Nonnegligible Seroprevalence and Predictors of Murine Typhus, Japan

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DOI: https://doi.org/10.3201/eid3002.230827

To the Editor: I was impressed by the recent publication by Aita et al. who reported a surprisingly high seroprevalence rate for *Rickettsia typhi* within resident populations on Honshu Island, Japan (*1*). The authors pointed out the possibility of murine typhus reemergence in Japan, where the disease has been reported only sporadically (*2*). However, the conclusions might be premature because the study was cross-sectional, and only 1 timepoint was evaluated. Many cases of murine typhus could have occurred in the distant past, which might not be reflected in this type of study. A previous study in Spain showed a high incidence rate in patients who were much younger (mean age of ≈46 years) (*3*) than those reported in this study (mean age of 67 years). A study in Greece showed frequent epidemiologic links to flea exposure (*4*), but the study in Japan did not investigate this apparent risk factor. I do not believe that age-related differences in flea exposures exist in Japan; hence, it is likely that exposures might have occurred in the past, when persons in Japan had a lower standard of hygiene. According to another study, the median half-life of *R. typhi* IgG was 177 days, and the median IgG titer was 800 at day 365 postinfection, suggesting long-lasting seropositivity (*5*). Therefore, the relatively stringent cutoff value of *R. typhi* serology in this study (*1*) could have overestimated the prevalence. To demonstrate that murine typhus is indeed a reemerging disease in Japan, further actual cases in Japan need to be identified, or similar seroprevalence studies should be repeated in other regions to determine trends in *R. typhi* seropositivity.

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DOI: https://doi.org/10.3201/eid3002.231465

In Response: We thank Dr. Iwata (*1*) for his remarks regarding our study of seroprevalence and predictors of murine typhus in Japan (*2*). In reference to long-term seropositivity, high seroprevalence of *Rickettsia typhi* might reflect distant past murine typhus (MT) infections rather than recent infections (*2*). We acknowledge the significance of this limitation in interpreting our results, which we first addressed in a preprint of the article (T. Aita et al., unpub. data, https://doi.org/10.1101/2023.01.12.2328449). Nonetheless, we posit that *R. typhi* seroprevalence would include some persons who have recently experienced MT. First, participants with remarkably high *R. typhi* IgG titers probably had recent MT infections, because *R. typhi* IgG titers generally undergo a continuous postinfection decline in diagnostic serologic assays. The percentage of persons with antibody titers of ≥1:3,200 in an indirect immunofluorescence assay was ≈85% at 4 weeks postinfection but decreased to ≈25% within 1 year (*3*). In addition, antibody titers continued to decrease over 3 years postinfection in an

enzyme-linked immunosorbent assay (*4*). In our study, using an indirect immunoperoxidase-based assay, 20 participants exhibited notably high antibody titers (1:1,280 to ≥1:40,960). Second, despite raising the diagnostic cutoff from 1:40 to 1:160, the preeminence of *R. typhi* seroprevalence persisted over that of *Orientia tsutsugamushi* (*2*), the causative agent of scrub typhus, which is the most frequent endemic rickettsiosis in Japan. Thus, excluding many persons with distant past infections did not influence the study's conclusion that *R. typhi* seroprevalence was significantly higher than that of *O. tsutsugamushi*. Therefore, the higher *R. typhi* seroprevalence indicates not only prolonged seropositivity but also recent *R. typhi* infections.

In conclusion, although Dr. Iwata's commentary is pivotal for a more precise interpretation of our results, our study indicates the occurrence of recent MT cases in Japan. We aim to elucidate this potential MT reemergence by conducting a case-based prospective study.

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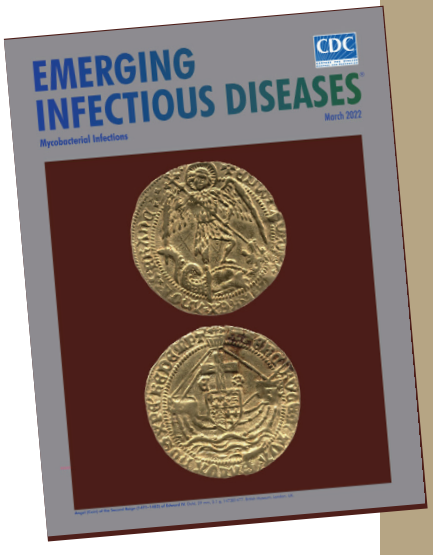

Originally published in March 2022

etymologia revisited

Schizophyllum commune

[skiz-of′-ĭ-ləm kom′-yoon]

Schizophyllum commune, or split-gill mushroom, is an environmental, wood-rotting basidiomycetous fungus. *Schizophyllum* is derived from "*Schíza*" meaning split because of the appearance of radial, centrally split, gill like folds; "*commune*" means common or shared ownership or ubiquitous. Swedish mycologist, Elias Magnus Fries (1794–1878), the Linnaeus of Mycology, assigned the scientific name in 1815. German mycologist Hans Kniep in 1930 discovered its sexual reproduction by consorting and recombining genomes with any one of numerous compatible mates (currently >2,800).

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