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RABIES IMMUNE GLOBULIN & VACCINE, WITH REFERENCE TO EGYPT

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Abstract

Rabies (Rhabdoviridae family) is a preventable viral disease commonly transferred by bite of a rabid animal. Dogs are the principal source of human rabies mortality, contributing up to 99% of all rabies transmissions to humans. Rabies virus infects the CNS of mammals, eventually causing infection in the brain and death. Rabies can affect all mammals, including humans, cats, dogs and farm wildlife like bats, raccoons, skunks, and foxes. In many other countries dogs still carry rabies, and most rabies deaths in people around the world are caused by dog bites. There is no effective treatment for rabies. Prevention is the mainstay of treatment including programs involving domestic animal vaccination, education, and monitoring

Key words: Rabies, Vaccine, Rabid Animals, Pathogenicity, Egypt, Nursing A review article.

Introduction

More than 3.3 billion people worldwide live in enzootic rabies areas. Human mortality from rabies is estimated at 59,000 deaths annually, mainly most cases occur in Africa and Asia, and result primarily from canine reservoirs (Hampson *et al,* 2015). In the United States, there has been an average of two fatal human rabies cases annually since 1980, 30% of them being imported cases with exposures occurring abroad; the majority of indigenous cases have been associated with exposure to bats. The incubation period is typically one to three months in humans, but may be as short as four days or longer than six years, depending on the location and severity of the wound and the amount of virus introduced (Singh *et al,* 2017)

Rabies is virtually always fatal, but infection can be prevented with proper wound care and prompt post-exposure prophylaxis. In the United States, approximately 16,000 to 39,000 patients with contact to potentially rabid animals receive rabies post-exposure prophylaxis annually (Manning *et al,* 2008).

Review and Discussion

Rabies biologics: Rabies vaccine and immune globulin are given to prevent rabies.

Rabies vaccines: Rabies vaccine is administered for pre- or post-exposure prophylaxis. The dosing schedule is determined by the intended use of WHO (2013) guidelines represent the standard of care in the jurisdiction. Rabies vaccines should be administered intramuscularly (IM) in the deltoid area, in doses of 1 ml according to the recommended schedules for pre- or post-exposure pro-phylaxis. Vaccine should never be administered in the gluteal area because this may result in lower antibody titers (Fishbein *et al,* 1988). For infants and younger children, the anterolateral aspect of the thigh is also acceptable; depending on the age and body mass (CDC, 2023).

Two licensed vaccines are currently available in the United States: 1- Human diploid cell vaccine (HDCV, Imovax Rabies, Sanofi Pasteur). 2- Purified chick embryo cell vaccine (PCECV, RabAvert, Novartis Vaccine and Diagnostics)

Shortages of rabies vaccine due to supply issues among licensed manufacturers in the United States have occurred and most likely will recur. If pre-exposure vaccination cann't be safely delayed, or post-exposure prophylaxis is required and vaccine is not readily available, the local public health authority

should be consulted. In the United States, the CDC maintains updates on availability on its rabies website. Rabies vaccines available outside USA include: PCECV (Rabipur), HDCV (Rabivac), the purified vero cell rabies vaccine (PVRV; Verorab; Imo-vax-Rabies Vero, Rabivax-S, TRC Verorab) and purified duck embryo vaccine (Lyssavac N).

In developing countries, PVRV & PCECV are most commonly used. These vaccines have generally replaced HDCV since they are less expensive and are as safe and effective (Wilde *et al,* 1999). However, the cost of PVRV & PCECV is still too high for many developing countries given the amount of post-exposure treatment that is needed. To further reduce costs, a reduced dose intradermal regimen is used in certain settings (WHO, 2010). Some countries have produced vaccine in sheep, goat, or suckling mouse nervous tissue to reduce costs, but these vaccines have unreliable potency and a high incidence of neurologic complications, with an international effort to eliminate such products (Hemachudha *et al,* 1987).

Experimental vaccines are under investigation, such as a rabies messenger RNA vaccine. In a phase 1 trial that included 101 healthy adults, this vaccine was generally found to be safe and immunogenic when administered with a needle-free device (Alberer *et al,* 2017).

Rabies immune globulin (RIG) is administered as part of a post-exposure prophylaxis regimen. RIG is derived from pooled plasma samples of hyper-immunized human donors (human RIG; HRIG) or from horses (equine RIG; ERIG). Both preparations are considered equally potent and effective. Although these products are derived from human donors or horses, they are treated in ways that eliminate infectious agents, and no transmission of infectious agents has yet been documented from either product. The recommended dose of HRIG is 20international units/kg in all age groups. Outside the United States, if ERIG is used (including F (ab') 2 products), the dose is 40international units/kg body weight. RIG can partially suppress antibody production, so no more than the single recommended dose should be administered (Cabasso *et al,* 1971). As much of RIG dose as is anatomically feasible should be infiltrated in the area in and around the wounds. Any remaining dose must be given intramuscularly and at a different intramuscular site than the vaccine (such as opposite deltoid). If there is no obvious wound (e.g., suspected bat exposure), the large volume of RIG should be administered into the anterolateral thigh or the deltoid muscle contralateral to the vaccine dose, according to product package inserts. But, historically, most clinicians and nurses have given immune globulin into gluteus muscle.

Three HRIG preparations are approved for use in USA (Tab. 3): 1-Hyper Rab S/D (Grifols Therapeutics Inc.) 150international units/ml. (2ml, 10ml); (solvent/detergent treated). 2-Imogam Rabies- HT (Sanofi Pasteur SA) 150 international units/mL (2ml, 10ml); (Heat treated). 3-KEDRAB (Kedrion BioPharma and Kamada, Ltd) 150 international units/ml (2ml, 10ml), received US/FDA approval in 2017 and expected to be available in 2018.

HRIG is also available outside the United States under a variety of trade names including: Bayrab, Berirab P, Imogam, and Imogam Rabies. However, imported HRIG is expensive and generic products (made in some blood banks abroad) are in scarce supply.

