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The Global Availability of Rabies Immune Globulin and Rabies Vaccine in Clinics Providing Direct Care to Travelers†

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Background. Rabies, which is globally endemic, poses a risk to international travelers. To improve recommendations for travelers, we assessed the global availability of rabies vaccine (RV) and rabies immune globulin (RIG).
Methods. We conducted a 20-question online survey, in English, Spanish, and French, distributed via e-mail to travel medicine providers and other clinicians worldwide from February 1 to March 30, 2011. Results were compiled according to the region.
Results. Among total respondents, only 190 indicated that they provided traveler postexposure care. Most responses came from North America (38%), Western Europe (19%), Australia and South and West Pacific Islands (11%), East and Southeast Asia (8%), and Southern Africa (6%). Approximately one third of 187 respondents stated that patients presented with wounds from an animal exposure that were seldom or never adequately cleansed. RIG was often or always accessible for 100% ($n = 5$) of respondents in the Middle East and North Africa; 94% ($n = 17$) in Australia and South and West Pacific Islands; 20% ($n = 1$) in Tropical South America; and 56% ($n = 5$) in Eastern Europe and Northern Asia. Ninety-one percent ($n = 158$) of all respondents reported that RV was often or always accessible. For all regions, 35% ($n = 58$) and 26% ($n = 43$) of respondents felt that the cost was too high for RIG and RV, respectively.
Conclusion. The availability of RV and RIG varied by geographic region. All travelers should be informed that RIG and RV might not be readily available at their destination and that travel health and medical evacuation insurance should be considered prior to departure. Travelers should be educated to avoid animal exposures; to clean all animal bites, licks, and scratches thoroughly with soap and water; and to seek medical care immediately, even if overseas.

Rabies is an acute, progressive, nearly universally fatal encephalomyelitis caused by neurotropic viruses (family *Rhabdoviridae*, genus *Lyssavirus*); transmission usually occurs through the bite from a rabid mammal. While rabies has one of the highest case-fatality ratios of any infectious disease, it is highly preventable with appropriate postexposure prophylaxis (PEP), which includes thorough wound washing and timely infiltration with rabies immune globulin (RIG) and administration of a series of rabies vaccine (RV) doses. An accurate rate of possible rabies exposures in travelers has not been calculated, although a recent study estimated from PEP records that 0.4% (range 0.01%–2.3%) of travelers receive an at-risk bite per month residence in a rabies-endemic country.[1] Canine rabies-endemic countries (ie, Africa, Asia, and parts of the Americas) remain the highest risk to most travelers.[2]

†The results of this study were presented at the XXII Rabies in the Americas Conference, October 16–21, 2011, San Juan, Puerto Rico.

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Health care providers advising travelers pre-travel to rabies-endemic areas might recommend rabies preexposure vaccination for certain travelers engaging in activities that may increase contact with wildlife (particularly bats) or staying in country for extended periods of time. However, even in industrialized countries, periodic supply limitations of RV can influence prioritization for preexposure vaccination. During periods of limited RV supply in the United States (eg, during 2008–2009), travelers who want or need preexposure vaccination may be assigned lower priority to ensure adequate vaccine for PEP and persons with high-risk occupational exposures (ie, rabies diagnostic laboratory workers).[3]

Currently, only human RIG (HRIG) products are licensed in the United States. While HRIG is the preferred product for PEP, it is expensive and typically in chronic limited supply, especially in nonindustrialized countries with the highest rabies burden. Equine RIG (ERIG) is used worldwide and is available in both purified and unpurified forms. Purified ERIG has a reported incidence of causing signs consistent with serum sickness ranging from 0.8% to 6%.[4] In contrast, unpurified ERIG has a reported incidence of causing signs consistent with serum sickness ranging from 15% to 46%.[4] World Health Organization (WHO) recommends that whenever ERIG is used appropriate precautions concerning anaphylaxis are taken. In the United States, two human RVs are licensed for preexposure vaccination or PEP use: human diploid cell and purified chick embryo cell.[5] Worldwide, these and other modern cell culture-based rabies vaccines (eg, Vero cell and purified duck embryo cell) that meet minimum potency requirements are recommended by WHO for use in human rabies preexposure vaccination and PEP.[1] In contrast, nerve tissue vaccines (NTV), produced in animals, are still used in some countries, but are associated with high rates of adverse events; WHO has recommended their use be discontinued.

Even when RV is readily available in the United States, most US international travelers are unvaccinated.[6] As the availability of RIG and RV for travelers abroad remains largely unknown, it is crucial for US international travelers to have an understanding of whether the vaccine is available and type used at their destinations or have an emergency evacuation health plan in case of an exposure. We sought to describe the availability, type, and costs of RIG and RV for travelers by conducting a survey of travel medicine practitioners and other health care providers, to improve travel recommendations for international travelers.

Methods

We developed a web-based survey, called the Evaluation of the Global Availability of Rabies Immune Globulin and Rabies Vaccine for Travelers: Direct Care Survey, and distributed the hyperlink to members of a travel medicine professional organization, an international evacuation and travel health insurance company, and members of international professional organizations specializing in rabies and PEP care. These organizations were chosen because of their geographic diversity and because their members might provide direct rabies postexposure care to travelers. Specifically, the survey asked respondents to provide information about their clinic's experiences in treating patients in 2010. The survey was available in English, Spanish, and French and accessible from February 1 to March 30, 2011. Two reminder e-mails were sent to encourage participation. This survey was determined to be a nonresearch activity by the US Centers for Disease Control and Prevention (CDC) Human Subjects Advisors.

