A Supplement to

IDSE Infectious Disease SPECIAL EDITION

PHARMACY PRACTICE NEWS

Special REPORT

Rabies Post-Exposure Prophylaxis: A Patient-Centric Approach to Care

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Rabies is an almost universally fatal neurologic infection caused by several species of virus in the genus *Lyssavirus*.[1] This zoonosis is spread from infected mammals to humans by saliva transmitted primarily through bites, although any form of internalized contact with infected saliva or neural tissue can lead to the development of rabies.[1] As one of the oldest recorded infectious diseases, rabies has been a source of widespread fear for centuries due to its extremely high case fatality rate and lack of documented therapy.[1-3] Although rates of infection and death in humans have declined in the United States due to widespread canine vaccination programs,[2,3] rabies is still a major cause of mortality worldwide, accounting for tens of millions of exposures and tens of thousands of deaths per year,[4] including 1 to 2 per year in the United States.[5] Wildlife, such as raccoons, foxes, skunks, and multiple species of bats, drive increases in US rabies infection rates,[6] while bites from rabid dogs continue to pose the greatest risk for disease in developing nations.[1] Elimination of human mortality from dog-mediated rabies by the year 2030 is a major goal of the World Health Organization (WHO) and other global welfare organizations.[7]

Symptoms of rabies at the outset of infection can be nonspecific and similar to other viral syndromes, and include fever, headache, and delirium.[2] As the virus spreads through the peripheral and central nervous system, classic symptoms of encephalitic (furious) rabies, such as hyperactivity, difficulty swallowing, and pharyngeal spasms due to the sight or sound of running water (ie, hydrophobia), emerge.[2] There is a second clinical type, paralytic rabies, which occurs less often compared with the furious type.[2]

Rabies is untreatable and universally fatal once symptoms appear.[2] Therefore, care must be initiated rapidly after a thorough risk assessment.[6] This includes several factors, such as the nature of the contact, the

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species in question, and the availability of the animal for diagnosis.[3,8] The incubation period—the time between exposure and symptom onset typically ranges from 4 to 6 weeks but could be as short as 10 days or in rare cases, more than a year in humans[1,2]—offers a critical window during which the progression of the disease can be interruputed.[6,8] A careful post-exposure prophylaxis (PEP) regimen of thorough wound washing, the infiltration of rabies immune globulin (RIG) if the patient was never vaccinated, and 4 doses of vaccine over a 14-day period are virtually 100% effective in preventing rabies.[8-10] Unfortunately, there are many barriers to the optimal implementation of appropriate PEP, including a low urgency to report among patients, improper wound care, cost, and supply chain issues, all of which can lead to increases in the risk for rabies virus infection.[11,12]

This special report reviews the current status of rabies PEP in the United States, with a focus on challenges in implementing an appropriate PEP regimen and strategies to overcome these challenges in the hospital setting. Through education, development of programs and services, and innovation, such as new or improved human RIG (HRIG) products, clinicians, researchers, and manufacturers have the potential to reduce the burden for patients with a rabies virus exposure.

Role of PEP in Rabies Prevention

An effective regimen of PEP following rabies virus exposure neutralizes virus at the local bite or wound site and halts viral progression toward the nervous system.[1] At presentation, wound care, consisting of immediate washing and flushing of the wound area thoroughly for at least 15 minutes with soap and water or a virucidal agent, should be initiated.[13] Vigorous washing and flushing has been shown to provide a major impact upon the risk for disease occurrence.[14] Furthermore, HRIG should be infiltrated at the wound site with as much of the dose volume as is possible, into the depth of the wound and around the site. Any remaining HRIG should be injected into an area separate from where rabies vaccine is given.[13] Immediate HRIG administration will help to eliminate the virus locally at the wound site, reducing the risk for nervous system acquisition.[8,15] Rabies vaccine should be administered at presentation on day 0 and at designated follow-up visits. Doses should not be missed or rescheduled to ensure the opportunity for the greatest induction of active immunity to the virus as possible.[9] Patients who have had prior rabies vaccination should only receive 2 doses of vaccine, 1 dose on day 0 and the second 3 days later, and will not require HRIG.[2]

