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Revisiting Rabies Post-Exposure Prophylaxis: Improving Adherence With Evidence-Based Care

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Rabies is a zoonotic infection caused by viruses in the *Lyssavirus* genus that is almost universally fatal once symptoms develop, since no treatment is available.[1-4] Rabies virus, the most common *Lyssavirus* species, is typically transmitted from infected mammals through a bite wound, with virions entering the peripheral nerves, with transit to the central nervous system (CNS), causing acute encephalopathy and meningoencephalitis.[1,3] Post-exposure prophylaxis (PEP) is almost universally effective when administered promptly; however, once symptoms of rabies develop, administration of PEP has repeatedly failed to improve the condition.[2,3,5]

In the United States, cases of human rabies are rare due to improved canine vaccination programs implemented after World War II.[3] Most reported cases in the United States occur in raccoons, skunks, foxes, and bats. Each year, only about 1 to 3 human cases are reported in the United States[6]; yet, in 2021, 5 cases of rabies were reported, which is a notable increase from 2019 and 2020 when no cases were reported.[7] During 1960-2018, among 125 reported human rabies cases, 89 were US acquired.[2] Among all US-acquired cases, 70% were caused by bat rabies virus variants.[2] Bats are currently the leading cause of human rabies deaths in the United States.[2] Despite the relatively low reported case load, between 30,000 and 60,000 people have potential exposures annually, requiring PEP.[6] Globally, rabies infections in humans account for approximately 59,000 deaths annually, primarily due to infections from rabid dogs.[8]

Initial symptoms of rabies infections are nonspecific and similar to those associated with other viral infections.[1] Neuropathic pain may be present around the bite wound, and patients may experience myoedema and pruritus around the wound extending into the limb.[1,9] As the infection progresses toward coma and death, most patients will develop agitation, delirium, and persistent fever.[10] Rabies

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encephalopathy is notably associated with hydrophobia, aerophobia, dysphagia, and hypersalivation.[1,10,11] A less common form of rabies, paralytic rabies, presents with paralysis, fever, piloerection, and fasciculations.[1]

The incubation period in humans is variable ranging from days to years, typically ranging from several weeks to months following exposure.[3] Careful patient assessment at the time of exposure is necessary for appropriate administration of PEP.[3] Due to cost and access barriers, emergency departments (EDs) are the primary setting for rabies PEP; however, ED providers have relatively infrequent experience with patients presenting with possible rabies virus exposures compared with other conditions.[12] Most failures of rabies PEP have resulted from not following proper guidelines, including a late start of prophylaxis, insufficient cleansing of the wound, total omission of human rabies immune globulin (HRIG) administration, or failure to inject RIG into all wound sites.[13] Concurrent immunosuppressive conditions or drugs might also be a factor.[13]

Opportunities for improved adherence to PEP in the United States have been reported.[14] A recent cross-sectional study at a major hospital system identified several areas of nonadherence to guideline recommendations from the CDC Advisory Committee on Immunization Practices (ACIP).[14] The majority of adherence failures were attributed to lack of education about PEP protocols and lack of communication within the healthcare team.[14] This Special Report reviews the PEP recommendations and implementation of rabies PEP in hospitals, and outlines best practices for achieving adherence to CDC ACIP guideline recommendations.

Overview of the PEP Regimen

Rabies PEP regimens consist of wound care, HRIG for immediate passive immunity, and vaccination for active immunity (Table 1).[3,15] When PEP is indicated, the ACIP recommends wound cleansing for all patients as the first step using soap and water, as well as a virucidal agent (eg, povidone-iodine) for irrigation; HRIG in patients who had not been vaccinated for rabies; and vaccination for all patients, with the schedule being based on previous vaccination and immunocompetency status.[3,15]

The World Health Organization (WHO) recommends PEP courses based on category of exposure.[16-18] For category I, which involves touching or feeding of animals and animal licks on intact skin—considered no exposure—PEP is not indicated.[16,18] Category II involves nibbling of uncovered skin or minor scratches or abrasions but no bleeding and is considered minor, for which wound washing and vaccination are recommended as PEP—to be treated as category III for exposure to a bat.[16,18] Category III encompasses single or multiple transdermal bites or scratches, contamination of mucous membranes or broken skin with saliva from animal licks, or exposure from direct bat contact.[16,18] This category is considered severe, for which wound washing, vaccination, and RIG are recommended.[16,18]