The survey contained approximately 20 questions, although the exact question count varied due to each participant's responses. Questions included whether the clinic evaluated patients for possible rabies exposure, whether they administered PEP, how accessible RIG and RV were when needed, the types of RIG and RV used, where travelers would be sent if RIG and RV were not available, and what barriers hindered obtaining the biologics. Accessibility was defined as being able to receive RIG or RV within 24 hours of the patient's seeking care for a potential rabies exposure.

Respondents were asked to register with a clinic name, city, and country. If more than one survey was completed for a clinic, one completed survey was randomly selected from each clinic. If two surveys were started by respondents from the same clinic, the more complete survey was retained. All identifying information was deleted before the analysis and results were compiled according to the region at the request of participants to ensure anonymity. The region classifications were those used previously for CDC Travelers' Health analyses, although some regions were combined if responses were limited. Data were described by using SAS 9.2 (SAS Institute, Cary, NC, USA) and ArcGIS (ESRI, Redlands, CA, USA).

Results

Approximately 5,314 surveys were distributed (Figure 1), but many surveys went to organization members who were not eligible for participation because they did not provide direct PEP patient care. This overdistribution was unavoidable because of inability of some participating organizations to distinguish their member's profession, current position, geographic location, or clinic services in e-mail listserv rosters. Therefore, the number of targeted individual e-mails was not known, and the survey distribution and subsequent response were understood to represent a convenience sample.

Although 341 persons started the survey, 41 surveys were excluded because of multiple responses per clinic ($n = 36$) or because no questions were answered ($n = 5$) (Figure 1). Further, only surveys from respondents indicating that they provided direct PEP patient care were included ($n = 190$; Figure 2). The largest number of responses came from North America (38%), Western

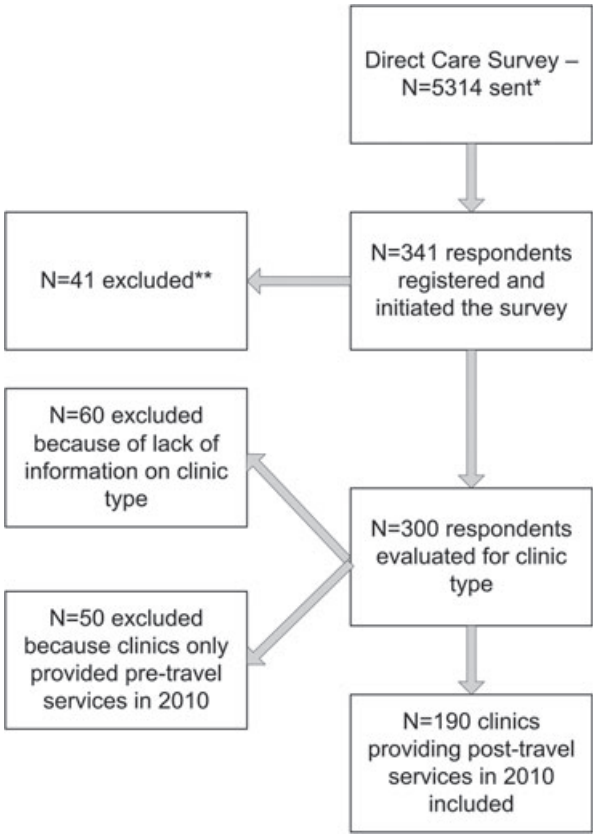

Figure 1 Direct care survey respondents to the Evaluation of the Global Availability of Rabies Immune Globulin and Rabies Vaccine for Travelers: Direct Care Survey, 2010. *Although 5,314 surveys were distributed by e-mail to the participating organizations, many surveys went to members of the organization that were not the target audience of the survey and that did not provide direct patient care. This was unavoidable as the organizations do not distinguish the member's profession or current position. The number of targeted individual e-mails is not known for an accurate response rate. Therefore, this survey distribution and response was understood to be a convenience sample. **Of the 41 that were initially excluded, 36 were excluded because of multiple clinic responses and 5 were excluded because although the respondent registered for the survey, no responses were recorded.

Europe (19%), Australia and South and West Pacific Islands (11%), East and Southeast Asia (8%), and Southern Africa (6%). Few respondents participated from clinics in West, Central, and East Africa, and Mexico, Central America, and the Caribbean regions, and none from clinics in the Indian Ocean Islands and Temperate South America.

Respondents reported that, in 2010, their clinics evaluated a median of 3,000 patients (range 12–90,000) for any inquiry or illness. Four clinics reported seeing over 50,000 patients a year: one each in Australia and South and West Pacific Islands ($n = 90{,}000$), Southern Africa ($n = 84{,}000$), North America ($n = 72{,}000$), and East and Southeast Asia ($n = 54{,}000$). Overall, a median of four patients per clinic (0–30,000) were administered PEP. Regions reporting the highest median number of patients that were administered PEP were South Asia (9 clinics, median = 400); West, Central, and East Africa (4 clinics, median = 15); and Southern Africa (11 clinics, median = 12).