Because rabies is essentially fatal once symptoms appear[1] and there are currently no effective treatments for rabies-induced encephalomyelitis,[15,16] rapid implementation of PEP is essential. However, not all patients with animal contact will require PEP. To avoid wastage of expensive resources and unnecessary PEP, risk assessments are needed to appropriately evaluate those patients who most need PEP.[8] Any rabies virus–suspect animal that exposes a patient should be euthanized, its brain removed and sent for rapid laboratory testing.[3] In the majority of cases, the diagnosis will be negative.[5]

Table 1 provides a global overview of current WHO recommendations for evaluating animal contact and determining when to administer PEP.[17] Evaluating the source of the wound is a key initial step: While canine rabies transmission has been eliminated in the United States,[8] unvaccinated dogs may still contract other variants of rabies virus from exposure to wildlife.[6] Because of this, dog, cat, and ferret bites should be considered for rabies PEP if the animal shows clinical signs of rabies during 10 days of observation following a bite or the suspect animal is not available for observation.[16,18] Bat bites are one of the main causes of human rabies virus exposure in the United States, responsible for approximately 70% of human rabies cases.[5] Any bite or scratch from a bat should be considered a potential rabies virus exposure.[2] Exposures from other wildlife, including skunks, foxes, and raccoons, are evaluated on a case-by-case basis and typically depend on geographic area and the results of laboratory testing.[2] If the animal is a dog, cat, or ferret and can be captured and observed, PEP can be postponed until the animal's status has been confirmed.[18]

It is also important to consider the nature of the wound when evaluating the need for PEP. Rabies virus is transmitted through saliva (or exposure to infectious neural tissue), when introduced through a bite wound, into open cuts, through mucous membranes, or rarely, via tissue/organ transplants.[1,6] Because of this, bites are the most common form of rabies virus transmission. Although possible, transmission through other routes is highly unlikely.[1] The contamination of an already present open wound and scratches that break the skin are 2 non-bite routes through which rabies virus can be transmitted. Although this is extremely rare, there are instances in which rabies virus has been transmitted in this manner and these exposures should be considered for PEP.[1,19] Any attack that occurs when a pet is being fed or handled may be considered a provoked exposure.[19] Other situations, such as petting or contact with other bodily fluids (eg, blood, urine, or feces), do not require PEP.[19]

Table 1. WHO Recommendations for Evaluation of Rabies Virus Exposure

Category	Type of Contact	Type of Exposure	Recommended PEP
I	Touching or feeding of animals; licks on intact skin	None	PEP not indicated
II	Nibbling of uncovered skin; minor scratches or abrasions without bleeding	Minor	Wound washing and vaccine only
III	Single or multiple transdermal bites or scratches, licks on broken skin; contamination of mucous membranes with saliva; exposure to bats	Severe	Wound washing, vaccine, and HRIG

PEP, post-exposure prophylaxis; **HRIG,** human rabies immune globulin; **WHO,** World Health Organization

Based on reference 17.

Appropriate PEP implementation ensures that the bite or wound is effectively disinfected, and first aid protocols along with HRIG and vaccinations prevent the virus from infecting the central nervous system. With such care, clinical symptoms do not present and mortality risk is virtually eliminated.[1,15] However, cases exist where PEP was initiated following exposure and patients developed rabies. Lack of proper wound care, misunderstanding or misrepresented HRIG or vaccine administration instructions, failure to inject HRIG into and around wound sites, and lack of access to modern intervention have all been cited as reasons for PEP failure.[20] Given the fatal course of rabies virus infection, it is critical for clinicians and health care providers to understand best practices in PEP administration to ensure its overall effectiveness.[20]

Best Practices for PEP

Once the need has been confirmed, PEP should begin immediately with prompt and thorough wound cleansing, followed by passive immunization with HRIG and active immunization with a series of rabies vaccinations.[6,8-10] If implemented early and followed correctly, rabies PEP protocols are almost always successful in preventing rabies.[10]

Wound Care

Proper wound care is the first extremely important step of rabies PEP. Wound care involves, at a minimum, thorough cleansing of the wound for at least 15 minutes with soap and water. When possible, a virucidal agent, such as povidone iodine solution, a quaternary ammonium compound, or 40% to 70% alcohol, also should be administered along with a local anesthetic and if indicated, a tetanus vaccination. Patients should be assessed for antibiotics after animal bite as well.[2,8,13,21] This should be done as soon as possible after rabies virus exposure.[13] After cleansing, wounds should be left open or covered with a simple dressing, rather than suturing closed, to avoid exposure of nerve endings to remaining virus.[13,21] Wound cleansing is a highly effective prevention method. Research using animal models have found that when done thoroughly and promptly after exposure, wound cleansing alone can prevent most productive rabies virus infections.[14]

