

Commentary

Human rabies, a disease of the poor — also in travelers?

Claudius Malerczyk

Medical Affairs Region Europe and International,
Novartis Vaccines & Diagnostics, Marburg, Germany

Invited Commentary on 'Imported human rabies cases worldwide, 1990–2012', Carrara et al.

Like other neglected zoonotic diseases, rabies is a disease of the poor. Of the worldwide estimated 55 000 human deaths, the majority of deaths occur in developing countries where rabies is endemic. India alone, for instance, accounts for about 20 000 annual human death cases. In particular, it is the less wealthy and less well-educated individuals that for a variety of reasons fail to seek the proper medical treatment after an exposure. However, an exposure in a rabies-endemic country may occur not only to local residents but also to travelers, and awareness among travelers from countries, where rabies is much less in focus, has led to deaths. We have published a list of 42 rabies cases in travelers from Europe, North America, or Japan to rabies endemic countries between 1990 and 2010. The majority of these travelers have been exposed in countries of Asia, Africa, or Latin America and unsurprisingly almost all of the individuals did not receive appropriate post-exposure prophylaxis (either not seeking medical attention or vaccination being withheld or incomplete).¹ Carrara and co-workers expand the list to worldwide cases between 1990 and 2012, adding a number of cases that we did not mention.² While it can be debated, who to include in such a survey (e.g. whether to include only travelers crossing state borders, or only crossing continents, etc.), the circumstances of the cases are similar. There are some distinct features that these may have in common, noteworthy of being discussed:

1. A significant proportion of the cases listed by Carrara *et al.* were observed in migrants or their descendants, or after a trip to visit friends and relatives (VFRs) (more than 40%).
2. Human cases also have occurred when the duration of the trip was short, potentially 2 weeks or less. This, in our opinion, questions previous

recommendations that pre-exposure vaccination should be considered only to long-term travelers or expatriates.

3. In endemic countries — except for maybe China — rabies is a disease of children. More than 50% of human rabies deaths are seen in children below the age of 15.³ This is usually less the case in travelers, and in our opinion, can be explained by the fact that the percentage of children among travelers is less than in a 'general population'. In addition, while children in their home surrounding play outside with animals — often without parental observation — in a travel situation, this may be different.
4. Even if travelers are aware of the risk of rabies, they may face difficulties in getting the necessary post-exposure prophylaxis (PEP). After a bite, they all of a sudden have to find the nearest hospital where high quality vaccine and rabies immunoglobulin (RIG) are available. This may not be the case everywhere, especially in rural areas. And RIG in particular may not be available at all or difficult to find. This is another good reason for pre-exposure prophylaxis before starting the journey, as it eliminates the need for RIG.

As a side note, for travelers from developed countries, pre-travel medical advice often includes rabies pre-exposure prophylaxis. Consequently, the percentage of travelers to a highly endemic country with a complete series of rabies shots may be higher than in the actual population residing in the country. Frequently travelers seek medical attention quite late before starting their journey, and for these individuals, a regular pre-exposure regimen may not be optimal, as it requires a period of 21 or 28 days to complete the necessary series of three vaccinations. Assuming adequate antibody levels are to be reached 1 week after the last dose, vaccination should be started 4 to 5 weeks before travel, which may be too long ahead of time, not only for last-minute travelers. An abbreviated traveler's regimen would be of advantage, e.g. completing a series of three injections within a shorter time frame, for instance, within 14 days or even 1 week. The Essen PEP Regimen is a good example that this can work. The first three doses are given on days 0, 3, and 7 and by day 14, usually an immune response of 0.5 IU/ml is achieved, which is considered adequate for protection.^{4,5} Whether these titers are maintained as long as with conventional pre-exposure schedules needs to be further investigated.

In any case, as important and tragic every human case in travelers is, the majority of travelers exposed to a suspect rabid animal, typically seek medical attention, and thus get proper PEP. Those contracting

Correspondence to: C. Malerczyk, Novartis Vaccines & Diagnostics GmbH, Emil-von-Behring-Str. 76, 35041 Marburg, Germany. Email: claudius.malerczyk@novartis.com

rabies are the travelers who are not reached by awareness campaigns by pre-travel advice or prophylactic vaccination, e.g. migrants or VFRs. In this regard, rabies in travelers is not different from rabies in residents: A lot of education and awareness are necessary and efforts have to be undertaken to reach those at highest risk.

References

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