The accessibility of RIG varied by region: RIG was often or always accessible for 100% ($n = 5$) of respondents in the Middle East and North Africa, 94% ($n = 17$) in Australia and South and West Pacific Islands, 91% ($n = 10$) in Southern Africa, and 89% ($n = 8$) in South Asia (Table 1; Figure 3a). Both clinics ($n = 2$, 100%) from Mexico, Central America, and the Caribbean and 80% ($n = 4$) of clinics from South America reported seldom or never having RIG accessible, respectively. Overall, the majority (76%; $n = 114$) of clinics reported using HRIG at their clinics (Table 1); 65 and 4% of these reported that an international pharmaceutical company or a local producer manufactured the HRIG, respectively (data not shown). However, 24% of those reporting the use of HRIG did not know the manufacturer. Of the clinics reporting the use of ERIG ($n = 15$), six also reported the use of HRIG. Clinics reporting only ERIG use were from South Asia ($n = 3$); Eastern Europe and Northern Asia ($n = 1$); Middle East and North Africa ($n = 2$); West, Central, and East Africa ($n = 1$); East and Southeast Asia ($n = 1$); and Tropical South America ($n = 1$). Of those using ERIG ($n = 15$), 80% reported using purified ERIG, 13% reported heat-treated digested ERIG FAB fragment, 7% reported heat-treated purified ERIG, and 7% reported not knowing the type of ERIG that was used. When asked where the travelers would be referred if RIG was not available, 63% ($n = 119$) of respondents reported that they would refer travelers to a clinic within the same city or elsewhere in their country, and 5% ($n = 9$) stated that they would refer only to clinics outside their country or send travelers back to their home country.

Ninety-one percent ($n = 158$) of all respondents reported that RV was often or always accessible (Table 2; Figure 3b). The use of human diploid cell and purified chick embryo cell vaccines was most common in North America (60 and 31% of respondents, respectively) and Western Europe (56 and 34%, respectively). Vero cell vaccine was the predominant vaccine reported in Asia and Africa. Four clinics, in Tropical South America ($n = 1$), Eastern Europe and Northern Asia ($n = 1$), and the Middle East and North Africa ($n = 2$), reported the continued use of NTV.

Most clinics (57%) responding to our survey indicated that they used the five-dose intramuscular administration schedule (Table 2). Thirty-two percent reported using the four-dose intramuscular administration schedule; 65% of these respondents were from North America. The Updated Thai Red Cross intradermal regimen was used by 56% of clinics in South Asia.

When asked where the travelers would be referred if RV was not available at their clinics, 69% ($n = 132$)

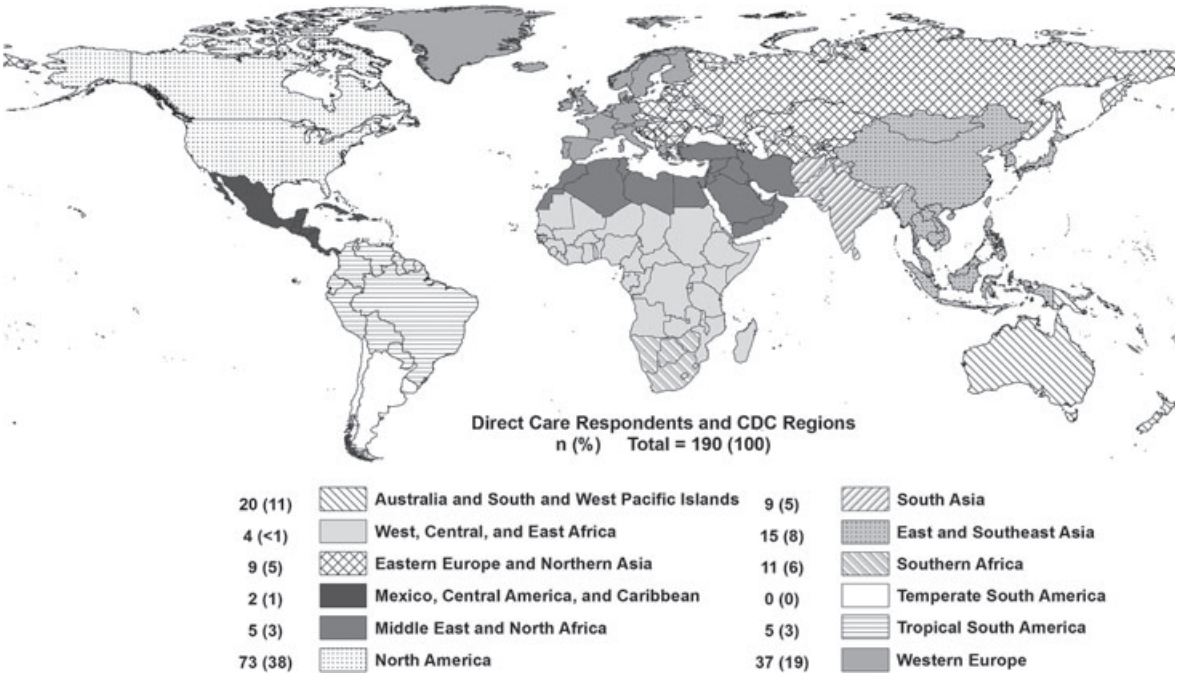

Figure 2 Participating clinic locations by region of those responding to the Evaluation of the Global Availability of Rabies Immune Globulin and Rabies Vaccine for Travelers: Direct Care Survey, 2010

reported that they would refer travelers to clinics in the same city or elsewhere in their country, and 1% ($n = 1$) stated that they would refer only to clinics outside their country or send travelers back to their home country.

