakes academic laboratory work in the Australian Rickettsial Reference Laboratory.

References

1. Watt G, Parola P. Scrub typhus and tropical rickettsioses. *Curr Opin Infect Dis.* 2003;16:429–36. <http://dx.doi.org/10.1097/00001432-200310000-00009>
2. Taylor AJ, Paris DH, Newton PN. A systematic review of mortality from untreated scrub typhus (*Orientia tsutsugamushi*). *PLoS Negl Trop Dis.* 2015;9:e0003971. <http://dx.doi.org/10.1371/journal.pntd.0003971>
3. Mahajan SK. Scrub typhus. *J Assoc Physicians India.* 2005;53:954–8.
4. Abhilash KP, Gunasekaran K, Mitra S, Patole S, Sathyendra S, Jasmine S, et al. Scrub typhus meningitis: An under-recognized cause of aseptic meningitis in India. *Neurol India.* 2015;63:209–14. <http://dx.doi.org/10.4103/0028-3886.156282>
5. 59 new cases of scrub typhus in Chitwan, Nepal. *myRepublica, Nepal.* 2016 [cited 2016 Dec 10]. <http://www.myrepublica.com/news/7173>
6. Dutt A. Scrub typhus outbreak in Himachal affects 700, kills 20. *Hindustan Times.* 2016 Sep 27, 2016 [cited 2016 Dec 10]. <http://www.hindustantimes.com/india-news/scrub-typhus-outbreak-in-himachal-affects-700-kills-20/story-6k5RvlnFLCIdePB-g2cxKAK.html>
7. Tshokey T, Choden T, Sharma R. Scrub typhus in Bhutan: a synthesis of data from 2009 to 2014. *WHO South East Asia J Public Health.* 2016;5:117–122.
8. Graves SR, Dwyer BW, McColl D, McDade JE. Flinders Island spotted fever: a newly recognised endemic focus of tick typhus in Bass Strait. Part 2. Serological investigations. *Med J Aust.* 1991; 154:99–104.
9. Tsay RW, Chang FY. Serious complications in scrub typhus. *J Microbiol Immunol Infect.* 1998;31:240–4.
10. Zhang L, Yu Q, He S, Wang S, Yu H, Li X, Zhang D, Pan L. Comparison of a rapid diagnostic test and microimmunofluorescence assay for detecting antibody to *Orientia tsutsugamushi* in scrub typhus patients in China. *Asian Pac J Trop Med.* 2011;4:666–8.

Address for correspondence: Tshokey Tshokey, Clinical Microbiologist, Department of Laboratory Services, Jigme Dorji Wangchuck National Referral Hospital, Thimphu, Bhutan; email: doc_tshokey@yahoo.com

Scrub Typhus as a Cause of Acute Encephalitis Syndrome, Gorakhpur, Uttar Pradesh, India

Mahima Mittal, Jeromie Wesley Vivian Thangaraj, Winsley Rose, Valsan Philip Verghese, C.P. Girish Kumar, Mahim Mittal, R. Sabarinathan, Vijay Bondre, Nivedita Gupta, Manoj V. Murhekar

Author affiliations: BRD Medical College, Gorakhpur, India (Mahima Mittal, Mahim Mittal); National Institute of Epidemiology, Chennai, India (J.W.V. Thangaraj, C.P. Girish Kumar, R. Sabarinathan, M.V. Murhekar); Christian Medical College, Vellore, India (W. Rose, V.P. Verghese); National Institute of Virology, Gorakhpur (V. Bondre); Indian Council of Medical Research, Delhi, India (N. Gupta)

DOI: <https://doi.org/10.3201/eid2308.170025>

Outbreaks of acute encephalitis syndrome (AES) have been occurring in Gorakhpur Division, Uttar Pradesh, India, for several years. In 2016, we conducted a case–control study. Our findings revealed a high proportion of AES cases with *Orientia tsutsugamushi* IgM and IgG, indicating that scrub typhus is a cause of AES.

Outbreaks of acute encephalitis syndrome (AES) with high case-fatality rates have been occurring in Gorakhpur Division of Uttar Pradesh, India, since 1978 (1). AES predominantly affects children ≤ 15 years of age (2), and its etiology has remained largely unknown (3,4). Studies focusing on AES in the region have documented that cases with unknown etiology accounted for 41.6% of cases in 2011–2012 (5) and 59% in 2013–2014 (6).

Investigations conducted during the 2015 outbreak revealed scrub typhus IgM in $>60\%$ of AES cases (7). The absence of information about IgM positivity from the general population, and the probability of high background antibody levels in areas to which scrub typhus is endemic, led us to conduct an unmatched case-control study in which we compared IgM and IgG seropositivity for *Orientia tsutsugamushi*, the causative agent of scrub typhus, in AES patients and healthy controls.

