of inappropriate antibiotic therapy for ASB.

**Note**

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

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**Seasonal Amplitude of Hemorrhagic Fever With Renal Syndrome in China: A Call for Attention to Neglected Regions**

**To the Editor—**Hemorrhagic fever with renal syndrome (HFRS), a rodent-borne viral disease characterized by fever, hemorrhagic, kidney damage, and hypotension, is caused by different species of hantaviruses [1]. Every year, HFRS affects thousands of persons in Asia, and >90% of cases are reported in China [2, 3]. Owing to its high fatality rates, HFRS has attracted considerable research attention, and prior studies have focused predominantly on quantifying HFRS morbidity [4], identifying high-risk areas [5] and populations [6], or exploring peak time of HFRS occurrence [3]. To our knowledge, no study to date has assessed the seasonal amplitude of HFRS in China, even though it reveals the seasonal fluctuation and thus may provide pivotal information on the possibility of HFRS outbreaks.

We collected data on monthly HFRS cases in 30 provinces of China from January 2005 to December 2013, and used a cosinor function combined with Poisson regression to quantify the seasonal parameters of HFRS, namely, peak time, trough time, and seasonal amplitude [7]. The seasonal amplitude was expressed as a proportion of mean HFRS cases to facilitate the comparisons between different provinces. We excluded 3 provinces (Qinghai, Ningxia, and Hainan) from the seasonal amplitude analysis because of very limited number of cases (<1 case annually). We also quantified the incidence of HFRS in each province, and we compared it with the spatial patterns of HFRS seasonal amplitude. We collected climatic (temperature, humidity, and rainfall) and geographic (latitude and longitude) data for each province and used regression tree analyses [8] to identify the putative drivers of HFRS incidence, peak time, trough time, and seasonal amplitude.

Figure 1 shows the spatial patterns of HFRS incidence and seasonal amplitude, revealing that HFRS occurred mainly in East China from January 2005 through December 2013. The comparison between HFRS incidence and seasonal amplitude shows that the seasonal fluctuation was very high in some provinces with a low or moderate incidence, such as Beijing, Hebei, Gansu, and Jiangsu. In contrast, although the incidence of HFRS was very high in Northeast China (eg, Heilongjiang, Jilin, and Liaoning), the seasonal amplitude there was moderate or low, indicating that the occurrence of HFRS in these regions was relatively consistent across different months and thus easier to predict. Unlike the high-incidence-but-low-amplitude provinces, Shaanxi had not only a high incidence of HFRS but also high seasonal amplitude. Results from the regression analyses suggest that longitude (threshold, 118° 0′) was associated with HFRS incidence, and latitude was associated with both peak time (threshold, 37° 3′) and trough time (threshold, 28° 54′) for the disease (Figure 1), with HFRS peaking earlier at higher latitudes (January–March) than at lower latitudes (November–December).

The great seasonal fluctuation in HFRS that we detected in Beijing echoes findings of another study [9], even though the underlying mechanism remains largely unclear. Currently, the majority of HFRS control and prevention resources have been allocated to Northeast China, given
its high HFRS incidence. However, some other provinces (eg, Hebei, Gansu, and Jiangsu) are neglected, and our findings indicate that they should receive much more attention. The longitude and latitude thresholds that we observed for HFRS incidence and peak times have practical implications for the development of future HFRS control and prevention measures.

Notes

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References

Uncultured Candidatus Neoehrlichia Mikurensis

TO THE EDITOR—I read with interest the article of Grankvist et al reporting new cases of infections caused by Candidatus Neoehrlichia mikurensis [1]. This bacterium had been detected several times before this name was proposed. It was found by molecular biology, initially in ticks in Holland in 1999 [2], then in Russia [3], then my laboratory detected it and proposed the name of Candidatus Ehrlichia walkerii [4], as we had not succeeded in cultivating it. Since then, this bacterium was renamed Candidatus Neoehrlichia mikurensis in 2004 and still has not been cultivated. It does not have an established species name because of this, culture failure explains the several successive names that were proposed. This present work is interesting because it highlights that this bacterium may not be rare in immunocompromised hosts in Europe [1]. Infection by this uncultured bacterium is difficult to diagnose because it relies only on the amplification and sequencing of the 16S ribosomal DNA gene. Indeed, this molecular method is less sensitive than specific gene detection by real time quantitative polymerase chain reaction for the diagnosis of intracellular bacterial infection in the blood [5]. This work passed an important remark, that the bacterium is described as being noncultivable [1]. This is erroneous; it is simply uncultivated, and we have good reason to think that, in the very near future, it will be cultivated. When a strain is established, it will become possible to name it, to test patients serologically, to use specific molecular tests, and to test the specific sensitivity to antibiotics for this bacterium. This study highlights how culture is still the key to diagnosis and treatment of bacterial infections.

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