Perspectives: Alternative Approaches to Rabies Immunization

Few topics in travel medicine prompt more concern and persistent questions than the prevention of rabies in travelers. Although we understand the basics of rabies prevention for travelers, the logistics of providing this care in a timely fashion remain a challenge. Unimmunized travelers who are exposed to rabies and other lyssaviruses require proper wound care, infiltration of human rabies immune globulin (RIG), and a series of 4 or 5 doses of rabies vaccine intramuscularly over a 2- to 4-week period. Travelers who receive 3 doses of rabies vaccine before travel need to receive 2 more doses of rabies vaccine, 3 days apart, after a viral exposure. Notably, human RIG and equine RIG are often unavailable in developing countries, although modern cell-culture rabies vaccines are increasingly available. Thus, preexposure rabies immunization can facilitate the traveler's access to adequate postexposure rabies prophylaxis.

Limiting the uptake of preexposure rabies immunization has been the cost of the vaccine in developed countries and the need for 3 clinic visits prior to travel. Three IM doses of rabies vaccine in the United States can now exceed $1,000 in cost. Even when modern cell-culture rabies vaccine was first introduced, at approximately $45 per dose in the early 1980s, many people already considered the vaccine too expensive. Thus, intradermal (ID) rabies immunization began almost as soon as the intramuscular (IM) human diploid cell vaccine (HDCV) was manufactured. By reconstituting the 1.0 mL of vaccine in the vial, practitioners could draw up approximately eight 0.1-mL doses. One problem was that the entire vial had to be used within a few hours of reconstituting, meaning that a provider had to either be in a busy clinic or line up groups of people, such as families, for rabies immunization at the same time.

Early studies of the immune response to ID rabies vaccine, using HDCV and later other rabies vaccines, were uniformly encouraging. Virtually 100% of vaccinees seroconverted. A 1982 statement by the US Advisory Committee on Immunization Practices (ACIP) reviewed data on >1,500 vaccinees and declared, "It appears that, with this vaccine, the 0.1-mL ID regimen is an acceptable alternative to the currently approved 1.0-mL IM regimen for preexposure prophylaxis." They called upon manufacturers to produce a product with appropriate packaging and labeling.

In 1986, the Mérieux Institute (now Sanofi Pasteur) received approval to market a 0.1-mL dose in an individual syringe. Sharing reconstituted vials of 1.0 mL between patients remained off-label. Although the new product solved the logistical problem of providing individual travelers with an ID dose, the cost of the prepackaged ID dose was 75% of the full 1.0-mL IM dose.

ACIP continued to endorse the concept of ID preexposure rabies immunization in a 1999 statement on rabies prevention. However, 3 lots of a prepackaged rabies ID vaccine were recalled in 2000 for having a potency that fell below the specification level before the expiration date. In 2001, the ID rabies vaccine was withdrawn from the market. Since then, authorities in the United States have not recommended sharing 1.0-mL vials for ID rabies immunization, as the manufacturer has not applied for the appropriate packaging and labeling to the Food and Drug Administration. This lack of endorsement of ID preexposure immunization has frustrated some travel medicine professionals.

With 2 decades more experience in using ID preexposure rabies immunization, the concept is fairly well accepted, but it remains off-label in the United States. Many clinics relying on preexposure ID dosing require the travelers to have a titer drawn after the series is completed to confirm seroconversion. This may save some money but requires a fourth clinic visit and even more time before travel.

Additional approaches have been taken to postexposure immunoprophylaxis, mainly driven by availability and cost of vaccine in resource-poor countries. Multi-dose ID and other abbreviated schedules have been used. From the point of view of the traveler, perhaps the best strategy would be to try to use postexposure regimens that are approved in the traveler's home country. This could create the most confidence and make it easier to complete regimens that have been started abroad in one's home country.

In late 2017, a World Health Organization (WHO) expert committee surprised many travel medicine practitioners by endorsing a 2-dose rabies preexposure immunization schedule. Although there have been some studies in limited numbers of subjects that support the notion that 2 doses may be adequate, the announcement seemed premature to some experts. In addition, WHO endorsed the use of wound-only administration of rabies immune globulin (RIG), an immunoglobulin-sparing technique in which RIG is injected around the wound (not to exceed the weight-calculated amount) but where the remaining calculated dose is not administered intramuscularly. This idea makes pathophysiologic sense, but there are many potential variables. Technique of the person injecting the RIG will be critical. With little written guidance available, some vaccine recipients may receive as little as 0.5 mL of RIG (in a small finger wound, for example), which may be <5% of historically recommended doses.

In the United States, practitioners should await ACIP and CDC guidance before adopting these new WHO recommendations. In the meantime, practitioners may face some challenging situations—treating people with a bite exposure who may have received the 2-dose preexposure regimen and having to decide how to proceed.

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Notes

Perspectives sections are written as editorial discussions aiming to add depth and clinical perspective to the official recommendations contained in the book. The views and opinions expressed in this section are those of the author and do not necessarily represent the official position of CDC.

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However, rabies vaccine adsorbed (RVA, Bioport Corporation) is no longer available for rabies postexposure or pre-exposure prophylaxis, and intradermal pre-exposure prophylaxis is no longer recommended because it is not available in the United States. Introduction. Rabies is a zoonotic disease caused by RNA viruses in the Family Rhabdoviridae, Genus Lyssavirus (1--4). Virus is typically present in the saliva of clinically ill mammals and is transmitted through a bite. After entering the central nervous system of the next host, the virus causes an acute, progressive encephalomyelitis that is al Forty-five persons severely bitten by rabid dogs and wolves in Iran were treated after exposure with a new rabies vaccine produced in cultures of human diploid cells. All except one also received one injection of rabies immune serum. This treatment, in contrast to past experience with other vaccines, resulted in protection of all individuals against rabies. Thus, almost a century after the postexposure treatment of humans was initiated, an effective tool for protecting man against rabies has finally been developed. Beran J, Honegr K, Banzhoff A, Malerczyk C. Potency requirements of rabies vacc Questions and answers (Q&As) about rabies vaccines and vaccination from IAC's immunization experts. Ninety-three percent of rabid animals were wildlife, with bats the most frequently reported animal in the United States at 33% of all reported rabid animals. In the last 100 years, the number of human deaths from rabies in the United States has fallen from 100 or more per year to an average of 2 or 3 per year. This decline is due to both the improved control and vaccination of domestic animals and to the development of effective postexposure treatment and vaccines.