Human Brucellosis, a Heterogeneously Distributed, Delayed, and Misdiagnosed Disease in China

To the Editor—Brucellosis is a common zoonotic disease worldwide [1]. The epidemiology of human brucellosis has drastically changed owing to changing sanitary and socioeconomic conditions, and the substantial increase in international travel. New foci of human brucellosis have emerged or reemerged, with brucellosis becoming a travel-related disease, particularly in nonendemic areas [2–4]. Awareness of the geographic distribution and characteristics of brucellosis is valuable not only for the disease control in endemic areas, but also for preventing and diagnosing travel-associated disease in nonendemic areas [5, 6].

To investigate the geographic distribution of the human brucellosis epidemic in China, data were extracted from the National Notifiable Disease Surveillance System and analyzed. From December 2004 to July 2010, 141 604 laboratory-confirmed cases were reported. A geographic distribution analysis showed that brucellosis is mainly distributed in some of the northern provinces of China. The 5 provinces with the highest incidence include Inner Mongolia (45.83%), Shanxi (13.94%), Heilongjiang (13.82%), Jilin (10.29%), and Hebei (6.31%); these provinces accounted for >90% of the reported cases. Nationwide, the annual incidence, at a county level, ranged from 0.00 to 1395.84 per 100 000 (Figure 1).

Timely diagnosis is important for treating brucellosis and preventing chronic infections [7]. We examined the case data for possible contributing factors to delayed diagnoses. Of these 141 604 confirmed cases, only 26.98% were diagnosed within 7 days of symptom onset, 43.83% within 14 days, and 2.39% longer than 6 months, indicating that a large proportion of the cases had a delayed diagnosis. Further analysis showed that the average diagnosis delay was shorter in the high-incidence areas than in the low-incidence areas (35 vs 59 days, $P < .001$), and shorter in urban areas than in villages (32.55 vs 40.62 days, $P < .001$). In addition, patients who traveled or migrated across provinces had longer delays than did patients residing within an area (43.54 vs 36.82 days, $P < .001$). These data indicated that diagnosis delays were multifactorial and may have contributed to the chronicity of brucellosis in some population segments.

Epidemiological information regarding 2060 cases were collected from brucellosis clinics and analyzed to investigate the reasons for the delays in diagnosis. Surprisingly, 57.62% of the patients had been misdiagnosed or suspected of having other diseases with similar clinical symptoms. Approximately 24.34% of the "delayed diagnosis" patients had traveled to or migrated from a high-risk area. All the patients had experienced direct contact with animals and/or consumed contaminated animal products prior to disease onset. The absence of characteristic symptoms and a general unawareness of epidemiological information contributed to the misdiagnoses.

The lack of typical clinical manifestations makes it difficult to diagnose brucellosis, primarily contributing to the misdiagnosis and delay. The availability of additional information regarding the geographic

