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**Reply**

Sir—We thank Drs. Mary and David Warrell [1] for noting the error in the percentage of patients with seroconversion presented in table 2 of our article [2]; the rate should have appeared as 27%, not 7%. On day 7 of the regimens, the levels of neutralizing antibodies (NAbs) in all patient groups ranged from undetectable to 0.4 IU/mL (geometric mean titer [GMT], 0.04 IU/mL) [3]. This titer is 10 times lower than the lowest acceptable titer (0.5 IU/mL) recommended by the World Health Organization (WHO) [4, 5].

In our study (F.K., H.W., Tepsumethanon S, Limusanno S, Tantawichien T, Wangroonsur Y, unpublished data), we compared levels of NAbs in patients on days 0, 5, 7, and 14 of each of the 4 regimens followed. The regimens included the Essen regimen, the Thai Red Cross regimen (TRC-ID), the Oxford 8-site regimen, and the “double-dose” TRC-ID (for dosages, see [2]). On day 5 of the regimens, NAb levels were undetectable. On day 7 of the regimens, the GMT was only 0.13 IU/mL (range, 0.03–0.5 IU/mL) in the group receiving the 8-site intradermal regimen. We suggest that these NAb levels are unlikely to intercept the virus before it enters the peripheral nerves [6]. If rabies immunoglobulin (RIG) was unavailable, use of the 8-site regimen was recommended by the WHO, but they cited no scientific evidence to support this recommendation [4].

We had reservations when Briggs et al. [7] performed a study in which only 0.1 mL of vaccine was used per injection site, rather than the WHO-recommended dose of 0.2 mL of vaccine from 1.0 mL of reconstituted purified chick embryo vaccine [7]. TRC-ID was developed for the use of purified Vero cell vaccine that is reconstituted in 0.5 mL of saline. Both vaccines have approximately equivalent antigen contents (6–14 IU), amounts that are several times greater than the WHO-recommended level of 2.5 IU. Briggs et al. [7], nevertheless, demonstrated that their vaccine regimen had good immunogenicity. This led to early application of TRC-ID with 0.1 mL of purified chick embryo vaccine per intradermal dose. There were no treatment failures among 7227 patients treated in a province in which canine rabies was endemic [8]. Only 216 (3%) of these 7277 patients also received RIG.

Unlike the Warrells, we are not aware of any confusion about these issues in Thailand. This country used TRC-ID for 5 years before it became the first intradermal regimen approved by WHO (in 1992). Use of this regimen made abolition of the use of neural rabies vaccines possible in 1992. We are convinced that RIGs will remain essential biological products. Further manipulation of vaccine administration schedules will not abolish the need to use these vaccines for optimal postexposure treatment, and we hope that an affordable immunoglobulin will soon reappear in the international marketplace.

**References**


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**Is There Hope for the Prevention of Future Antimicrobial Shortages?**

Sir—Shlaes and Moellering [1] recently described the impact of using a 10% delta for the lower limit of the 95% CI for clinical trials of noninferiority when a newly developed antibiotic is compared with a previously approved agent. The authors discussed the high number of patients required for statistically significant data in clinical trials that use a 10% delta, and they accurately described the impracticality of conducting a clinical trial using a 10% delta for an infection such as acute meningitis, for which >700 patients would be needed. Such a trial would require a large number of sites and would take several years to complete. Shlaes and Moellering [1] emphasized that the costs of conducting such a study and the potentially low financial return to the sponsor are

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