Window of Treatment Initiation for Human Brucellosis, Implications for Treatment Efficacy, and Prevention of Chronic Infection

To the Editor—Brucellosis is a common zoonotic infectious disease, with >500 000 new cases reported annually worldwide [1, 2]. Brucellosis is caused by the intracellular bacterial pathogen *Brucella*.
Because of *Brucella*’s unique interaction with the human immune system, brucellosis is prone to become a chronic infection, which is difficult to cure. Timely diagnosis and treatment are considered to be the most efficient strategies to prevent chronic infections [3]. Although several treatment regimens have been recommended [4], treatment failure and relapse occur at high frequency [5], resulting in increased medical cost and patient suffering [1]. Whether the treatment delay results in treatment failure and relapse remains unknown, and the optimal treatment initiation time will be valuable for efficient treatment and prevention of chronic infection.

To analyze the treatment delay, we first examined the distribution of time to treatment among 160,826 cases of brucellosis reported in the national surveillance system of China from January 2005 to July 2010. Average time from onset of symptoms to initiation of treatment was 36.82 days. Of these, 929 patients were treated with streptomycin plus tetracycline for 6 weeks. Patients were followed up for regimen adherence, recovery, alleviation of symptoms, and relapse. A total of 793 patients completing the full treatment course were included for treatment efficacy analysis. Cure rates decreased with increasing time to treatment (Figure 1). Time to treatment was inversely correlated with cure rate ($P < .001$). When the time to treatment is $>2$ months, the cure rate is significantly lower than that for treatment within 2 months (46.51% vs 87.43%, $P < .001$). Cure rates showed a larger decrease with $>3$ months of time to treatment as compared to $<3$ months (38.18% vs 85.06%, $P < .001$).

Based on the above results, human brucellosis treatment delay exists in a great proportion of patients. Approximately 8% of the patients were treated 3 months after the onset of symptoms. This is consistent with the average of relapse incidence [5]. As shown by our subsequent observational study, treatment delay resulted in decreased cure rate. Therefore, there is an optimal treatment window of 3 months for human brucellosis. Treatment onset after 3 months usually resulted in a significantly lower cure rate. In addition to the treatment delay, we also found that other factors are involved in the treatment failure, including shortened treatment course, abandonment after alleviation of symptoms, or improvement of disease. Therefore, we suggest to clinicians that the treatment window is important for human brucellosis.

**Notes**

**Financial support.** This work was supported by the National Basic Research Program of China (grant number 2009CB522602), National Natural Science Foundation of China (31000548, 31000041, 81071320, 81171530, 31272592), and National Key Program for Infectious Diseases of China (2013ZX10004-203, 2013ZX10004-217-002, 2013ZX10004-4805-006).

**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.

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Clinical Infectious Diseases 2013;56(9):1350–2
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DOI: 10.1093/cid/cit014