Best Practices for Patient Assessment And Appropriate Selection for PEP

Each patient presenting with a possible rabies virus exposure should undergo thorough risk assessment to determine whether PEP is indicated.[3,15] Providers should balance the risks of PEP (eg, adverse effects, time, and costs) versus benefits of providing PEP in accord with the principle of "first, do no harm."[3]

Both HRIG and vaccines are primarily accessible at EDs due to costs.[12] In addition, vaccines are associated with high copays and out-of-pocket costs to patients.[12] Since many patients may need to return to EDs for completion of vaccination series, PEP is associated with additional time in the ED and/or time out of work.[12] Therefore, clinicians must ensure supply and access to individuals who need PEP.[3]

For each patient, the following criteria should be assessed[3]:

- type of exposure (ie, bite vs non-bite);
- epidemiology of animal rabies in the local region (ie, local patterns of rabies virus infection and animals affected);
- circumstances regarding the exposure incident (eg, animal

Table 1. ACIP PEP Regimen

Treatment	Not previously vaccinated against rabies	Previously vaccinated against rabies
Wound cleansing	All patients should receive thorough and immediate cleansing with soap and water and a virucidal agent if available.	
Rabies immune globulin	20 IU/kg infiltrated into wound, if anatomically feasible. Any remaining dose should be administered IM at anatomic site distant from vaccine administration.[a]	Should not be administered.
Vaccine	HDCV or PCECV 1.0 mL IM on days 0, 3, 7, and 14.[b]	HDCV or PCECV 1.0 mL IM on days 0 and 3.

ACIP, Advisory Committee on Immunization Practices; **HDCV,** human diploid cell vaccine; **IM,** intramuscularly; **PCECV,** purified chick embryo cell vaccine; **PEP,** post-exposure prophylaxis.

[a] Administration of vaccine and HRIG should occur at separate anatomic sites and use a different needle/syringe during preparation. This is done to eliminate the possibility for HRIG to neutralize rabies antigens in the vaccine, rendering it ineffective.

[b] For immunosuppressed patients, administer vaccine on days 0, 3, 7, 14, and 28.

Based on references 3 and 15.

behavior, signs of illness, potential for animal to be exposed to rabies virus); and
- availability of the animal for observation and/or brain analysis for rabies infection.

State and local health departments are available to assist in evaluating cases of exposure, especially in atypical scenarios.[3]

Wounds should be infiltrated with as much of the full dose of HRIG with consideration for multiple factors, including[3,19]:
- the exposure route;
- wound severity and depth;
- contamination, viral load, and proximity to highly innervated areas and the CNS;
- the number of wounds; and
- injuries in areas of high neural density.

In cases of bat exposures, where there is no visible wound, such as an exposure following the discovery of a bat in the same room as a person unaware of contact (eg, sleeping in a bedroom), the entire dose of HRIG should be administered if anatomically feasible into or around the wound, with the remaining product adminstered in the quadriceps or deltoids.[3] In these cases, more concentrated immune globulin formulations would be preferred.[19] Currently, 150- and 300-IU/mL FDA-approved HRIG products are available, with the latter concentration delivering twice as much rabies virus antibody to the affected area per volume unit.[19-22] The higher concentrated product would have half the volume, which is advantageous in anatomically constrained areas requiring infiltration (eg, a finger pad, the tip of the nose).