Approximately one third of 187 respondents stated that patients presenting with wounds from an animal exposure seldom or never adequately cleansed those wounds (Table 3). Sixty-nine percent of respondents stated that approximately 0%–10% of their patients seeking care for a possible rabies virus exposure had been previously immunized against rabies.

Barriers to the availability of RIG and RV were assessed among respondents (Figure 4). For RIG, the most common responses to the barriers of availability were the high cost (35%), not being stocked because the need for it was not regular (32%), and not having enough supply (26%). For RV, the high cost (26%), the lack of supply (18%), and problems with ordering (15%) were the most common barriers for all respondents (Figure 4).

Discussion

Current information on RIG and RV availability worldwide has been limited, and to our knowledge, no study or survey has described the availability and types of rabies biologics when traveling abroad. The interpretation and discussion of the data presented here must take into account several factors. First and foremost, this survey represented a convenience sample of travel medicine and other medical staff who belong to several international health care organizations that deal with rabies prevention. This resulted in broad distribution, but lacked specificity for targeting eligible participants (ie, clinicians who saw patients during or after travel). The inclusion of travel medicine organizations likely biased responses toward travel medicine clinics that are primarily in North America and Western Europe (where canine rabies is controlled) and located in urban areas, have higher access to medical services in general, and see patients with financial means to pay for international travel and more extensive medical care. In addition, our survey was limited to clinicians who spoke English, Spanish, or French and had access to e-mail and the internet. The survey findings are likely to be more representative of what is available in more developed urban settings and likely available to international travelers, rather than the general availability of RIG and RV to the broad population. Small sample size for each country and region might limit the representativeness of these findings. Specifically, the canine rabies-endemic areas of Africa, Asia, and parts of the Americas are underrepresented in this survey. In addition, results were compiled into regions; countries within these defined regions might differ from each other. Furthermore, this survey asked clinicians their experience only in 2010. Because the availability of rabies biologics can vary temporally, our study may not be representative of past, current, or future situations.

Understanding these constraints, we found that the availability and type of RIG and RV varied geographically. Despite its expense and limited supply,

Table 1 The accessibility to and type of rabies immune globulin used by region, reported by respondents providing direct patient care to travelers in the Evaluation of the Global Availability of Rabies Immune Globulin and Rabies Vaccine for Travelers: Direct Care Survey, 2010

	Region											
	Australia and South and West Pacific Islands	North America	Mexico, Central America, and Caribbean	Tropical South America	Western Europe	Eastern Europe and Northern Asia	South Asia	East and Southeast Asia	Middle East and North Africa	West, Central, and East Africa	Southern Africa	Total
In your clinic in 2010, how accessible*was rabies immune globulin when it was needed for patients?†												
Number of responses‡	18	68	2	5	36	9	9	15	5	4	11	182
Never or seldom, *n* (%)	1 (6)	13 (19)	2 (100)	4 (80)	8 (22)	4 (44)	0	5 (33)	0	1 (25)	0	38 (21)
Sometimes, *n* (%)	0	5 (7)	0	0	0	0	1 (11)	0	0	1 (25)	1 (9)	8 (4)
Often or always, *n* (%)	17 (94)	50 (74)	0 (0)	1 (20)	28 (78)	5 (56)	8 (89)	10 (67)	5 (100)	2 (50)	10 (91)	136 (75)
In your clinic during 2010, what type of rabies immune globulin was used as a part of postexposure prophylaxis for rabies?§												
Number of responses¶	17	56	1	3	31	5	9	10	4	3	11	150
HRIG, *n* (%)	17 (100)	42 (75)	1 (100)	1 (33)	24 (77)	3 (60)	6 (67)	8 (80)	2 (50)	1 (33)	8 (82)	114 (76)
ERIG, *n* (%)	0	0	0	1 (33)	0	1 (20)	8 (89)	2 (20)	2 (50)	1 (33)	0	15 (10)
Other, *n* (%)	0	7 (13)	0	0	1 (3)	1 (20)	0	1 (10)	0	0	0	10 (7)
I don't know, *n* (%)	0	6 (11)	0	0	4 (13)	0 (0)	0	0	0	0	2 (18)	12 (8)

HRIG = human rabies immune globulin; ERIG = equine rabies immune globulin.

*Accessibility was defined as being able to receive rabies immune globulin in 24 hours.

†Never was defined as occurring 0% of the time; seldom was defined as occurring 1%–24% of the time; sometimes was defined as occurring 25%–74% of the time; often was defined as occurring 75%–99% of the time; and always was defined as occurring 100% of the time.

‡Only one response per clinic was allowed.

§Respondents were asked this question if they answered that rabies immune globulin was always, often, sometimes, or seldom accessible when it was needed for patients in the previous question listed above.

¶More than one response allowed; however, those responding "I don't know" did not choose other responses.