ERIG is a less expensive but safe and effective alternative for RIG in some resource-limited settings (Chantanakajornfung *et al,* 1999). Despite the potential advantages of ERIG, during the past two decades several major manufacturers didn't continue ERIG production because of costs, pressures from animal rights activists, and more requirements from national regulatory authorities (Wilde *et al,* 2002). Due to global shortages of HRIG and ERIG and the expense of production, alternate means of prophylaxis are being sought. Human monoclonal antibodies (CR57 & CR4098) demonstrated in-vitro

neutralization against rabies virus (Goudsmit *et al*, 2006). In an animal model, these monoclonal antibodies provided protection a level against lethal rabies virus challenge as that of HRIG.

In the first clinical study among healthy adults in the United States and India, CR57 and CR4098 were safe and well tolerated (Bakker *et al,* 2008). All subjects had adequ ate neutralizing activity against rabies virus from day 14 onward when given in combination with rabies vaccine. Another neutralizing monoclonal antibody (SII RMAb) has also showed promise and appeared safe, but not inferior to HRIG in rabies virus neutralizing antibody activity as measured by the rapid fluorescent focus inhibition test (Gogtay *et al,* 2012). In 2016, the first rabies monoclonal antibody product using SII RMAb was licensed for use in India as the passive antibody component of the post-exposure prophylaxis (Gogtay *et al,* 2018).

Regimens for pre-exposure prophylaxis: Pre-exposure rabies prophylaxis must be given to individuals who are at high risk of exposure to rabies (Strady *et al,* 1998). The primary series for pre-exposure prophylaxis includes 3 doses of rabies vaccine (Tab. 1).

Routine testing after pre-exposure prophylaxis is generally not needed since antibody responses in the vast majority of patients are predictable and relatively long-lived (Mansfield *et al,* 2016). However, monitoring is warranted for: 1- Those with ongoing risk, and a booster vaccine should be administered when neutralizing antibodies decline to less than protective levels (Tab. 4). 2- Immunocompromised hosts if the pre-exposure is administered. Typically, the immunocompromised patients should avoid activities that put them at risk for exposure to rabies, and, thus, they would not require pre-exposure prophylaxis. But, if the risk of exposure to rabies is unavoidable, response to pre-exposure prophylaxis should be assessed.

Multiple studies in humans demonstrate that vaccination with human diploid cell vaccine (HDCV) or purified chick embryo cell vaccine (PCECV) results in significant titers of neutralizing antibodies by day 14 (Sabchareon *et al,* 1999). Studies have showed that antibody kinetics and persistence of antibody over several years are similar between these two types of cell culture vaccine preparations (Nicholson *et al,* 1987). Studies in animals have also showed protective levels of antibody after immunization with HDCV (Lodmell and, Ewalt, 2000). In addition, one study demonstrated protection against challenge with rabies viruses after primary vaccination with PCECV or HDCV in all animals, except in one group that had been challenged through an intracranial route, which had 5% mortality rate (Brookes *et al,* 2005).

Post-exposure prophylaxis: Post-exposure prophylaxis includes proper wound care and administration of rabies biologics. Approach to post-exposure prophylaxis is based upon guidelines from Advisory Committee on Immunization Practices (ACIP). The full guidelines can be accessed at: www.cdc.gov/mmwr/pdf/rr/rr57e507.pdf (with updated vaccine schedule recommendations at www.cdc. gov/mmwr/pdf/rr/rr5902). No post-exposure vaccine failures have occurred in the United States; however, occasional case reports of rabies in vaccinated individuals have occurred elsewhere.

Wound care: One of the most important initial steps to prevent rabies is wound care. Thorough washing of bite wounds, scratches, and non-bite exposures with soap and water is recommended, if feasible. When available, a virucidal agent such as povidone-iodine should also be used. Tetanus prophylaxis, as well as antibiotics, should also be considered, depending on the type of wound, as tetanus-diphtheria toxoid vaccination in adults and soft tissue infections due to dog and cat bites (Havers *et al,* 2020).

In animal studies of rabies, wound cleansing alone reduced the likelihood of rabies by up to 90% (Dean *et al,* 1963). However, a survey of the international travel medicine providers suggested that many of those presenting with wounds from an animal expo-

sure didn't perform adequate wound cleaning (Jentes *et al,* 2013).

Post-exposure immunization: Post-exposure prophylaxis includes rabies vaccine (active immunization) with or without rabies Ig (passive immunization). The use of these agents elicits neutralizing antibodies after rabies exposure and prevents infection. Rabies vaccine induces the production of protective virus-neutralizing antibodies within about 7 to 10 days; measurable antibody generally persists for several years, although individual variability exists (Fishbein *et al,* 1986). The administration of rabies Ig (RIG) provides immediate virus-neutralizing antibodies until protective antibodies are generated in response to vaccine. Human RIG (HRIG) has a half-life of about three weeks (Hanna *et al,* 2018). The regimen for post-exposure prophylaxis depends primarily upon the patient's previous immunization history, the schedules, doses, and routes of administration (Tab. 2)

Immunization time: Once it has been decided that a patient should receive rabies post-exposure prophylaxis, prophylaxis must begin as soon as possible after the exposure (Ahmad *et al,* 2022). Decision to start prophylaxis requires a thorough risk assessment, which depends upon the type of exposure, the local rabies epidemiology, the circumstances of the exposure incident, and the availability of animal for observation or rabies testing; algorithm 1 (Crump *et al,* 2021).

Post-exposure prophylaxis must be administered following a rabies exposure, even if there is a delay; post-exposure prophylaxis is only too late when signs of clinical rabies develop. Average incubation period is 45 days, although latency periods between exposure and onset of disease as long as one to eight years have been reported (Boland *et al,* 2014). No post-exposure prophylaxis failures were reported in the United States despite an average delay to initiation of approximately five days.

The State and Local Public Health officials are typically available to assist with risk assessments. In the United States, contacts can be found on the CDC (1999).

