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Reply to Willoughby

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We thank Willoughby for his thoughtful comments regarding rabies post-exposure prophylaxis (PEP) schedules for elderly persons [1]. Indeed, people are living longer, some with health conditions or treatments that can negatively impact vaccination response.

Over the past 30 years, among an estimated 1.8 million people in the United States who received modern cell-culture rabies vaccines as part of rabies PEP, no breakthrough infections attributed to being elderly were identified [2]. While it is true that a recent systematic review that evaluated the immunogenicity after rabies vaccines [3] found that the geometric mean titer (GMT) after rabies vaccinations is lower for persons aged >60

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years compared with younger persons, the median peak GMT among these persons was still substantially higher (13.2 IU/mL) than the Advisory Committee on Immunization Practices (ACIP) targeted antibody titer of 0.5 IU/mL [4]. In the absence of an immunocompromising condition, being elderly alone does not appear to be a risk factor for suboptimal immune responses after rabies vaccination. The same publication identified the GMT after intramuscular administration of rabies vaccines to be higher for longer periods of time than those after intradermal administration. Since rabies vaccines in the United States are administered intramuscularly, these data further indicate that the vaccination strategy facilitates appropriate GMTs in elderly persons. While data indicate that it takes longer (42 days vs 30 days) to reach peak levels among older persons compared with younger persons, the wide availability of rabies immune globulin in the United States is further expected to facilitate adequate protection.

In addition to the currently recommended vaccination schedule likely being effective for elderly persons, the costs of titer checks for elderly persons may be a deterrent if such a broad recommendation were made. As Willoughby emphasizes, nearly 25% of people receiving PEP in the United States are likely aged >65 years. However, if all approximately 15 000 elderly PEP patients were to receive an antibody titer (estimated at $400 in medical-associated costs from a commercial laboratory), this recommendation would result in an additional $180 million in titer-related costs over 30 years. Research for alternate rabies vaccine schedules and development of future rabies vaccines for humans and animals should continue. However, at present, the current vaccines have proven efficacious. Developing a messenger RNA (mRNA) vaccine for approximately 60 000 patients per year is unlikely; this would involve multiyear clinical trials, US Food and Drug Administration approvals, and ACIP guidelines. With an estimated 30 million people getting rabies PEP globally, perhaps mRNA vaccine development holds more promise from a global approach [5].

The concern of an expanding elderly population in the United States deserves more attention. To prevent host-mediated vaccine failures, we should expand our understanding of the efficacy of vaccines in elderly populations, improve our understanding of commonly overlooked immunological disorders in this population, and provide clinician education regarding when titers are necessary. With the limited data available and the rarity of rabies vaccine failure, we reiterate our suggestion that persons with concerning rabies exposures be evaluated, regardless of age, for immunocompromise.

Potential conflicts of interest.

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