HRIG

Following wound cleansing, patients with a high suspicion of rabies virus exposure who have not previously been vaccinated against the virus should receive a HRIG product.[2] There are 3 HRIG products currently available for use in the United States (Table 2).[22-25] HRIG is given at a dose of 20 IU/kg and should be administered through local infiltration around the wound, with as much of the HRIG dose volume given at the wound site as possible.[13,22] In the case of multiple bites and scratches, it is important for every wound to be infiltrated.[20] If additional HRIG remains after infiltration of the wound(s), the remaining dose should be given via intramuscular injection.[13] Ideally, HRIG should be given immediately following wound cleansing and prior to vaccination. If the patient does not receive HRIG at this time, however, it may be given for up to 7 days after administration of the first rabies vaccine.[2]

In the case of small bites or scratches, particularly those of bats, it may be challenging to administer the entire dose of HRIG. For the deltoid and lateral thigh muscles, current recommendations for a safe injection volume in a single intramuscular injection are 1 and 3 mL, respectively.[26] Older adults and patients with low body mass index may only tolerate up to 2 mL in a single injection.[26] Such injection volume limits could make locating sufficient sites for intramuscular injection challenging. While 2 of the 3 HRIG products currently available have a potency of 150 IU/mL, a recently approved formulation of HyperRAB® (rabies immune globulin [human]) 300 IU/mL (Grifols) has a potency of 300 IU/mL.[22] HyperRAB® is indicated for PEP, along with rabies vaccine, for all persons suspected of exposure to rabies virus.[23] This higher concentration product allows both, the delivery of more of the dose volume at the wound site, and the administration of the required dose of HRIG in a lower overall volume.[22]

When selecting a HRIG product, it is extremely important to be certain of the potency required. Currently, some HRIG products offer a potency of 150 IU/mL and HyperRAB® is offered at a higher potency of 300 IU/mL.[22] If both product types are available, select the formulation most appropriate

Table 2. Rabies Immune Globulins and Vaccines Approved in the United States

Agent	Type	Potency	Dose	Presentation
Imovax® (HDCV); Sanofi Pasteur	Vaccine	≥2.5 IU of rabies antigen	NA	1.0-mL prefilled syringe
RabAvert® (PCECV); Bavarian Nordic	Vaccine	≥2.5 IU of rabies antigen	NA	1.0-mL prefilled syringe
Imogam® Rabies-HT; Sanofi Pasteur	Human immune globulin	150 IU/mL	20 IU/kg	2-mL vial
KEDRAB™; Kedrion Biopharma	Human immune globulin	150 IU/mL	20 IU/kg	2- and 10-mL vials
HyperRAB®; Grifols	Human immunoglobulin	300 IU/mL	20 IU/kg	1-, 3-, and 5-mL vials

HDCV, human diploid cell vaccine; **NA,** not applicable; **PCECV,** purified chick embryo cell vaccine

Based on references 22-25, 30, and 31.

for the wound type and size. Additionally, the 300-IU/mL HyperRAB® can be diluted as needed, if a larger volume is required to appropriately infiltrate multiple wounds. If dilution is required, using dextrose 5% in water (D5W) is recommended by the manufacturer.[23] Dilution is not recommended for the 2 lower potency 150-IU/mL HRIG products—KEDRAB™ (rabies immune globulin [human]) (Kedrion Biopharma) and rabies immune globulin (human) USP, heat treated, Imogam® rabies–HT (Sanofi Pasteur). Regardless of which potency product is used, the dosage should never change from 20 IU/kg, as this is the safest and most effective dose.[8] Higher doses may suppress immune responses to rabies vaccination, and lower doses are associated with PEP failure.[2,20]