Regimen for patients not vaccinated before: For patients who have not completed a rabies vaccine series (e.g., pre-exposure prophylaxis), post-exposure prophylaxis should always include both passive and active immunization (Tab. 2). Studies evaluated efficacy of RIG plus vaccine include: 1- Combination of five intramuscular (IM) doses of human diploid cell vaccine (HDCV) and HRIG prophylaxis was evaluated in 90 persons treated after expo-sure to rabies, 21 of whom were bitten by proven rabid animals (Anderson *et al,* 1980). All 87 persons tested developed protective titers of antibody (≥0.5 international units/mL). A year after vaccination, all 33 persons who had follow-up testing had detectable antibodies to rabies virus. 2- Forty-five persons bitten by rabid dogs and wolves in Iran were treated with HDCV, and all except one also received RIG (Bahm anyar *et al,* 1976), none of the exposed persons developed rabies. 3- In 40 patients with rabies exposure, all who received HDCV, with or without RIG, seroconverted but, those who received both had significantly higher antibody titers (Navarrete-Navarro *et al,* 1999). 4- A study reported no human rabies cases among 45 patients receiving six intramuscular doses of purified chick embryo cell vaccine (PCECV) and HRIG after exposed to biopsy-proven rabid animals (Bijok *et al,* 1984). 5- In 171 Chinese patients with severe rabies exposure who received five IM purified vero-cell rabies vaccine (PVRV) & equine RIG (ERIG) showed protective neutralizing antibodies of more than 0.5international units/ml by day 14 in all 171 cases. None developed rabies up to six months after treatment (Wang *et al,* 2000).

Administration of rabies Ig: Rabies immune globulin (RIG) should be administered to patients who have not completed a rabies vaccine series. RIG should always be given in a different syringe from the vaccine.

Rabies vaccine for unvaccinated persons: After a rabies exposure, immunocompetent

patients should receive rabies vaccine starting promptly after exposure (day 0) and on days 3, 7, and 14 (table 2).

For immunocompromised hosts, a 5th dose on day 28 must be administered (Deshpande *et al,* 1998). Besides, these patients must have antibody titers checked to assess their response. Although data are limited corticosteroids, other immunosuppressive drugs, and immunocompromising illnesses may prevent the immune response to rabies vaccination to the point of insufficient neutralizing antibody (Kopel *et al,* 2012).

Earlier guideline recommendations included a fifth dose of rabies vaccine on day 28 for all patients (Rupprecht *et al,* 2010), which consisted with the package inserts from both manufacturers that provide vaccine in the United States (Novartis and Sanofi Pasteur). The decision to reduce the regimen to a four-dose series for immunocompetent patients is based upon global epidemiologic studies, which found that rabies did not develop in any patient who received appropriate wound care, HRIG, and four doses of vaccine; in addition, immunologic studies found the fifth dose did not lead to a further increase in antibody titers (Rupprecht *et al,* 2009) However, the manufacturers' recommendations are not expected to change.

Reducing the number of clinic visits for rabies prophylaxis can help improve completion of post-exposure dosing schedules, especially in areas where access to medical care is limited and requires significant travel. Preliminary results from one study in healthy volunteers suggest that a one-week schedule of prophylaxis increases neutralizing antibody levels compared with standard regimens (Shantavasinkul *et al,* 2010), but this was not adopted by either the US/CDC or WHO.

Regimen for patients received prior rabies vaccine: After an exposure, vaccine alone (i.e., no RIG) is a must for the following patients: 1- Exposed persons who have completed a full pre-exposure or post-exposure prophylaxis vaccine series with a cell culture or chick embryo cell vaccine. 2- Rabies vaccines' exposed persons who were vaccinated with other types of rabies vaccine followed by a documented neutralizing antibody response. Such patients should receive two intramuscular doses of vaccine. The first dose is administered on day 0, as soon after exposure as possible, and the other three days later (Tab. 2). RIG is not needed in these patients because the anamnestic response to vaccine is sufficient in persons who were effectively vaccinated previously. Similarly, routine serologic testing after boosting is not recommended because of the uniformity of the antibody response.

Resource-limited settings: While post-exposure prophylaxis can prevent deaths in patients exposed to rabies, the treatment regimen is expensive, costing over USD $3000 per person for biologics alone (Vora *et al,* 2015). The annual expenditure for rabies globally has been estimated at USD $8.6 billion in direct costs and lost productivity, with Asia and Africa accounting for the majority. The cost of post-exposure prophylaxis with rabies immune globulin and vaccine accounts for a significant proportion of this expenditure. To address these cost-related issues in resource-limited settings, the WHO and other agencies have developed protocols to help reduce the costs associated with rabies prophylaxis.

Dosing schedule: All patients who require post-exposure prophylaxis should receive proper wound care. However, for patients who have never received rabies vaccine, the post-exposure immunization regimen depends upon the type of exposure (WHO, 2017): 1-For those who had single or multiple transdermal bites or scratches, licks on broken skin, contamination of mucous membrane with saliva, or exposures to bats, the WHO recommends vaccine and RIG.
The WHO guidelines recommend the five-dose schedule for IM rabies immunization for this type of exposure (one dose administered on each of days 0, 3, 7, 14, & 28). They also cite the four-dose IM schedule

(days 0, 3, 7, & 14) as an alternative regimen for exposed patients who are immunocompetent and receive wound care plus high quality RIG. 2- For patients who had an exposure that occurred via nibbling of uncovered skin by an animal or sustained minor scratches or abrasions (without bleeding), the WHO recommends vaccine alone.

Five doses of the rabies vaccine should be administered intramuscularly (one dose administered on each of days 0, 3, 7, 14, & 28). An alternative four-dose IM regimen (two doses on day 0 [one into each of the two deltoids] and one dose on days 7 & 21) can also be administered. Additional information on the WHO four-dose regimen can be accessed.