Optimizing Adherence to Recommended Wound Care

Immediate wound cleansing is recommended for all animal bites, along with irrigation using povidine-iodine solution.[3,15] Studies have shown that thorough cleansing of wounds, with or without RIG, significantly reduced the risk for rabies virus infection.[3,23,24] Recommendations from the WHO include washing and flushing wounds for at least 15 minutes using water with or without soap.[18,25] Wound washing is proven to reduce viral load at the wound site, and insufficient wound cleansing may contribute to PEP failure.[3,10,18] All patients should receive wound cleansing as standard of care, regardless of previous PEP administration.[3]

Bleeding typically indicates a more severe wound, and potentially a higher risk exposure to rabies virus.[25] Suturing of wounds should be avoided or postponed when possible to prevent further viral contamination of wounds and to allow for sufficient infiltration of RIG.[3,25] If suturing is necessary, RIG should still be applied into and around the wound.[25] Additional wound care considerations include administration of tetanus toxoid vaccine, wound debridement, and use of antibiotic prophylaxis, and should be individualized based on wound characteristics.[3,26-28]

Optimizing Adherence to Recommended Use Of HRIG

During PEP, HRIG provides immediate passive immunity to bridge patients until active immunity develops from vaccination, which begins 7 days after the initial vaccine dose.[3,15] The HRIG is indicated for patients without prior rabies vaccination when PEP is administered, and is not indicated after 7 days post-initial vaccination.[10] The rationale here is to avoid immunologic interference or suppression of active immunity from the rabies vaccination series.[3,10] Several products are available in the United States (Table 2).[20-22,29,30]

The HRIG is dosed as 20 IU/kg for 1 dose only on the first day of PEP, but may be administered up to 7 days after initiation of the PEP vaccine series.[3,15,31] Higher HRIG doses may reduce the immune response to vaccination.[10] In contrast, lower doses have been associated with PEP failure.[13] The full dose of HRIG should be infiltrated into and around the wound if anatomically feasible.[3] The ACIP recommends that the remaining dose be administered intramuscularly in an anatomic site distant from vaccination.[3] If multiple wounds exist, each should be infiltrated with HRIG.[13]

Although generally well tolerated, safety considerations include injection site reactions (pain and soreness), systemic allergic reactions, and risks associated with human plasma products.[10]

Overcoming Barriers to Guideline Adherence On Infiltration

Clinical practice guidelines emphasize the importance of infiltration for optimizing efficacy of PEP.[3,15,18] Current WHO

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
KEDRAB, Kedrion Biopharma	Human rabies immune globulin	150 IU/mL	20 IU/kg	2- and 10-mL vials
HyperRAB, Grifols	Human rabies immune globulin	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 20-22, 29, and 30.

recommendations noted that local infiltration is the primary mode of protection.[18] Despite the availability of evidence-based recommendations, several challenges are associated with adherence to infiltration, including a lack of detailed administration guidance, institutional differences in who provides HRIG administration (nurse vs provider), and a lack of continuing education.[14,32]

Both ACIP and WHO guidelines recommend infiltration of as much of the HRIG dose to the extent that is anatomically feasible into the wound.[3,15,18] Yet, there is a common misconception to administer 50% of the dose through infiltration and 50% of the dose through intramuscular administration due to prior recommendations, which were not supported by evidence. One study at a major US-based health system determined that infiltration of the full HRIG dose only occurred in 26% (37/143) of patients, while 52% (74/143) received no infiltration.[14] Of those with partial infiltration, approximately 32% of the dose was infiltrated (using a 150-IU/mL product).[14]

There also can be significant difficulty infiltrating large volumes into small wounds/anatomic spaces (eg, fingertips, nose, ears), due to the risk for compartment syndrome with excessive volume administration.[32] Pediatric management of rabies PEP has nuances as well because of the patient's size and development.[32] Obese patients generally require larger doses since HRIG dose is based on actual weight.[32] Robust evidence-based guidelines on minimum and maximum infiltration volume are lacking; however, volume- and wound-based guidelines have been suggested by a Dutch advisory committee based on data from 1,091 cases, a survey of clinicians, and 2 published studies.[33-35]

Selection of the most appropriate product based on wound size enhances guideline adherence. Products with the higher concentration of 300 IU/mL permit infiltration using 50% less volume compared with 150-IU/mL formulations.[20] Products can be diluted for large wounds.[25]

Other efforts to improve adherence to the recommended PEP regimen include the use of clinical decision support in the electronic health record (EHR).[12] Clinical decision support interventions include order sets to help with medication selection, dosing, and administration, as well as standardization of orders to provide instructions on every order with appropriate administration recommendations.[12]