HRIG is generally safe, with mild injection site reactions such as pain and soreness at the injection site as the most commonly cited adverse events (AEs).[2] However, there are some patients for whom HRIG should be used with caution because of the risk for serious AEs. Risks and benefits of PEP should be carefully considered in these patients, including patients who have previously had a systemic allergic reaction following use of human immune globulin products and patients with an immunoglobulin A (IgA) deficiency, who are at risk for developing antibodies against IgA.[23] It is important to note that HRIG is a human plasma product and, as such, carries the potential for transmission of certain viral or prion diseases.[23] Although plasma donors are screened prior to donation, there is still a small chance for disease transmission.[23] The manufacturing and purification processes for the available HRIG products are different, resulting in varying levels of residual aggregates and procoagulant activity in each.[23-25] The HyperRAB® manufacturing process has demonstrated the capacity to inactivate prions, which may cause transmissible spongiform encephalopathies, such as Creutzfeldt-Jakob disease (CJD), and variant CJD in humans. These studies provide reasonable assurance that low levels of vCJD/CJD, if present in the starting material, would be removed by the caprylate/chromatography manufacturing process.[23] These risks should be discussed with patients prior to administration.

Rabies Vaccination

Following wound cleansing and administration of HRIG, US patients should begin a 4-dose rabies vaccine series.[27] In healthy, immunocompetent patients, the first vaccine is given on day 0, concurrently with HRIG, and remaining vaccines are administered on days 3, 7, and 14.[8,27] For patients who are immunocompromised due to illness or medication use, a fifth vaccine dose should be given on day 28, noting that protection against a productive infection may still be lacking due to a compromised immune response.[27] The location of intramuscular vaccine administration is highly important. In adults, rabies vaccines should only be given in the deltoid area, and children may receive vaccination in the outer thigh.[27] In both adults and children, vaccination should never be administered in the gluteal region, as this is associated with lower anti-rabies virus antibody titers and a potential risk for sciatic nerve damage.[28,29] The vaccination site should be far from the area where HRIG was administered, ideally in a different muscle group, as there is a risk that the antibodies from the HRIG will bind to the vaccine antigen when administered in the same region.[13]

Currently, there are 2 inactivated cell culture rabies vaccines approved in the United States: Imovax® rabies vaccine (Sanofi Pasteur), a human diploid cell vaccine, and RabAvert® rabies vaccine (Bavarian Nordic), a purified chick embryo cell vaccine (Table 2).[22,30,31] Both vaccines are equally safe and effective, and selection between the 2 vaccines is primarily based on availability and clinician preference. Ideally, the vaccination series should be completed using the same vaccine product throughout. However, there have been no documented instances of decreased efficacy or increased AEs when the vaccine series is initiated with one product and completed with another.[6] In the case that the rabies virus–exposed individual has previously completed a rabies vaccine series, they should receive 2 doses of vaccine given on days 0 and 3. In this case, no HRIG should be given.[2]

Rabies vaccines have been shown to be safe when used for appropriate PEP, with the incidence of AEs occurring most often in young children (<5 years of age).[32] The most common AEs associated with rabies vaccines include injection site reactions, headache, nausea, abdominal pain, muscle aches, and dizziness.[30,31] Although it is extremely rare, there is also a risk for Guillain-Barré syndrome following rabies vaccination, but this is usually transient.[30,31] Because of the life-threatening nature of rabies virus infection, there are no contraindications for vaccine administration other than those with life-threatening hypersensitivity systemic reactions to a particular vaccine.[30,31] Rabies vaccine may be administered to anyone, including pregnant women.[31] Administering clinicians should be prepared to manage anaphylactic reactions, particularly in patients with a history of allergic response to vaccination.[30]

Addressing Challenges in PEP

When rabies PEP is given as advised by the WHO and the Advisory Committee on Immunization Practices (ACIP), a committee within the CDC, it is nearly 100% effective in preventing rabies.[8-10] However, rabies PEP can be challenging to administer, and failures of PEP sometimes arise. Instances in which PEP fails to prevent rabies deaths almost always involve failure to follow PEP protocols, such as inadequate wound cleansing, failure to administer correct doses of HRIG, and incomplete rabies vaccine series.[20] Current barriers to appropriate rabies PEP in the United States can be examined in terms of obstacles that prevent appropriate administration by providers and those that prevent patients from seeking care.

Barriers for Providers

Because rabies virus exposure is less common in the United States compared with other infections,[5] many clinicians are not familiar with appropriate PEP protocols and fail to adequately follow them.[33,34] In particular, clinicians should gain awareness of the vaccination protocol and the need to administer an entire vaccine series, including follow-up on days 3, 7, and 14.[8,27] When these doses are missed, the immune response to the rabies virus is incomplete, and there is a risk both for PEP failure[20] and the possibility that patients may incorrectly believe they are protected from future rabies virus exposures.