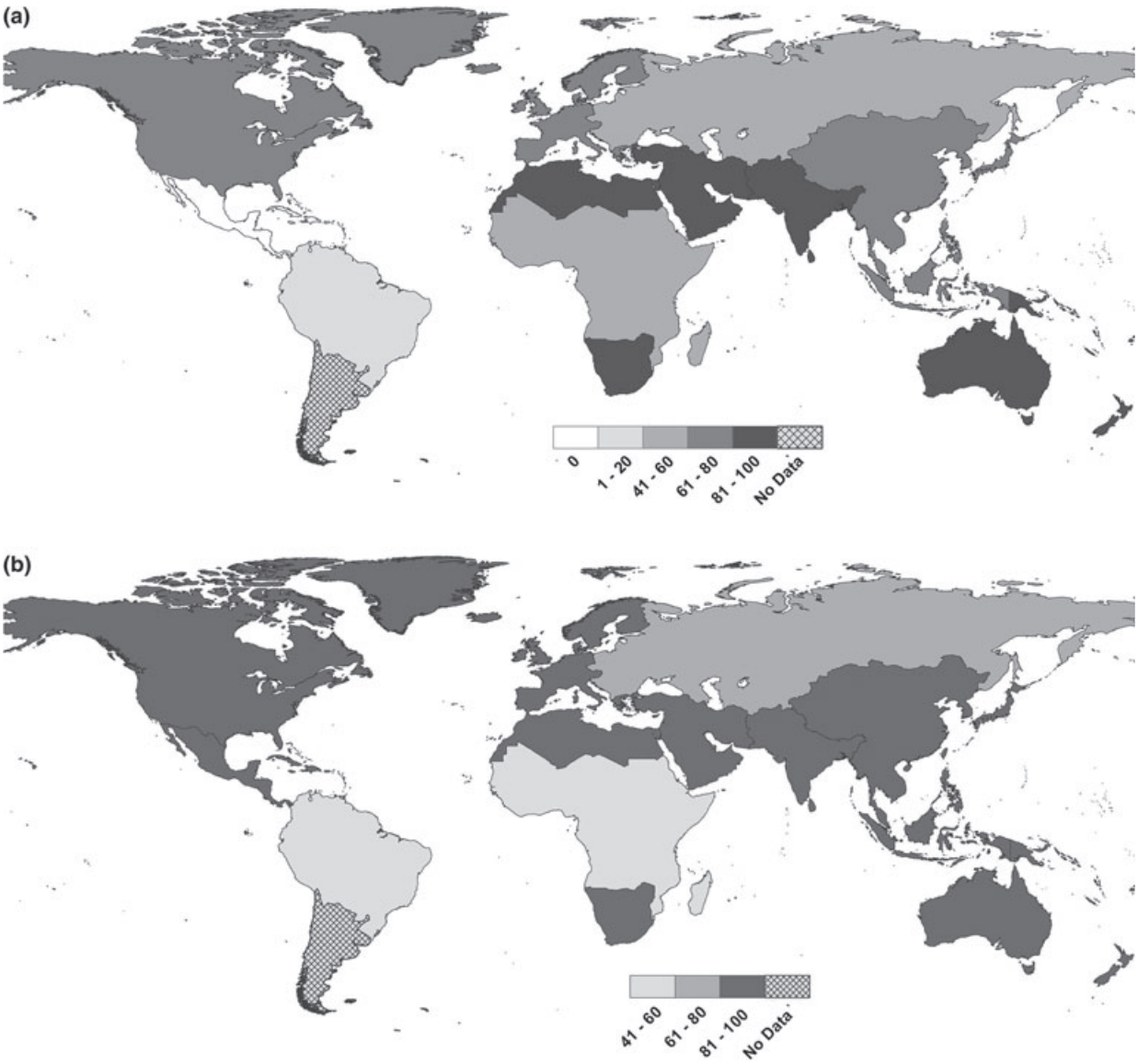

Figure 3 (a) Percentage of respondents for whom rabies immune globulin was often or always accessible when needed for patients in those providing direct patient care to travelers in the Evaluation of the Global Availability of Rabies Immune Globulin and Rabies Vaccine for Travelers: Direct Care Survey, 2010. (b) Percentage of respondents for whom rabies vaccine was often or always accessible when needed for patients as reported by respondents providing direct patient care to travelers in the Evaluation of the Global Availability of Rabies Immune Globulin and Rabies Vaccine for Travelers: Direct Care Survey, 2010.

HRIG was the most commonly reported RIG used overall. However, this finding is not surprising, as 68% of our respondents were from Australia and the South and West Pacific Islands, North America, and Western Europe, and for many countries in these areas, only HRIG is licensed or approved for use.[7] The majority of clinics reporting the use of ERIG were in Asia and Africa, similar to previous descriptions of the ERIG manufacturing in countries such as China, India, and Thailand.[8,9] Fortunately, most clinics reporting the use of ERIG reported using its purified or FAB fragment form, which are associated with a lower incidence of serum sickness and anaphylaxis. Not unexpectedly, cost was the most common reason respondents reported that RIG was not available, as cost has long been a factor in obtaining rabies biologics.[8]

In our study, four clinics reported the use of NTVs, despite recommendations from WHO to discontinue their use; this underscores the need for travelers to be proactive after a possible exposure and aware of the type of vaccine being offered to them as PEP. If the only vaccine available is NTV, travelers should seek prompt medical evacuation to a location where an alternative vaccine can be provided. Vero cell vaccines

Table 2 The accessibility of and type of rabies vaccine used by region, reported by respondents providing direct patient care to travelers in the Evaluation of the Global Availability of Rabies Immune Globulin and Rabies Vaccine for Travelers: Direct Care Survey, 2010