Optimizing Adherence to Recommended PEP Vaccination

Vaccination for PEP consists of a 4-dose regimen administered intramuscularly on days 0 (as soon as possible after exposure), 3, 7, and 14 for patients who had never received rabies vaccination.[15] Previously vaccinated patients should receive a 2-dose regimen administered on days 0 and 3.[15] Patients are considered *previously vaccinated* if they received an ACIP-recommended pre- or PEP regimen with a cell culture vaccine or received another vaccine regimen with a documented adequate rabies virus–neutralizing antibody response.[15] Patients with an immunocompromising condition or who are taking an immunosuppressant medication should receive a fifth dose given 28 days after the first dose, due to the possibility of an insufficient immune response.[15]

Available vaccine products in the United States include IMOVAX (Sanofi Pasteur) human diploid cell vaccine and RabAvert (Bavarian Nordic) purified chick embryo cell vaccine (Table 2).[20,29,30] The vaccine dose is the same for children and adults, regardless of which product is used.[3,15]

The deltoid muscle is the recommended site of administration.[15] The anterolateral aspect of the thigh also may be used for children.[15] The gluteal area should not be used to avoid a diminished immune response, risk of injury to the sciatic nerve, and possible PEP failure.[15,36]

Serological testing for post-vaccination antibodies is not necessary; however, serological testing should be performed on immunocompromised patients.[15] Insufficient response should be managed in collaboration with public health officials.[15]

Optimizing Completion of Vaccine Series

Adherence to and completion of the recommended vaccination schedule is important to ensure effective PEP.[3,15,37] Access to rabies vaccines in the United States is typically limited to the ED, and in some cases specialty travel pharmacies.[12] Consequently, many patients must return to the ED for follow-up vaccination series, placing undue stress on the ED; the staff must ensure an appropriate plan at discharge for patients to receive their remaining vaccine series.[12]

While variation and delays in vaccine schedule by a few days may not notably affect efficacy, the effects of longer delays of weeks are unknown.[3,37] If administration deviates from the recommended schedule by several days, vaccination can resume as if the patient were on schedule using the same dosing intervals.[3] If there are substantial deviations in administration schedule, serological testing may be considered 7 to 14 days after the final vaccine dose.[3]

Several institutions have reported implementing system-level initiatives aimed to improve vaccine follow-up and adherence.[12] These initiatives include providing a hard copy of the vaccine schedule to patients, detailing when and where to obtain follow-up vaccines, including the use of affiliated outpatient facilities and urgent care centers.[12] One health system collaborated with its affiliated outpatient pharmacy to develop a program in which the pharmacy contacted patients if doses were missed.[12] Other standardized interventions included order sets that advise clinicians on appropriate administration, including site of administration, and order sets targeting continuity of care for the remaining vaccine doses.[12]

Cost barriers may affect patient follow-up.[12,38] The average cost of a PEP regimen in the United States is about $3,800, not including hospital treatment and wound care costs.[38] Cost barriers for uninsured and underinsured patients may be alleviated by patient assistance programs, when available.[39] Currently, patient assistance programs are provided by Sanofi (IMOVAX), Grifols (HyperRAB), and Kedrion BioPharma (KEDRAB).[39] Informing patients about patient assistance programs and facilitating the application process can negate concerns and fears about cost that may interfere with patient follow-up.

Managing HRIG and Vaccine Stock And Ensuring Availability

Due to the biologic nature of HRIG and rabies vaccinations, inventory shortages have occurred and are a persistent issue globally.[17] Patient assessment evaluating risks associated with the offending animal can help to divert product to patients who need it most. As of January 2023, no rabies

biologics shortages have been reported in the United States.[40] However, institutions should take measures to ensure consistent supply to patients, especially since availability is typically limited to EDs.[12,17] To ensure appropriate inventory, institutions should review utilization reports to understand trends in administration and determine appropriate stock levels. Once minimum inventory levels have been set, processes should be established to ensure reordering to avoid stockouts. Furthermore, since dosing of HRIG is weight-based, it is important to consider patients with obesity who may require larger doses and product quantity when setting inventory levels.[32,41] Also, in situations that involve bat exposures, an entire family may require PEP at the same time—pharmacies should always be prepared to address these occurrences.