Inadequate wound care is a common cause of PEP failures. Incomplete washing, poor technique, and lack of infiltration of the wound with HRIG are all contributing factors.[20] In particular, proper and adequate infiltration of the wound site with HRIG is one of the major challenges in appropriate rabies PEP. In one study, only a small percentage of patients was found to have received full infiltration at the wound site alone rather than at the wound and via intramuscular injection,[35] and other studies

have reported that less than half of patients receive the appropriate HRIG dose through either route.[36] A common misperception is for 50% of the dose to be administered at the wound site with 50% at distant sites; this practice is not recommended by current PEP guidelines.[27]

Because many wound sites may be very small, particularly in the case of bat exposure,[19] or may occur on smaller anatomic sites, such as the fingertip or nose,[35] it may be difficult to administer the entire volume of HRIG at the wound site. Injection of large volumes of fluid into small anatomic locations is associated with an increased risk for compartment syndrome.[17] Clinicians may incompletely infiltrate rabies virus–prone wounds out of fear of these complications. ACIP recommendations stress the importance of administering as much of the HRIG dose at the wound site with any remaining volume to be administered in a large muscle group distant from the vaccine administration site.[27] Consider the use of a more concentrated HRIG product for wounds that are small and difficult to infiltrate due to the reduced volume needed to inject the entire dose.[22] If compartment syndrome is a concern based on the location of the wounds, a more concentrated product is an option as the volume required to complete the dose becomes an important consideration.

Finally, issues of product supply can greatly affect a clinician's ability to appropriately administer rabies PEP. As of July 2020, there are no shortages of HRIG or rabies vaccines in the United States,[37] but this has not always been the case. In the past 2 years alone, there have been shortages of both rabies vaccines and 2 of 3 brands of HRIG (KEDRAB™ and Imogam®).[37] Although extra caution should be employed to avoid rabies virus exposure during times of shortage, consistent supply of rabies PEP is the only way to ensure appropriate protocols are followed in exposed patients. In times of shortages, clinicians should carefully evaluate each patient for risk for rabies virus exposure prior to administering PEP and prioritize those with the highest risk, such as patients with transdermal exposure.[17] However, it is important that supply issues do not impair delivery of rabies PEP, given the fatal nature of this infection.[1] Efforts by manufacturers to overcome supply chain issues are needed to ensure a constant supply of HRIG and vaccine. Because HRIG is manufactured using human plasma, the supply chain involved in ensuring a reliable supply of HRIG is more complex than that of traditional pharmaceutical agents. It is very much dependent on a consistent supply of US plasma donations and management of many variables from plasma testing to manufacture and distribution. The fewer variables and control over the uncertainties within that process, the more reliable is the supply likely to be.

Barriers for Patients

Lack of education is unquestionably the biggest barrier to appropriate rabies PEP among exposed individuals. In particular, a low urgency to seek care is a major cause of rabies mortality,[11,12] particularly among patients with exposure through bats.[38] This is due to a number of causes, including a lack of awareness in the general population that rabies can occur after bat exposures and a difficulty in identifying bat bites or scratches, partly due to their small size.[38] Today, the majority of rabies deaths in the United States occur from rabid bat exposures.[5] Often, bat-related rabies death occurs when individuals are unaware that bats are potential vectors for rabies virus transmission as the majority of bats are not rabid,[5] or the individual does not believe they had been bitten due to the small size of the bite wound and fails to seek care.[38]

Another key barrier is a fear of needles and multiple injections, which prevents some patients from seeking rabies PEP following an exposure,[39] although this also can be attributed to a lack of education.[11] Many patients believe that rabies PEP injections are extremely painful and given "into the stomach" (intraabdominally) over the course of a month.[39] Advances in technology with inactivated cell culture vaccines,[22,30,31] and higher-potency HRIG formulations,[22] mean these beliefs are outdated, but fear of needles is very pervasive, and there has been relatively little population-wide education on the ease and safety of rabies PEP. Population-wide educational programs designed to inform the public about the risk for rabies virus infection, when to seek medical care, and addressing misconceptions about HRIG and rabies vaccines would be an ideal way to improve the urgency and willingness to seek medical intervention in rabies virus–exposed individuals.[11]