	Region											
	Australia and South and West Pacific Islands	North America	Mexico, Central America, and Caribbean	Tropical South America	Western Europe	Eastern Europe and Northern Asia	South Asia	East and Southeast Asia	Middle East and North Africa	West, Central, and East Africa	Southern Africa	Total
In your clinic in 2010, how accessible*was rabies vaccine when it was needed for patients?†												
Number of responses‡	18	66	1	5	34	9	9	15	4	4	9	174
Never or seldom, *n* (%)	0	4 (6)	0	2 (40)	1 (3)	3 (33)	0	0	0	0	0	10 (6)
Sometimes, *n* (%)	0	4 (6)	0	0	0	0	0	0	0	2 (50)	0	6 (3)
Often or always, *n* (%)	18 (100)	58 (88)	1 (100)	3 (60)	33 (97)	6 (67)	9 (100)	15 (100)	4 (100)	2 (50)	9 (100)	158 (91)
In your clinic during 2010, what type of rabies vaccine was used as a part of postexposure prophylaxis for rabies?§												
Number of responses¶	17	62	1	5	32	9	9	15	4	4	9	167
Vero cell, *n* (%)	7 (41)	3 (5)	0 (0)	4 (80)	5 (16)	5 (56)	8 (89)	11 (73)	3 (75)	3 (75)	4 (44)	53 (32)
Human diploid cell, *n* (%)	9 (53)	37 (60)	1 (100)	1 (20)	18 (56)	2 (22)	1 (11)	3 (20)	1 (50)	1 (25)	2 (22)	76 (46)
Purified chick embryo cell, *n* (%)	4 (24)	19 (31)	0 (0)	0 (0)	11 (34)	2 (22)	5 (56)	4 (27)	0	0	0 (0)	45 (27)
Purified duck embryo cell, *n* (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (33)	0	0	0	0 (0)	3 (2)
Nervous tissue, *n* (%)	0 (0)	0 (0)	0 (0)	1 (20)	0 (0)	1 (11)	0 (0)	0	2 (50)	0	0 (0)	4 (2)
Other, *n* (%)	1 (6)	3 (6)	0 (0)	0 (0)	3 (9)	1 (11)	0 (0)	0	0	1 (25)	0 (0)	10 (6)
I don't know, *n* (%)	0 (0)	11 (18)	0 (0)	0 (0)	5 (16)	1 (11)	0 (0)	0	0	1 (25)	3 (33)	21 (13)
In your clinic during 2010, which rabies vaccine administration schedule did you typically prescribe for postexposure prophylaxis?‖												
Number of responses‡	17	62	1	4	31	9	9	15	4	4	8	164
Four-dose intramuscular, *n* (%)	0	34 (55)	1 (100)	0	5 (16)	2 (22)	1 (11)	3 (20)	1 (25)	1 (25)	4 (50)	52 (32)
Five-dose intramuscular, *n* (%)	17 (100)	23 (37)	0	4 (100)	23 (74)	6 (67)	3 (33)	10 (67)	2 (50)	2 (50)	3 (38)	93 (57)
Zagreb, *n* (%)	0	0	0	0	2 (6)	1 (11)	0	0	1 (25)	1 (25)	0	4 (2)
Updated Thai Red Cross, *n* (%)	0	0	0	0	0	0	5 (56)	1 (7)	0	0	0	7 (4)
Eight-site intradermal, *n* (%)	0	0	0	0	0	0	0	0	0	0	0	0
Other, *n* (%)**	0	5 (8)	0	0	1 (3)	0	0	1 (7)	0	0	1 (13)	8 (5)

*Accessibility was defined as being able to receive rabies vaccine in 24 hours.

†Never was defined as occurring 0% of the time; seldom was defined as occurring 1%–24% of the time; sometimes was defined as occurring 25%–74% of the time; often was defined as occurring 75%–99% of the time; and always was defined as occurring 100% of the time.

‡Only one response per clinic was allowed.

§Respondents were asked this question if they answered that rabies vaccine was always, often, sometimes, or seldom accessible when it was needed for patients in the previous question listed above.

¶More than one response allowed; however, those responding "I don't know" did not choose other responses.

‖Vaccine administration schedules were defined as follows: four-dose intramuscular regimen ("0–3–7–14" or four-dose Essen regimen); five-dose intramuscular regimen ("0–3–7–14–28" or five-dose Essen regimen); Zagreb regimen or abbreviated multisite intramuscular regimen ("2–1–1"); Updated Thai Red Cross intradermal regimen ("2–2–2–0–2" regimen); eight-site intradermal regimen ("8–0–4–0–1–1" regimen) or other.