Intradermal administration of vaccine: Intradermal routes of vaccine administration are not used for products licensed in the United States. However, in areas where vaccine and financial resources are in short supply, intradermal administration of vaccine can reduce costs by up to 80%: 1-For patients who have not received pre-exposure prophylaxis, the "Thai Red Cross" intradermal schedule ("2-2-2-0-2" regimen) has proven to be efficacious when used with PVRV or PCECV vaccine. The recommended regimen is one injection of 0.1 ml at each side of the upper arm (i.e., two injections at each visit) on days 0, 3, 7, & 28. 2- For patients who received pre-exposure prophylaxis, WHO (2018) guidelines suggested one of two different intradermal regimens: one intradermal injection of 0.1 ml rabies vaccine at a single site on days 0 & three; or four intradermal injections of 0.1 ml rabies vaccine in the upper arm or thigh, all given on the same day (Harverson and Wasi, 1984)

The effectiveness of all cell culture vaccines given intradermal with or without RIG among rabies-exposed humans was demonstrated in several studies with different schedules (Warrell *et al,* 1985; Chutivongse *et al,* 1990; Quiambao *et al,* 2005). Intradermal administration for the pre-exposure prophylaxis was evaluated (Recuenco *et al,* 2017).

For travelers who received post-exposure prophylaxis in a resource-limited setting, receipt of vaccine by intradermal method may not be sufficient justification in and of itself to recommend re-administration (Kerdpanich *et al,* 2018).

Deviations from immunization regimens: Every attempt should be made to administer pre- and post-exposure prophylaxis according to the appropriate the CDC or WHO schedule. However, deviations of a few days from the immunization schedule don't require the complete re-initiation of vaccination (Rupprecht and Gibbons, 2004). If a patient misses an injection, the immunization series should be continued until all doses have been administered according to the regular intervals (e.g., if day 7 vaccine is given on day 10, next dose should be on day 17, 7 days later…etc.). For more significant deviations from the schedule, antibody testing by using the rapid fluorescent focus inhibition test (RFFIT) should be conducted at least 14 days after initiation and again 7 to 14 days after the final dose is given (CDC, 2016). Serologic testing is given below.

Another area of potential concern is when different vaccine formulations are used. Although the vaccine formulations are essentially equivalent in immunogenicity, and theoretically can be substituted for one another, there are scant data on this approach. Thus, when feasible, use of the same vaccine formulation is recommended during the entire immunization series (Briggs *et al,* 2000). However, this may not be possible, particularly in returning travelers who need to complete a vaccine series. In this setting, patients should typically complete the immunization series with intramuscularly administered rabies vaccine and document protective RFFIT antibody titers.

Pregnancy: There is no evidence that rabies vaccination is associated with fetal abnormalities or adverse pregnancy outcomes of any kind (Chutivongse *et al,* 1995). Pregnancy is therefore not a contraindication to post-exposure prophylaxis if a rabies expos-

ure has occurred. The danger of rabies after a significant exposure far outweighs any theoretical risk from administration. For patients in a continuous risk category, pre-exposure prophylaxis might also be necessary during pregnancy (Varner *et al,* 1982).

Antimalarial prophylaxis: Little data showed that antimalarial prophylaxis with chloroquine may blunt the immune response to rabies vaccine, which is considered a concern primarily with pre-exposure prophylaxis regimens. So, when possible, patient receiving pre-exposure prophylaxis should complete the series prior to begin the antimalarial. Also, the WHO recommends that patients receiving antimalarial prophylaxis be given rabies vaccine intramuscularly (not intradermally) as a precaution. Because intramuscular administration is the only appropriate method for United States products, no special recommendations apply.

In a randomized controlled study of 51 veterinary students, antibody responses to intradermal HDCV were assessed when chloroquine was given (Pappaioanou *et al,* 1986). Although all achieved an adequate vaccine response according to CDC criteria, the mean neutralizing antibody titers were significantly lower in 26 individuals who also received malaria prophylaxis. Decreased antibody titers have not been documented with other anti-malarials as mefloquine, although it is theoretically possible; this is currently being studied.

Prophylaxis failure Risk: Recommended post-exposure prophylaxis regimens appear uniformly effective. No post-exposure vaccine failures have occurred in the United States. However, occasional case reports of rabies in vaccinated individuals have occurred outside the United States, when ACIP recommendations have not been followed. Failure of prophylaxis was associated with: 1- Improper wound cleaning, 2- Inadequate dosing of RIG, 3- Absence of RIG administration in the wound site, & 4- Vaccine administration in the gluteal area. To reduce the failure risk, an antibody titer should be checked if a post-exposure prophylaxis regimen using unknown or nonstandard biologics was administered.

If the serologic response was appropriate, no additional immunization is needed. However, if the response was not adequate, post-exposure prophylaxis should be readministered in consultation with the local or state public health department or the CDC.

Post-vaccination serologic testing: In general, routine postvaccination serologic testing is not necessary. Rabies vaccine induces protective neutralizing antibodies in the vast majority of patients. Questions as to whether a particular patient should have response to prophylaxis monitored should be directed to public health authorities or the US/CDC.
However, serologic testing using the rapid fluorescent focus inhibition test (RFFIT) is reasonable in the following groups of patients: 1- Patients with ongoing risk: Patients who received pre-exposure prophylaxis and have ongoing risk may need a booster dose of vaccine. Intervals for serologic testing & guidance regarding booster doses are found in the tables (tables 1 & 4). 2- Immunocompromised patients: Immunocompromised patients should ideally avoid activities that put them at risk for exposure to rabies. However, if that is not possible and prophylaxis was administered, it is important to assess the vaccine response. In post-exposure prop -hylaxis, testing should be performed on day 14 of the vaccine series and again 7 to 14 days after the final dose is given (table 2). Response to pre-exposure prophylaxis must be assessed in a sample drawn 7 to 14 days following the third dose (table 1). 3- Patients received inadequate prophylaxis: Assessment response to post-exposure prophylaxis in patients who may have received a regimen that provided suboptimal protection (e.g., prophylaxis regimen didn't include human rabies immune globulin (HRIG) or substituted equine RIG (ERIG); the patient received any part of the post-exposure regimen in a resource-limited setting where vaccine hand ling and storage may have been compromised or