Lastly, the cost of PEP is a major obstacle for many patients.[39] The average cost of rabies PEP in the United States is estimated at $3,800 for the biologics alone, not including the cost of hospital stays or wound care.[40] The CDC estimates between $245 million and $510 million is spent annually on rabies infection diagnostics, prevention and control.[40] Reducing the burden of cost for rabies virus–exposed individuals is extremely important to improve patient access to PEP. Currently, several manufacturers, including Grifols (HyperRAB®), Sanofi Pasteur (Imovax® and Imogam®), and Bavarian Nordic (RabAvert®), offer assistance programs that can help cover the cost of rabies PEP for uninsured or underinsured patients,[41] and thereby also decreasing the cost burden for hospitals. Ensuring patients are aware of these programs and are able to access necessary information can help allay fears regarding PEP cost.

Case Study:

Identifying and Correcting Shortcomings in PEP in a Major Hospital System

The many challenges faced by providers when administering PEP are well illustrated by a case study carried out by researchers at the Houston Methodist Hospital in Houston, Texas.[42] This retrospective, cross-sectional study evaluated outcomes in 246 patients treated for potential rabies virus exposure in a multihospital health system.[42] When evaluating patients included in this study, the authors identified several incidents of nonadherence to ACIP guidelines in the implementation of rabies PEP. Of note, appropriate infiltration of the wound site with HRIG occurred in only 56% of patients in the study (Figure).[42] Additionally, when HRIG was administered in distant muscle sites, selection of the injection site did not follow current recommendations. For example, 17% of patients received HRIG in the buttock,[42] which is associated with decreased efficacy of HRIG and increased risk for sciatic nerve damage.[28,29] Furthermore, 10% of patients received HRIG and rabies vaccination in the same muscle group, which is not recommended due to the risk that these complementary actions may negatively impact one another.[42] Other instances of provider failure to follow ACIP recommendations for rabies PEP included failure to administer HRIG in 21 patients for whom it was indicated and 4 errors in dosing.[42]

Among 143 patients with wounds and documented volumes of HRIG administration at each administration site, the proportion of HRIG dose that was infiltrated into and around the wound was full (100%) for 37 patients, partial (>0% and <100%) for 32 patients, and none (0%) for 74 patients.[42] Patients who received partial infiltration of HRIG into and around the wound indicated that the clinician intended to perform appropriate infiltration, but was unable to adequately infiltrate the full dose of HRIG potentially due to concerns related to injection volume constraints, risk for compartment syndrome, or risk for injection site reactions.[42] The authors of this study determined that among these 32 patients with partial infiltration, only 32% of the volume of the HRIG dose was infiltrated into and around the wound.[42] This proportion could possibly have been doubled to 64% using the concentrated, 300-IU/mL product,[22] without increasing the physical volume of HRIG injected.[42]

The authors also determined that the majority of failures to adhere to ACIP recommendations in their study arose from lack of education among providers regarding appropriate PEP protocols and lack of communication within the health care team.[42] At the time, the hospital system had not included recommendations for rabies PEP in its electronic health record (EHR) system.[42] Integrating clinical decision support tools related to rabies PEP into EHRs is an excellent method of improving adherence to ACIP recommendations. Tools can be designed to identify patients in need of rabies PEP and to prompt providers when HRIG is appropriate. Additionally, education related to dosage, administration, and selection of injection sites can be included to ensure the provider is aware of specific protocols and best practices. This is particularly important in cases where the patient has received a previous rabies vaccination, as recommendations differ and few providers are aware of the intricacies of these protocols.[42] In addition to integrating support tools into hospital EHR systems, the authors recommended an organization-wide educational campaign for emergency department clinicians to update them on the most recent guidance.[42]

Conclusion

Rabies is a universally fatal viral infection that can easily be prevented through public education, proper animal vaccination programs, and appropriate PEP measures.[1,3,8-10] Unfortunately, there are many barriers to appropriate implementation of rabies PEP. Low urgency to seek care, fear of vaccination protocols, ignorance about the disease, and substantial health care cost may prevent individuals who have been exposed from receiving PEP.[11,12] Similarly, disruptions in supply chains, incorrect techniques, and lack of knowledge regarding exposure risk among clinicians may prevent patients from receiving appropriate care.[11,12] To prevent unnecessary and preventable deaths from rabies infection, it is important to recognize risk factors associated with viral exposure, partner with manufacturers who bring focus to patient care and provide health care providers with education regarding the need for PEP, ensure consistency of supply, and implement protocols to ensure all exposed patients receive timely and successful PEP.[20] Health care providers and select manufacturers are uniquely positioned to improve access and understanding of appropriate rabies PEP through customer-centric innovation, resulting in development of products and programs that reduce the burden on the patient and improve adherence.