**When prompted, none of the eight clinics that selected "other" described the regimen used.

Table 3 Previous immunization and frequency of adequately cleansed wounds among patients presenting with possible rabies exposures reported by respondents providing direct patient care to travelers in the Evaluation of the Global Availability of Rabies Immune Globulin and Rabies Vaccine for Travelers: Direct Care Survey, 2010

	Region											
	Australia and South and West Pacific Islands	North America	Mexico, Central America, and Caribbean	Tropical South America	Western Europe	Eastern Europe and Northern Asia	South Asia	East and Southeast Asia	Middle East and North Africa	West, Central, and East Africa	Southern Africa	Total
In your clinic during all of 2010, how often did patients present with adequately cleansed wounds due to an animal exposure?*												
Number of responses†	20	71	2	5	36	9	9	15	5	4	11	187
Never or seldom, *n* (%)	4 (20)	21 (30)	1 (50)	0	17 (47)	3 (33)	3 (33)	4 (27)	1 (20)	0	7 (64)	63 (34)
Sometimes, *n* (%)	6 (30)	12 (17)	0	2 (40)	2 (6)	2 (22)	4 (44)	4 (27)	0	0	3 (27)	35 (19)
Often or always, *n* (%)	10 (50)	38 (54)	1 (50)	3 (60)	17 (47)	4 (44)	2 (22)	7 (47)	4 (80)	2 (50)	1 (9)	89 (48)
In your clinic during 2010, approximately what percentage of the patients presenting with possible rabies exposure had been previously immunized against rabies?												
Number of responses†	19	68	1	5	36	9	9	15	5	4	11	183
0%–10%	13 (68)	52 (76)	1 (50)	3 (60)	25 (69)	8 (89)	4 (44)	9 (60)	2 (40)	1 (25)	8 (72)	127 (69)
11%–20%	1 (5)	4 (6)	0	2 (40)	3 (8)	1 (11)	5 (56)	1 (7)	2 (40)	1 (25)	0	20 (11)
21%–30%	1 (5)	3 (4)	0	0	2 (6)	0	0	1 (7)	0	1 (25)	0	8 (4)
31%–40%	1 (5)	1 (1)	0	0	0	0	0	0	0	1 (25)	0	3 (2)
41%–50%	1 (5)	2 (3)	0	0	3 (8)	0	0	3 (20)	0	0	0	9 (5)
>50%	2 (11)	2 (3)	0	0	2 (6)	0	0	1 (7)	0	0	0	7 (4)
I don't know	0	4 (6)	0	0	1 (3)	0	0	0	1 (20)	0	3 (27)	9 (5)

*Never was defined as occurring 0% of the time; seldom was defined as occurring 1%–24% of the time; sometimes was defined as occurring 25%–74% of the time; often was defined as occurring 75%–99% of the time; and always was defined as occurring 100% of the time.

†Only one response per clinic was allowed.

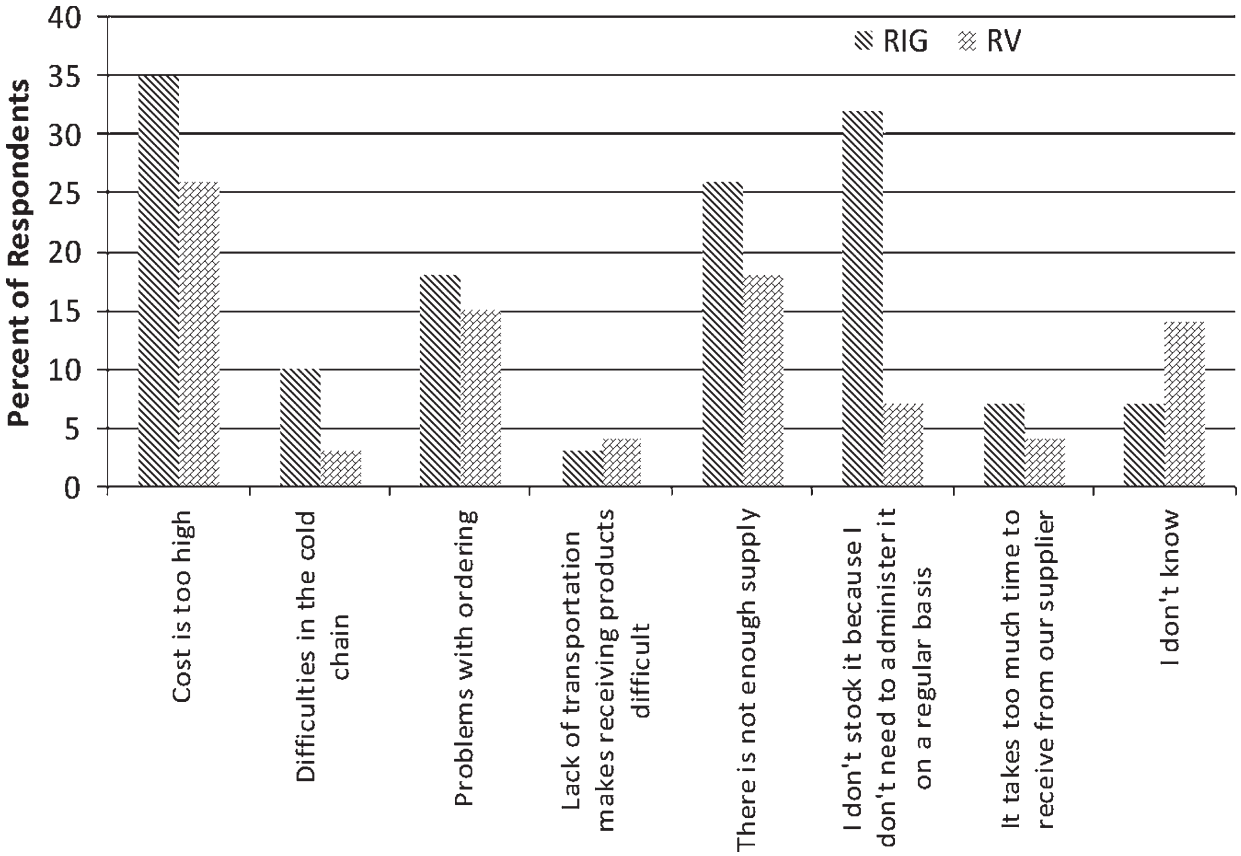

Figure 4 Reported barriers to availability of rabies immune globulin (RIG) and rabies vaccine (RV) by respondents providing direct patient care to travelers in the Evaluation of the Global Availability of Rabies Immune Globulin and Rabies Vaccine for Travelers: Direct Care Survey, 2010.