Some institutions report dose rounding of HRIG, so that it is within 10% of the recommended 20-IU/kg dose.[14,42] HRIG products with more vial size options and enhanced storage conditions, such as longer shelf-life and room temperature storage, can be considered to reduce waste, discard, and optimize storage space.

Best Practices for Team-Based Care

Given the adherence barriers to recommended PEP guidelines and high consequences of PEP failure, leveraging team-based care can optimize PEP administration and reduce guideline deviations. Using a team-based approach for patient assessment, decision making about initiation of care, resource acquisition, and continuity of care can ensure comprehensive patient care. Local and state health departments can be consulted for their expertise in assessing patients with possible rabies exposure, and the CDC can be consulted for assistance in atypical scenarios.[3,15]

Interdisciplinary care within the health system can streamline PEP administration, standardize the care process, and ensure adequate resources. Pharmacists can play a role in the development of rabies PEP policies and procedures, including development of EHR pathways; standardized order sets with clear directions, dosing, and administration instructions; and processes for determining follow-up for vaccination series, based on a patient's healthcare coverage.[43]

Conclusion

Rabies PEP is universally effective when administered appropriately.[2,3,5,15] Given the fatal nature of a rabies virus infection once it has developed and the rarity of cases, providers require education to ensure appropriate recognition of high-risk rabies virus exposures. In the United States, PEP is primarily administered in EDs and associated with high costs, time, and ED resource utilization.[12] In addition, institutions may stock a limited supply based on prior utilization reports and product shelf-life, emphasizing the importance of discretionary PEP administration and careful patient assessment.[12] Adherence to all steps of PEP administration recommendations, including thorough wound cleansing, is imperative to ensure effectiveness.[3,15] Providers should be aware of common downfalls associated with HRIG administration and vaccination, such as recommended administration sites, dosing, route of HRIG administration, and completion of vaccination series. In addition, providers should take care to infiltrate as much of the HRIG dose as anatomically feasible into and around the wound areas and administer any remaining HRIG via the intramuscular route, with consideration to dose volume.[13,41] Standardization within the EHR and employment of PEP bundles, including considerations for concentrations of HRIG used, can improve adherence to ACIP guideline recommendations.[3,41]

Case Study:

Implementation of Rabies PEP Bundle in a Major Hospital System

A quality improvement initiative targeting improved rabies PEP in the ED was implemented and evaluated in a major US-based health system in Houston, Texas.[41] A before-and-after quality improvement study was implemented to test the hypothesis that a rabies PEP bundle in the ED would improve full adherence to the ACIP guideline recommendations.[3,41] The study was implemented throughout the entire health system consisting of 15 EDs.[41] The rabies PEP bundle comprised[41]:

1. EHR enhancements (eg, PEP order set with clinical decision support and administration instructions, fields for administration documentation, and a discharge order set);
2. ED staff education through live presentations and tip sheets; and
3. Patient education to help ensure that follow-up visits for subsequent vaccines were scheduled.

Methods

In this study, HRIG 150 and 300 IU/mL (HyperRAB, Grifols Therapeutics), rabies human diploid cell culture vaccine (IMOVAX, Sanofi), and rabies chick embryo cell–derived vaccine (RabAvert, Bavarian Nordic) were used.[41] Patients who received PEP between January 2015 and June 2018 were identified using reports extracted from the EHR and included in the pre-implementation group.[41] Following implementation of the PEP bundle in December 2019, patients treated from then through November 2020 were included in the post-implementation group.[41] In 2019, the formulary also expanded to update the preferred HRIG product to the 300-IU/mL formulation to increase the amount of HRIG dose infiltrated into the wound because a smaller volume is required.[41]