We conducted the study during August 17–October 16, 2016. Children ≤ 15 years of age with AES admitted to the BRD Medical College in Gorakhpur during the study period were recruited to the study if their parents consented to a blood draw and they had siblings ≤ 15 years of age. We defined a case of AES as an acute onset of fever and change in mental status or new onset seizures, excluding febrile seizures (8), with cerebrospinal fluid pleocytosis (cell counts $>5/\text{mm}^3$). Controls were healthy children ≤ 15 years of age residing in the home (sibling controls) or village (community controls) of AES case-patients. We interviewed mothers and caretakers for information on case-patients and controls.

We collected 2-mL blood samples from case-patients and controls and tested the samples for *O. tsutsugamushi* IgM and IgG using commercial ELISAs (Scrub Typhus Detect; InBios International Inc., Seattle, WA, USA). We considered an optical density value >0.5 to be a positive result (9). We compared IgM and IgG positivity among AES case-patients and their controls by calculating crude and adjusted odds ratios (ORs) with 95% CIs.

We enrolled 46 case-patients and 151 controls (69 sibling and 82 community controls) in the study. The

median age was 5 (interquartile range 3–9) years for patients and 7 (interquartile range 4–10) years for controls. The case-patients and controls did not differ by age group or sex (Table). The mothers of 54 (35.8%) of the control children reported a history of fever in the past 6 months.

Common symptoms among the 46 AES case-patients included seizures (69.6%), altered sensorium (52.2%), and vomiting (37%); physical examinations revealed hepatomegaly (43.4%), cervical or inguinal lymphadenopathy (39.1%), and periorbital edema (54.3%). Cerebrospinal fluid was clear in appearance in 43 of the patients we tested. Cell counts ranged from 5–100/ mm^3 in 41 (95.3%) and were $>100/\text{mm}^3$ in 2 patients. Protein levels in fluid were ≤ 45 mg/dL in 8 patients, 46–100 mg/dL in 15, and >100 mg/dL in 20 patients. All AES case-patients were given intravenous azithromycin; 20 patients also received injected ceftriaxone. Eight patients died.

O. tsutsugamushi IgM was detected in 29 (63%) case-patients and IgG in 38 (82.6%). For controls, IgM was detected in 7 (4.6%) and IgG in 64 (42.4%) children. Of the 8 fatal cases, 6 patients had *O. tsutsugamushi* IgM and all had IgG. The distribution of optical density values for IgM and IgG among cases and controls are shown in the Appendix (online Technical Appendix, <https://wwwnc.cdc.gov/EID/article/23/8/17-0025-Techapp.pdf>). Twenty-eight of the 29 IgM-positive cases and 6 of the 7 controls with IgM seroreactivity were also positive for IgG. Of the 7 controls with IgM seroreactivity, 3 had a history of febrile illness in the past 6 months.

The odds of IgM scrub typhus positivity were 35.1 (95% CI 13.4–92.3) times higher among AES case-patients than among controls; when adjusted for age, the odds were 29.9 (95% CI 9.6–92.9) times higher for case-patients. The odds of IgG positivity were 6.5 (2.8–14.8) times higher among AES case-patients than controls, and when adjusted for age, the odds were 3.8 (95% CI 1.4–10.9) times higher for case-patients. When analyzed separately, AES case-patients had higher odds for IgM positivity compared with

Table. Characteristics of patients with scrub typhus and controls in study of acute encephalitis syndrome, Gorakhpur, Uttar Pradesh, India, 2016

Characteristic	No. (%) patients	No. (%) controls	Odds ratio (95% CI)	p value	Adjusted odds ratio (95% CI)
Age group, y					
≤ 5	24 (52.2)	53 (35.1)	2.0 (0.8–5.2)	0.152	7.4 (1.8–31.0)
6–10	15 (32.6)	67 (44.4)	1.0 (0.4–2.7)	0.987	1.8 (0.5–6.8)
11–15	7 (15.2)	31 (20.5)	1		1
Sex					
M	28 (60.9)	82 (54.3)	1.3 (0.7–2.6)	0.433	
F	18 (39.1)	69 (45.7)	1		
<i>Orientia tsutsugamushi</i> IgM					
Positive	29 (63.0)	7 (4.6)	35.1 (13.4–92.3)	0.000	29.9 (9.6–92.9)
Negative	17 (37.0)	144 (95.4)	1		1
<i>O. tsutsugamushi</i> IgG					
Positive	38 (82.6)	64 (42.4)	6.5 (2.8–14.8)	0.000	3.8 (1.4–10.9)
Negative	8 (17.4)	87 (57.6)	1		1

sibling (OR 25.1, 95% 6.3–99.8) or community (OR 13.2, 95% 2.27–76.7) controls.

Our study had 1 main limitation: patients and controls were selected from the same village and shared the same environmental risk factors. Despite overmatching that underestimates the strength of association, the odds ratios for *O. tsutsugamushi* IgM and IgG positivity were significant. We concluded that the presence of higher levels of *O. tsutsugamushi* IgM and IgG among AES case-patients than among controls indicates a role for scrub typhus in the etiology of AES in Gorakhpur.