were reported more commonly from respondents in Eastern Europe, Asia, and Africa, in contrast to clinics in North America and Western Europe, which primarily reported using human diploid cell and purified chick embryo cell vaccines. Three clinics in North America reported using Vero cell vaccines, which are not licensed in either the United States or Canada, but it is unclear if these vaccines were actually used in these clinics or whether the clinician erroneously reported their use. Most clinics worldwide used the five-dose intramuscular regimen. The four-dose series was introduced in 2010 in the United States, during our study period.[7] Fifty-five percent of respondents in North America reported using this regimen, which suggests robust adoption of the new recommendations in the United States.[7]

Notably, 8 and 13% of respondents did not know what type of RIG or RV, respectively, was used in their clinics. Although specific reasons for these responses were not collected during our survey, the differences in potential serious adverse events (ie, anaphylaxis) for RIG and administration schedules for RV warrant concern. These findings are similar to studies that evaluated the knowledge of travel medicine providers and found that among providers, the appropriate use and administration of RIG and RV was often not known.[10,11] All health care providers, even those familiar with travel medicine, should be familiar with rabies biologics, their potential side effects, and PEP administration schedules, both in their geographic area and internationally. This information, in addition to being critical for patient care, needs to be explained thoroughly to patient-travelers, if they decide to continue the prophylaxis series in their own country. Postgraduate refresher training in proper PEP administration, such as the online course *Rabies Postexposure Prophylaxis (PEP) Basics: Case Illustrations of the 2010 Advisory Committee on Immunization Practices (ACIP) Guidelines* (http://ideha.dhmh.maryland.gov/training/rabies/default.aspx), should be encouraged among providers who may see travelers during or after travel.

We found that among respondents providing PEP, most travelers requiring such care had not received preexposure vaccination. Research has found that most travelers do not seek pre-travel health consultations before traveling; therefore vaccination opportunities can be limited.[12,13] Lack of preexposure vaccination in travelers is probably due to several other factors, including cost, insufficient time for vaccine administration before travel, the perception that the

traveler is at low risk while traveling, and a general lack of rabies knowledge.[14] A study of French travelers found that only 6.7% of travelers to rabies-risk countries knew the risk of rabies was important, 24.7% had no idea how to avoid rabies, and more than 57% had visited the clinics within 3 weeks of travel, making complete preexposure vaccination difficult.[15] Recent discussions have suggested that providers should consider aggregate travel rather than each trip individually, and that rabies vaccination might be a sound investment for those who travel frequently to rabies-endemic areas.[16]

Further, 34% of travelers in our study did not adequately cleanse their wounds before seeking care for PEP. This was potentially because of not seeking pre-travel consultations with health care providers before travel or not receiving proper information at that consultation. A study of backpackers in Southeast Asia found that of those who sought pre-travel health information, only 55.6% had received information about rabies and 41% of all travelers did not know that rabies could be transmitted from licks on broken skin.[17] As RIG is not often available in remote locations, proper wound cleansing is a critical component of PEP and should be covered in detail by providers at pre-travel consultations.

Travelers should seek a pre-travel health consultation from their health care provider 4–6 weeks before travel, especially if rabies preexposure vaccination is warranted as multiple visits to the provider are needed. Providers need to discuss, in detail, the traveler's itinerary and activities to provide customized recommendations, including the consideration of preexposure vaccination, education on the endemicity of rabies at the destination, the limited availability of RIG and RV at some locations around the world, avoidance of animal bites, and proper actions should a potential rabies exposure occur. Updated travel recommendations for travelers and providers can be found at www.cdc.gov/travel. Providers should also emphasize that, if bitten or licked on broken skin, travelers should thoroughly clean the wound with soap and water and seek medical attention immediately. If possible, the animal should be tested for rabies, or if a cat or dog, should be observed for 10 days by an appropriate local authority to rule out the possibility the cat or dog was shedding rabies virus during the time the potential exposure occurred.[18] Finally, travelers need to be aware that both RIG and RV might not be available at their destinations, that different products may be more accessible than what is recommended in their home country, and that such biologics might vary considerably in quality and safety.

Conclusion

We found that the availability and type of RV and RIG varied by geographic region and that a few responding clinics reported the continued use of NTV. Further, one third of responding clinics reported that travelers were not cleaning wounds adequately. Travelers should be educated to avoid animal exposures; clean all animal bites, licks, and scratches thoroughly with soap and water; and seek medical care immediately, even if overseas. All travelers should be informed that RIG and RV might not be readily available at their destination and that travel health and medical evacuation insurance should be considered prior to departure.

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Declaration of Interests

The authors state they have no conflicts of interest to declare.

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