where vaccine production was not well regulated; there were significant deviations from the vaccine schedule). Testing should be performed at least 14 days after initiation and may be performed again 7 to 14 days after the final dose is given if the first titer is below 0.5international units/ml as measured by RFFIT. The minimum acceptable antibody level, as recommended by CDC, is complete virus neutralization at a 1:5 serum dilution by the RFFIT. Serological methods for monitoring rabies-specific antibody titers in dogs can be carried out using enzyme-linked immunosorbent assay (ELISA) methods as recommended by the World Organization for Animal Health (Fitria *et al,* 2023). For immunocompromised patients and those who may have received a suboptimal regimen, failure to demonstrate an adequate immune response when tested may indicate the need for additional vaccination. Such patients should be managed in the consultation with State Public Health Authorities or the CDC.

Rabies vaccine adverse reactions: Patients who receive the rabies vaccine can have a variety of adverse reactions depending upon the type they receive: 1- Human diploid cell vaccine (HDCV): Local reactions, including pain at the injection site, redness, swelling, and induration, have been reported in many patients. Most are mild and resolve in a few days. Systemic reactions are less common and include mild fever, headache, dizziness, and gastrointestinal symptoms (Fishbein *et al,* 1989). However, allergic reactions can occur, and patients who develop a hypersensitivity to this vaccine can receive purified chick embryo cell vaccine (PCECV) formulation if future doses are needed. During surveillance for adverse events following HDCV immunization from 1980 to 1984, CDC (1984) received reports of 108 systemic allergic reactions, ranging from hives to anaphylaxis, for a rate of approximately 11/10,000 vaccines Also, systemic hypersensitivity reactions have been reported in up to 6 percent of persons receiving a booster vaccination with HDCV following primary rabies prophylaxis (Fishbein *et al,* 1993). 2- Purified chick embryo cell vaccine (PCECV): PCECV is also associated with local reactions at injection site. A retrospective review of adverse events following immunization with PCECV was conducted using data from the Vaccine Adverse Event Reporting System (VAERS) over an eight-year period (Dobardzic *et al,* 2007). Mild side effects included headache, fever, myalgia, nausea, and weakness. Serious adverse events were uncommon (3 per 100,000 doses distributed). Hypersensitivity to PCECV is less well described (Dreesen *et al,* 1989) but, HDCV vaccine can replace PCECV if hypersensitivity develops with the use of that product as the initial vaccine. 3- Purified vero cell rabies vaccine (PVRV): Like HDCV and PCECV, PVRV is associated with both local and systemic reactions (Kulkarni *et al,* 2013). In 60 healthy adult volunteers received a pre-exposure vaccine series of a new PVRV vaccine either intramuscularly or intradermally, or a previously licensed PVRV vaccine intramuscularly, 116 adverse events were reported across all three groups. Twenty-eight local reactions included pain at the injection site, erythema, pruritus, induration, and edema. All local reactions were judged to be relatively mild and resolved rapidly. Eighty-eight systemic reactions were comprised primarily of headache, arthralgia, and myalgia and were self-limiting. There were no significant differences in the type of rate of reported local or system reactions between the three groups. Rare case reports of neurologic adverse events (e.g., acute disseminated encephalomyelitis, Guillain-Barré) following rabies vaccination have also been reported; however, causality has not been established.

Clinicians in the United States who require assistance in the management of a patient with significant hypersensitivity should contact their state health department rabies consultant or the CDC. All serious vaccine reactions should be reported to VAERS, phone

number 800-822-7967,

Although severe reactions are rare, a study found that about 50% of individuals receiving either pre- or post-exposure prophylaxis experienced at least one systemic reaction, and that 5% of individuals actually discontinued the vaccine series due to their reaction. Individuals who have had a rabies exposure and who experience a systemic reaction may need to be encouraged to complete post-exposure series (Mattner *et al,* 2007).

Rabies immune globulin adverse reactions: Human rabies Ig (HRIG) is associated with local reactions including pain and tenderness, erythema, and induration. Headache is the most commonly reported systemic side effect (Lang *et al,* 1998). There has never been evidence of transmission of any known virus or infectious agent by HRIG approved for use in the United States. Use of equine rabies Ig (ERIG) products can be associated with hypersensitivity reactions and must be administered under close medical supervision. But, most of the available preparations are associated with very few adverse reactions. The purified immunoglobulin cleavage fragment products may be less reactogenic. In a retrospective study at the Thai Red Cross, adverse events to HRIG & ERIG were reviewed in more than 70,000 patients (Suwansrinon *et al,* 2007). A higher number of side effects occurred among those who had received ERIG (1.83 versus 0.09%). General observations also included a higher risk of hypersensitivity to either product among females and a lower risk of serum-sickness in children less than 10 years of age. Only one patient developed anaphylaxis associated with ERIG administration.

In Egypt, Botros *et al.* (1988) isolated Nineteen street rabies virus strains, from humans (two), dogs (nine), cats (two), farm animals (two), gerbils (three), and a jackal were antigenically analyzed. Raybern *et al.* (2020) in USA reported that on 2019, rabies was diagnosed in a dog out of 26 vaccined imported from Egypt, represented the third canine rabies case imported from Egypt in 4 years. FAO (2021) in the World Rabies Day was celebrated in the presence of a large number of parties involved in combating this disease in Egypt. The Strategic Framework for Elimination of Dog-Mediated Human Rabies in Egypt was developed in cooperation between the Ministry of Health (MOPH), the Ministry of Agriculture and Land Reclamation (MoALR) and the Ministry of Environment (MOE) with support of the (WHO) and the Food and Agriculture Organization of the United Nations (FAO). This national strategic framework aims at zero human dog-mediated rabies deaths by 2030, a goal consistent with the global action plan set in 2015 by WHO, OIE, FAO & GARC. Egypt's strategic framework consists of seven pillars and requires utmost efforts by all actors in a multi-sectoral partnership in order to realize its goal. Taha et al. (2023) in Benha evaluated the effect of health educational programs for rural population on prevention of rabies, they reported a highly significant correlation between the rural population's total knowledge level and total practices level and total attitude level preprogram and post program implementation. CDC (2024) reported that as in most other low-income countries, rabies is endemic throughout Egypt, where rabies vaccine is available for pre-exposure and post-exposure prophylaxis; human rabies immune globulin