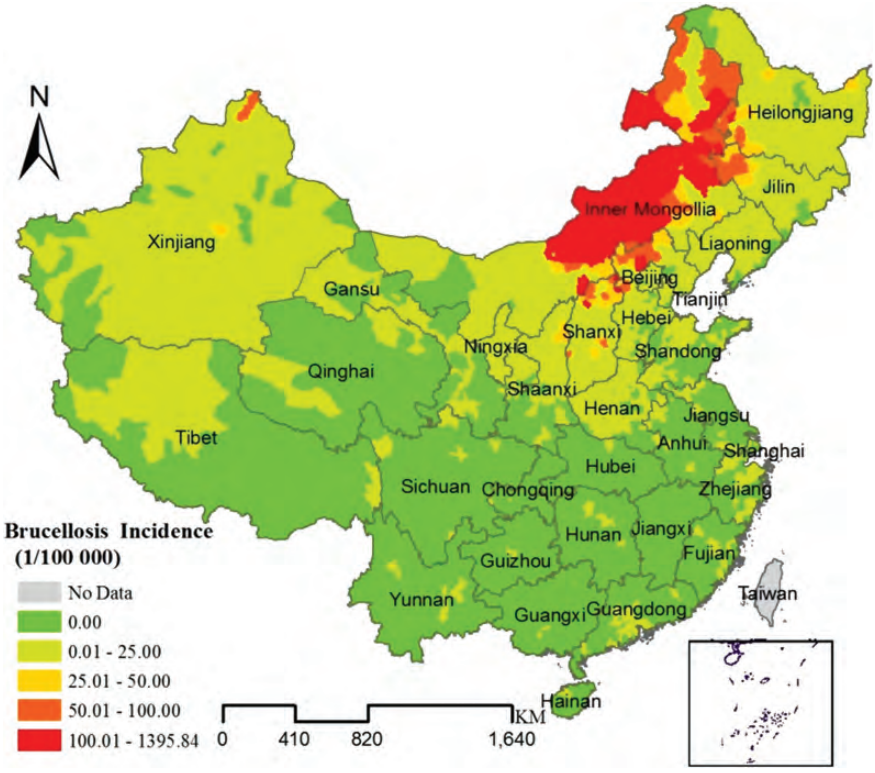

Figure 1. Geographic distribution and annual incidence of brucellosis, by province, in China. Geographic information of the confirmed cases was extracted. Average annual incidence for each county were calculated and mapped. Greatly higher incidences were observed in counties from some northern provinces of China.

distribution of the disease and its associated epidemiological information might help improve diagnosis. The presence of a fever of unknown origin, particularly when associated with travel to, or residence in, a high-risk region and contact with or consumption of products derived from potentially contaminated animals should alert health professionals to the possibility of brucellosis [2].

Notes

Financial support. This work was supported by National Basic Research Program of China (grant number 2009CB522602), National Natural Science Foundation of China (31000548, 31000041, 81071320, 81171530), National Key Program for Infectious Diseases of China (2013ZX10004-203, 2013ZX10004-217-002, 2013ZX10004805-006).

Potential conflicts of interest. All authors: No reported conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

Yufei Wang,[1,a] Wenyi Zhang,[1,a] Yuehua Ke,[1,a] Qing Zhen,[3] Xitong Yuan,[1] Wen Zou,[1] Shenlong Li,[1] Yingjie Sun,[4] Zhonghai Wang,[4] Dali Wang,[5] Buyun Cui,[2] Hongbin Song,[1] Liuyu Huang,[1] and Zeliang Chen[1]

[1]Institute of Disease Control and Prevention, Academy of Military Medical Science, and [2]National Institute for Communicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention, Changping, Beijing; [3]Department of Epidemiology and Biostatistics, Key Laboratory of Zoonosis, Ministry of Education, School of Public Health, Jilin University, Changchun, [4]Songyuan Centers for Disease Control and Prevention, Songyuan, and [5]Plague and Brucellosis Prevention and Control Base, Chinese Center for Disease Control and Prevention, Baicheng, Jilin, People's Republic of China

References

1. Pappas G, Papadimitriou P, Akritidis N, Christou L, Tsianos EV. The new global map of human brucellosis. Lancet Infect Dis **2006**; 6:91–9.
2. Memish ZA, Balkhy HH. Brucellosis and international travel. J Travel Med **2004**; 11: 49–55.
3. Egli A, Khanna N, Schmid T, Rudin S, Frei RBlaich A. Recurrent fever after a holiday in Turkey. BMJ **2011**; 343:d7832.
4. Chuang YC, Chen SC, Mu JJ, et al. Brucellosis, Taiwan, 2011. Emerg Infect Dis **2011**; 17:2374–5.
5. Fosgate GT, Carpenter TE, Chomel BB, Case JT, DeBess EE, Reilly KF. Time-space clustering of human brucellosis, California, 1973–1992. Emerg Infect Dis **2002**; 8:672–8.
6. Flores-Figueroa J, Okhuysen PC, von Sonnenburg F, et al. Patterns of illness in travelers visiting Mexico and Central America: the GeoSentinel experience. Clin Infect Dis **2011**; 53:523–31.
7. Drapkin MS, Kamath RS, Kim JY. Case records of the Massachusetts General Hospital. Case 26–2012. A 70-year-old woman with fever and back pain. N Engl J Med **2012**; 367:754–62.

[a]Y. W., W. Zhang, and Y. K. contributed equally to this work. Correspondence: Zeliang Chen, Institute of Disease Control and Prevention, Academy of Military Medical Science, No. 20, Dongdajie, Fengtai District, Beijing 100071, PR China (zeliangchen@yahoo.com).

Clinical Infectious Diseases 2013;56(5):750–51

DOI: 10.1093/cid/cis980