The primary end point was the proportion of patients who achieved full adherence to 6 recommendations for RIG administration, based on guideline and prescribing information.[41] These recommendations included: 1) appropriate patient selection, 2) appropriate dose, 3) appropriate timing, 4) administration into and around the wound if anatomically feasible, 5) administration distant from rabies vaccine, and 6) administration that avoids the buttock, unless the wound is near the buttock.[41]

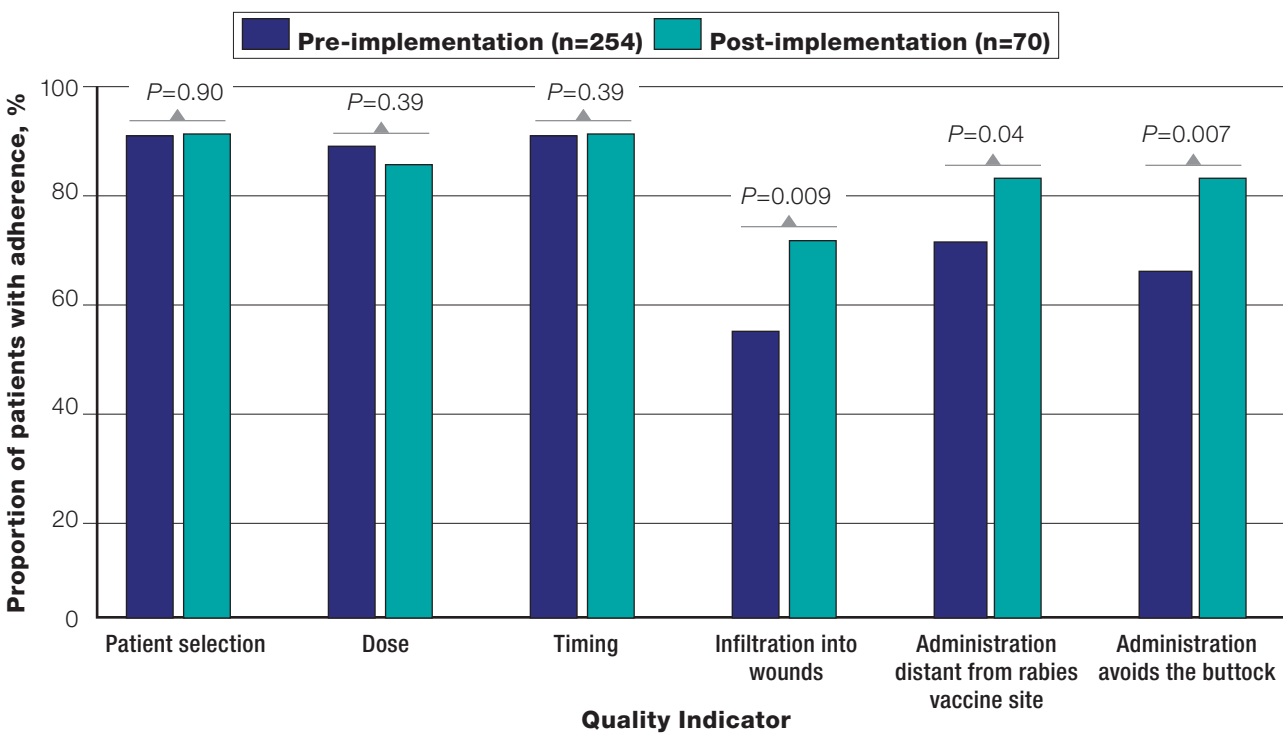
Patient Characteristics and Results

The study included 324 patients with 254 patients in the pre-implementation group and 70 in the post-implementation group.[41] Of these patients, 76% had been bitten by an animal and 71% sought care in the EDs of community hospitals.[41] A history of rabies prophylaxis was reported in 5 patients (1%), including 2 in the pre-implementation group and 3 in the post-implementation group.[41] A total of 8 patients (2%) were immunocompromised, of which 7 were in the pre-implementation group.[41] With the exception of exposing animal type and presence of wound—the post-implementation group had more bat exposures (53% vs 25%; *P*<0.001) and a decreased presence of wounds (63% vs 84%; *P*<0.001)—patient characteristics were similar between the 2 groups.[41] Patients in the post-implementation group also had more exposure to high-risk animals (63%) compared with the pre-implementation group (32%; difference, 31%; 95% CI, 18%-44%; *P*<0.001).[41] High-risk animals included bats, followed by coyotes, foxes, raccoons, and skunks.[41]