Nursing management

A patient with rabies include: 1- History, **i**dentify the following in any suspected case of rabies virus exposure: the nature of the interaction with the animal (recall that "provocation" is not an indication of rabies risk, since humans may not understand what is provocative to a wild animal); strange animal behavior; vaccination status of animal for rabies; and availability of animal for testing, 2- Physical examination with furious rabies, patients present with episodic delirium, psychosis, restlessness, thrashing, muscular fasciculations, seizures, and/or aphasia; autonomic instability is observed with the furi-

ous rabies.

Major nursing diagnosis are: 1- Ineffective breathing pattern related to asphyxia, 2- Imbalanced nutrition, 3- Hyperthermia related to viremia, 4- Anxiety of family related to information exposure, 5- Risk for injury related to seizures and weakness, & 6- Risk for infection associated with open wounds.

Major nursing care plan goals include: 1- Patient displays to improve breathing pattrn, 2- Takes adequate amount of calories or nutrients, 3- Maintains body temperature below 39° C (102.2° F), 4- Identifies strategies to reduce anxiety, 5- Remains free of injuries, and infection.

Nursing interventions are: 1- Improve patient breathing pattern, 2- Improve his/her nutritional intake, 3- Maintain normal body temperature, 4- Reduce all anxiety, 5- Prevent injury, and infection.

Summary and Recommendations

Rabies is virtually always fatal, but infection can be prevented with proper wound care and post-exposure prophylaxis using rabies biologics (rabies vaccine, rabies immune globulin, RIG).

Several rabies vaccine and RIG formulations are available, but administration is critical to optimize the protective efficacy and prevent vaccine failure. Vaccines must be administered intramuscularly. The deltoid is the only acceptable intramuscular site for vaccine administration in adults and older children, although the outer aspect of the thigh can be used for young children. The gluteal muscle should not be used for rabies vaccine since antibody responses have been lower after administration at that site.

If RIG is required, the wound should be infiltrated with RIG; any remaining dose should be given intramuscularly and at a different intramuscular site than the vaccine.

Pre-exposure rabies prophylaxis should be administered to individuals who are at high risk of being exposed to rabies. The primary series for pre-exposure prophylaxis includes three doses of rabies vaccine. A booster vaccine should be administered to those with ongoing risk when neutralizing antibodies decline to less than protective levels. Post-exposure prophylaxis includes proper wound care and giving of rabies biologics (rabies vaccine with or without RIG) to elicit neutralizing antibodies after a rabies exposure.

Once determined that the patient should receive rabies post-exposure prophylaxis, prophylaxis should begin as soon as possible after the exposure. Decision to initiate prophylaxis requires a careful risk assessment and depends upon the type of exposure, the local rabies epidemiology, the circumstances of the exposure incident, and the availability of animal for observation or rabies testing (algorithm 1).

Regimen used for post-exposure prophylaxis depends upon patient's previous immunization history. Dosing schedules and administration routes are given, but, in certain resource-limited settings, may be modified to maximize vaccine availability.

Immunization schedules must be adhered to as closely as possible but, if a delay of only a few days occurs, schedule simply resume with intervals preserved within the new schedule. By contrast, antibody titers are assessed to evaluate efficacy if the dosing schedule has been significantly violated. Both rabies immunoglobulin and rabies vaccines are associated with local reactions

. References

Ahmad, N, Nawi, AM, Jamhari, MN, Nurumal, SR, Mansor, J, *et al,* 2022: Post-exposure prophylactic vaccination against rabies: A systematic review. Iran J. Publ.Hlth. 51, 5:967-77.

Alberer, M, Gnad-Vogt, U, Hong, HS, *et al,* 2017: Safety and immunogenicity of a mRNA rabies vaccine in healthy adults: an open-label, non-randomised, prospective, first-in-human phase 1 clinical trial. Lancet 390:1511.

Anderson, LJ, Sikes, RK, Langkop, CW, *et al,* 1980: Postexposure trial of a human diploid cell strain rabies vaccine. J. Infect. Dis. 142:133.

Bahmanyar, M, Fayaz, A, Nour-Salehi, S, *et al,* 1976: Successful protection of humans exposed to rabies infection: Postexposure treatment with the new human diploid cell rabies vaccine and antirabies serum. JAMA 236:2751.

Bakker, AB, Python, C, Kissling, CJ, *et al,*

2008: First administration to humans of a monoclonal antibody cocktail against rabies virus: safety, tolerability, and neutralizing activity. Vaccine 26:5922.

Bijok, U, Vodopija, I, Smerdel, S, *et al,* 1984: Purified chick embryo cell (PCEC) rabies vaccine for human use: clinical trials. Behring Inst. Mitt. 84:155.

Boland, TA, McGuone, D, Jindal, J, *et al,* 2014: Phylogenetic and epidemiologic evidence of multiyear incubation in human rabies. Ann. Neurol. 75:155.

Botros, BA, Salib, AW, Mellick, PW, Linn, JM, Soliman, AK, *et al,* 1988: Antigenic variation of wild and vaccine rabies strains of Egypt. J. Med. Virol. 24, 2:153-9.

Briggs, DJ, Dreesen, DW, Nicolay, U, *et al,* 2000: Purified chick embryo cell culture rabies vaccine: Interchangeability with human diploid cell culture rabies vaccine and comparison of one versus two-dose post-exposure booster regimen for previously immunized persons. Vaccine 19:1055-12.