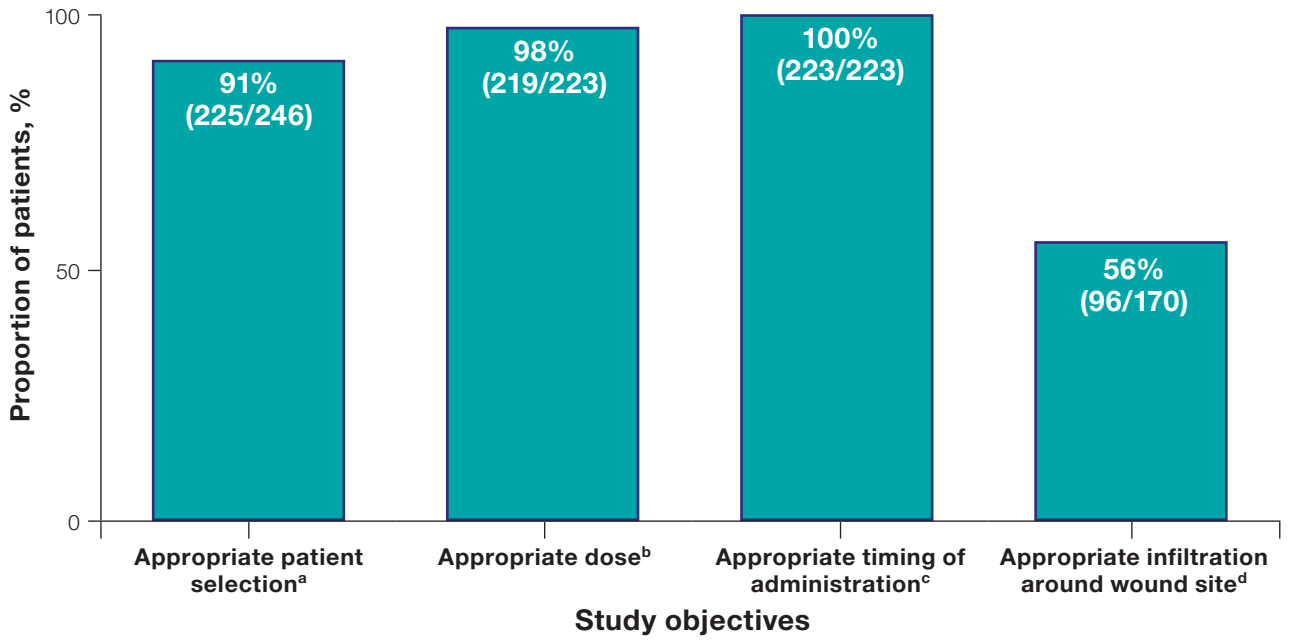

Figure. Proportion of patients who achieved adherence to guideline recommendations for HRIG patient selection, dosing, timing, and anatomic site of administration in rabies PEP.

[a] Proportion of patients who were treated according to guideline recommendations on patient selection for HRIG administration.
[b] Proportion of patients who received a HRIG dose that was within 10% of the FDA-approved dose of 20 IU/kg.
[c] Proportion of patients who received HRIG within 7 days of the first dose of rabies vaccine.
[d] Proportion of patients who received HRIG infiltration into and around the wound among patients who had a wound and documented HRIG administration sites.

PEP, post-exposure prophylaxis; **HRIG,** human rabies immune globulin

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US-HB3-2000063 SEPTEMBER 2020 SR201

Disclosures

Dr Rupprecht reported that he is a consultant to AHA Inc, and has received speaking fees from Grifols.

Dr Scholand reported that he has received speaking fees from Grifols, Pfizer, and Sanofi Pasteur.

Dr Singh reported no relevant financial conflicts of interest.

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