Full adherence to the 6 quality indicators was observed in 37% of the pre-implementation group and 61% of the post-implementation group (*P*<0.001), resulting in an absolute increase of 24% with implementation of the ED PEP bundle.[41] When adjusted for differences between the groups (animal type [bat vs other] and animal exposure [bite vs other]), the association between the implementation of the PEP bundle and improved adherence remained significant (adjusted odds ratio, 2.32; 95% CI, 1.32-4.07; *P*=0.003).[41]

Secondary end points included analysis of adherence to each quality indicator.[41] Increased adherence was observed with 3 quality indicators (Figure).[41] Indicators with a significant improvement in adherence included the following: Infiltration into wounds increased from 54% to 71% (absolute difference, 17%; *P*=0.009); administration distant from rabies vaccine site increased from 71% to 83% (absolute difference, 12%; *P*=0.04); and administration that avoided the buttocks increased from 66% to 83% (absolute increase, 17%; *P*=0.007).[41] Other quality indicators that were not associated with significant improvement had a high baseline adherence rate, including patient selection (91%), dosing (89%), and timing (91%).[41]

A subgroup analysis of 172 patients with clear administration site documentation showed that 43% of patients in the post-implementation group achieved infiltration of the entire HRIG dose compared with 24% in the pre-implementation group (*P*=0.03).[41] In a post hoc analysis evaluating patients with active wounds that were visible and unhealed, full adherence to quality indicators increased significantly from the



The absolute difference in adherence was significant for infiltration into wounds (17% [95% CI, 5%-30%]; *P*=0.009), administration distance from the rabies vaccine site (12% [95% CI, 2%-22%]; *P*=0.04), and administration avoiding the buttock (17% [95% CI, 6%-27%]; *P*=0.007).

Figure. Adherence to individual HRIG quality indicators following implementation of a PEP bundle.

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

Based on reference 41.

pre-implementation group (38%) to the post-implementation group (56%; absolute difference, 19%; 95% CI, 1%-37%; *P*=0.04).[41] There were no significant differences in full adherence between ED settings (*P*=0.34).[41] Full adherence was achieved in 65% of patients when the order set was used appropriately (ie, ordering through order set and selecting appropriate clinical pathway) compared with 40% when such protocols were not used (absolute difference, 25%; 95% CI, –8% to 58%, not significant).[41]

Study Conclusions and Discussion

Overall, implementation of a rabies PEP bundle in the ED was associated with improved patient selection and delivery of HRIG universally across a multi-hospital health system.[3,41] In addition to improved adherence in 6 quality indicators, implementation of the bundle was associated with improvements in 3 individual quality indicators that had been targeted as an opportunity for improvement when creating the bundle.[41] The observed improvement in adherence to quality indicators was likely driven by the EHR implementation of standardized order sets and clinical decision support, rather than the ED staff education and patient education at discharge.[41]

As a critical component of PEP in preventing the spread of virions from the wound into the CNS, infiltration of the full HRIG dose into the wound significantly increased in the post-implementation phase (43%) compared with the pre-implementation phase (24%), which may be attributed to the use of the concentrated HRIG 300-IU/mL product as the preferred HRIG formulation during the post-implementation phase rather than the 150-IU/mL formulation used during the pre-implementation phase.[13,41]

Additional considerations for minimum inventory requirements and dosing for obese patients should be evaluated by institutions.[32,41] Administration of HRIG can be challenging in patients with obesity due to depletion of inventory, as well as dosing errors and high injection volumes.[32] During the study period, 2 dosing errors occurred as a result of insufficient inventory at a single ED that treated 2 concurrent patients with obesity.[41] In this instance, the available inventory was 4,500 IU of HRIG, and an inventory of 5,100 IU would have been sufficient to prevent the error.[41] Future research should evaluate the effect of clinical decision support on PEP adherence at other health systems.[41]

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