Brookes, SM, Parsons, G, Johnson, N, *et al,* 2005: Rabies human diploid cell vaccine elicits cross-neutralising and cross-protecting immune responses against European and Australian bat lyssaviruses. Vaccine 23:4101.

Cabasso, VJ, Loofbourow, JC, Roby, RE, Anuskiewicz, W, 1971: Rabies immune globulin of human origin: preparation and dosage determination in non-exposed volunteer subjects. Bull. WHO 45:303.

CDC, 1984: Systemic allergic reactions following immunization with human diploid cell rabies vaccine. MMWR Morb Mortal Wkly Rep 1984; 33:185.

CDC, 1999: Human rabies prevention--United States, 1999: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm. Rep. 48:1.

CDC, 2016: Rabies Specimen Submission Guidelines https://www.cdc.gov/rabies/specific_groups/hcp/serology.html

CDC, 2023: Vaccine Administration https://www.who.int/health-topics/rabies.

CDC, 2024: Egypt: Yellow Book 2024 https://wwwnc.cdc.gov/travel/destinations/traveler/none/egypt.

Chantanakajornfung, A, Naraporn, N, Khumphai, W, *et al,* 1999: A study of human rabies immune globulin manufactured by the Thai Red Cross. Vaccine 17:979.

Chutivongse, S, Wilde, H, Benjavongkulchai, M, *et al,* 1995: Postexposure rabies vaccination during pregnancy: effect on 202 women and their infants. Clin. Infect. Dis. 20:818.

Chutivongse, S, Wilde, H, Supich, C, *et al,* 1990: Post-exposure prophylaxis for rabies with antiserum and intradermal vaccination. Lancet 335:896.

Crump, L, Maidane, Y, Mauti, S, Tschopp, R, Ali. SM, *et al,* 2021: From reverse innovation to global innovation in animal health: A review. Heliyon. 2021 Sep 21; 7, 9:e08044. doi: 10.1016/j.heliyon.2021.e08044. eCollection 2021.

Dean, DJ, Baer, GM, Thompson, WR, 1963: Studies on the local treatment of rabies-infected wounds. Bull. WHO 28:477.

Deshpande, A, Briggs, DJ, Dietzschold, B, *et al,* 1998: Immune response to purified chick embryo cell vaccine (PCECV) in HIV-infected individuals in Mumbai India using a simulated rabies post-ex-posure regimen. In: Proc. IX Inter. Meet. Res. Adv. Rabi. Contr. Americas, Puerto Vallarta Mexico.

Dobardzic, A, Izurieta, H, Woo, EJ, *et al,* 2007: Safety review of the purified chick embryo cell

Dreesen, DW, Fishbein, DB, Kemp, DT, Brown, J, 1989: Two-year comparative trial on the immunogenicity and adverse effects of purified chick embryo cell rabies vaccine for pre-exposure immunization. Vaccine 7:397-404.

Fishbein, DB, Bernard, KW, Miller, KD, *et al,* 1986: The early kinetics of the neutralizing antibody response after booster immunizations with human diploid cell rabies vaccine. Am. J. Trop. Med. Hyg. 35:663-9.

Fishbein, DB, Dreesen, DW, Holmes, DF, *et al,* 1989: Human diploid cell rabies vaccine purified by zonal centrifugation: a controlled study of antibody response and side effects following primary and booster pre-exposure immunizations. Vaccine 7:437-46.

Fishbein, DB, Sawyer, LA, Reid-Sanden, FL, Weir, EH, 1988: Administration of human diploid-cell rabies vaccine in the gluteal area. N. Engl. J. Med. 318:124.

Fishbein, DB, Yenne, KM, Dreesen, DW, *et al,* 1993: Risk factors for systemic hypersensitivity reactions after booster vaccinations with human diploid cell rabies vaccine: a nationwide prospective study. Vaccine 11:1390.

Fitria, Y, Febrianto, N, Putri, RE, Rahmadani, I, Subekti, DT, 2023: Evaluation of in-house

elisa for anti-rabies antibodies detection in domestic canine. Vet. Med. Int. 2023 Jan 25; 2023: 4096258. doi: 10.1155/2023/4096258

FOA-Egypt, 2021: World Rabies Day 2021 Celebration- Egypt presents the Strategic Framework for Elimination Rabies by 2030

Gogtay, N, Thatte, U, Kshirsagar, N, *et al,* 2012: Safety and pharmacokinetics of a human monoclonal antibody to rabies virus: a randomized, dose-escalation phase 1 study in adults. Vaccine 30:7315.

Gogtay, NJ, Munshi, R, Ashwath Narayana, DH, *et al,* 2018: Comparison of a novel human rabies monoclonal antibody to human rabies immunoglobulin for postexposure prophylaxis: A phase 2/3, randomized, single-blind, noninferiority, controlled study. Clin. Infect. Dis. 66: 387.

Goudsmit, J, Marissen, WE, Weldon, WC, *et al,* 2006: Comparison of an anti-rabies human monoclonal antibody combination with human polyclonal anti-rabies immune globulin. J. Infect. Dis. 193:796.

Hampson, K, Coudeville, L, Lembo, T, *et al,* 2015: Estimating the global burden of endemic canine rabies. PLoS Negl. Trop. Dis. 9: e0003-709.

Hanna, K, Cruz, MC, Mondou, E, Corsi, E, Vandeberg, P, 2018: Safety and neutralizing rabies antibody in healthy subjects given a single dose of rabies immune globulin caprylate/ chromatography purified. Clin. Pharmacol. 10:79-88.

Harverson, G, Wasi, C, 1984: Use of post-exposure intradermal rabies vaccination in a rural mission hospital. Lancet 2:313.

Havers, FP, Moro, P, Hunter, P, *et al,* 2020: Use of Tetanus Toxoid, Reduced Diphtheria Toxoid, and Acellular Pertussis (Tdap) Vaccines:Updated Recommendations of the Advisory Committee on Immunization Practices. MMWR Morb. Mortal. Wkly, Rep. 69, 3:77-83.