Acknowledgments

We thank the members of the expert group on Research-Cum-Intervention project on AES/JE for their inputs on the study findings. We are grateful to Anita Mehta, S.K. Srivastava, and Bhoopendra Sharma for their cooperation. Thanks are also due to Mr. Karunakaran and Mr. Magesh for their technical support.

The study was funded from an extramural grant by the Indian Council of Medical Research, New Delhi.

Dr. Mittal is the head of the Department of Pediatrics at BRD Medical College, Gorakhpur, India. Her research interests include central nervous system infections among children.

References

- Mittal M, Kushwaha KP. AES: Clinical presentation and dilemmas in critical care management. *J Commun Dis* 2014; 46: 50–56
- Ranjan P, Gore M, Selvaraju S, Kushwaha KP, Srivastava DK, Murhekar M. Changes in acute encephalitis syndrome incidence after introduction of Japanese encephalitis vaccine in a region of India. *J Infect*. 2014;69:200–2. <http://dx.doi.org/10.1016/j.jinf.2014.03.013>
- Bhatt GC, Bondre VP, Sapkal GN, Sharma T, Kumar S, Gore MM, et al. Changing clinico-laboratory profile of encephalitis patients in the eastern Uttar Pradesh region of India. *Trop Doct* 2012;42:106e8. <http://journals.sagepub.com/doi/pdf/10.1258/td.2011.110391>
- Joshi R, Kalantri SP, Reingold A, Colford JM Jr. Changing landscape of acute encephalitis syndrome in India: a systematic review. *Natl Med J India*. 2012;25:212–20.
- Jain P, Jain A, Kumar A, Prakash S, Khan DN, Singh KP, et al. Epidemiology and etiology of acute encephalitis syndrome in North India. *Jpn J Infect Dis*. 2014;67:197–203. <http://dx.doi.org/10.7883/yoken.67.197>
- Gupta S, Shahi RK, Nigam P. Clinico-etiological profile and predictors of outcome in acute encephalitis syndrome in adults. *International Journal of Scientific Study*. 2016;3:78–83. http://www.ijss-sn.com/uploads/2/0/1/5/20153321/ijss_feb_oa16_2016.pdf
- Murhekar MV, Mittal M, Prakash JA, Pillai VM, Mittal M, Girish Kumar CP, et al. Acute encephalitis syndrome in Gorakhpur, Uttar Pradesh, India - Role of scrub typhus. *J Infect*. 2016;73:623–6. <http://dx.doi.org/10.1016/j.jinf.2016.08.014>
- World Health Organization. Acute Encephalitis Syndrome. Japanese encephalitis surveillance standards. January 2006. From WHO-recommended standards for surveillance of selected vaccine-preventable diseases. WHO/V&B/03.01 [cited 2016 Oct 14]. http://apps.who.int/iris/bitstream/10665/68334/1/WHO_V-B_03.01_eng.pdf
- Blacksell SD, Tanganuchitcharnchai A, Nawtaisong P, Kantipong P, Laongnualpanich A, Day NP, et al. Diagnostic accuracy of the InBios scrub typhus detect enzyme-linked immunoassay for the detection of IgM antibodies in northern Thailand. *Clin Vaccine Immunol*. 2016;23:148–54. <http://dx.doi.org/10.1128/CVI.00553-15>

Address for correspondence: Manoj V. Murhekar, National Institute of Epidemiology, Indian Council of Medical Research R-127, Tamil Nadu Housing Board, Ayapakkam Chennai 600077, India; email: mmurhekar@nieicmr.org.in

Human Infection with *Burkholderia thailandensis*, China, 2013

Kai Chang, Jie Luo, Huan Xu, Min Li, Fengling Zhang, Jin Li, Dayong Gu, Shaoli Deng, Ming Chen, Weiping Lu

Author affiliations: Third Military Medical University, Chongqing, China (K. Chang, J. Luo, H. Xu, M. Li, F. Zhang, J. Li, S. Deng, M. Chen, W. Lu); Shenzhen Academy of Inspection and Quarantine, Guangdong, China (D. Gu)

DOI: <https://doi.org/10.3201/eid2308.170048>

Burkholderia thailandensis infection in humans is uncommon. We describe a case of *B. thailandensis* infection in a person in China, a location heretofore unknown for *B. thailandensis*. We identified the specific virulence factors of *B. thailandensis*, which may indicate a transition to a new virulent form.

Burkholderia thailandensis is closely related to *B. pseudomallei*, the causative agent of melioidosis (1). *B. thailandensis* shares most virulence factors and extensive genomic similarity with *B. pseudomallei* but can be distinguished by its ability to assimilate arabinose and different rRNA sequences (2,3). Little is known about *B. thailandensis* infection in humans. Two case reports described soft tissue infection and pneumonia with sepsis in Thailand and the United States (4,5). We describe a clinical investigation of human infection with *B. thailandensis* in Chongqing, China.

In October 2013, a 67-year-old man in Chongqing was hospitalized with a 13-day history of fever, productive