Hemachudha, T, Phanuphak, P, Johnson, RT, *et al,* 1987: Neurologic complications of Semple-type rabies vaccine: clinical and immunologic studies. Neurology 137:550.

Jentes, ES, Blanton, JD, Johnson, KJ, *et al,* 2013: The global availability of rabies immune globulin and rabies vaccine in clinics providing direct care to travelers. J. Travel Med. 20:148.

Kopel, E, Oren, G, Sidi, Y, David, D, 2012: Inadequate antibody response to rabies vaccine in immunocompromised patient. Emerg. Infect Dis. 18:1493.

Kerdpanich, P, Chanthavanich, P, De Los Reyes, MR, Lim, J, Yu, D, *et al,* 2018: Shortening intradermal rabies post-exposure prophylaxis regimens to 1 week: Results from a phase III clinical trial in children, adolescents and adults. PLoS Negl Trop Dis. 2018 Jun 6;12, 6: e0006340. doi: 10.1371/journal.pntd.0006340.

Kulkarni, PS, Sapru, A, D'costa, PM, *et al,* 2013: Safety and immunogenicity of a new purified vero cell rabies vaccine (PVRV) administered by intramuscular and intradermal routes in healthy volunteers. Vaccine 31:2719.

Lang, J, Gravenstein, S, Briggs, D, *et al,* 1998: Evaluation of the safety and immunogenicity of a new, heat-treated human rabies immune globulin using a sham, post-exposure prophylaxis of rabies. Biologicals 26:7.

Lodmell, DL, Ewalt, LC, 2000: Rabies vaccination: comparison of neutralizing antibody responses after priming and boosting with different combinations of DNA, inactivated virus, or recombinant vaccinia virus vaccines. Vaccine 18:2394.

Manning, SE, Rupprecht, CE, Fishbein, D, *et al,* 2008: Human rabies prevention--United States, 2008: recommendations of the Advisory Committee on Immunization Practices. MMWR Recomm. Rep. 57:1.

Mansfield, KL, Andrews, N, Goharriz, H, *et al,* 2016: Rabies pre-exposure prophylaxis elicits long-lasting immunity in humans. Vaccine 34:5959.

Mattner, F, Bitz, F, Goedecke, M, *et al,* 2007: Adverse effects of rabies pre- and post-exposure prophylaxis in 290 health-care-workers exposed to a rabies infected organ donor or transplant recipients. Infection 35:219.

Moro, PL, Lewis, P, Cano, M, 2019: Adverse events following purified chick embryo cell rabies vac-cine: Data from the vaccine adverse event reporting system (VAERS), 1997-2005. Vaccine 25: 4244.

Nurse Study Guides, 2023: Infectious & Communicable diseases. https://nurseslabs.com/rabies/

Navarrete-Navarro, S, Aguilar-Setién, A, Avila-Figueroa, C, *et al,* 1999: Improved serological response to human diploid cell rabies vaccine when given simultaneously with antirabies hyperimmune globulin. Arch. Med. Res. 30:332.

Nicholson, KG, Farrow, PR, Bijok, U, Barth, R, 1987: Pre-exposure studies with purified chick embryo cell culture rabies vaccine and

human diploid cell vaccine: serological and clinical responses in man. Vaccine 5:208.

Pappaioanou, M, Fishbein, DB, Dreesen, DW, *et al,* 1986: Antibody response to preexposure human diploid-cell rabies vaccine given concurrently with chloroquine. N. Engl. J. Med. 314: 280.

Quiambao, BP, Dimaano, EM, Ambas, C, *et al,* 2005: Reducing the cost of post-exposure rabies prophylaxis: efficacy of 0.1 ml PCEC rabies vaccine administered intradermally using the Thai Red Cross post-exposure regimen in patients severely exposed to laboratory-confirmed rabid animals. Vaccine 23:1709.

Raybern, C, Zaldivar, A, Tubach, S, Ahmed, FS, Moore, S, *et al,* 2020: Rabies in a Dog Imported from Egypt - Kansas, 2019. MMWR Morb. Mortal. Wkly. Rep. 69, 38:1374-7.

Recuenco, S, Warnock, E, Osinubi, MOV, Rupprecht, CE, 2017: A single center, open label study of intradermal administration of an inactivated purified chick embryo cell culture rabies virus vaccine in adults. Vaccine 35:4315.

Rupprecht, CE, Briggs, D, Brown, CM, *et al,* 2009: Evidence for a 4-dose vaccine schedule for human rabies post-exposure prophylaxis in previously non-vaccinated individuals. Vaccine 27:7141.

Rupprecht, CE, Briggs, D, Brown, CM, *et al,* 2010: Use of a reduced (4-dose) vaccine schedule for postexposure prophylaxis to prevent human rabies: recommendations of the advisory committee on immunization practices. MMWR Recomm. Rep. 59:1.

Rupprecht, CE, Gibbons, RV, 2004: Clinical practice: Prophylaxis against rabies. N. Engl. J. Med. 351:2626.

Sabchareon, A, Lang, J, Attanath, P, *et al*, 1999: A new Vero cell rabies vaccine: results of a comparative trial with human diploid cell rabies vaccine in children. Clin. Infect. Dis. 29:141.

Shantavasinkul, P, Tantawichien, T, Wilde, H, *et al,* 2010: Postexposure rabies prophylaxis completed in 1 week: preliminary study. Clin. Infect. Dis. 50:56.

Singh, R, Singh, KP, Cherian, S, Saminathan, M, Kapoor, S, *et al,* 2017: Rabies, epidemiology, pathogenesis, public health concerns and advances in diagnosis and control: a comprehensive review. Vet. Q. 37, 1:212-51.

Smith, JS, Fishbein, DB, Rupprecht, CE, Clark, K, 1991: Unexplained rabies in three immigrants in the United States. A virologic investigation. N. Engl. J. Med. 324:205.

Strady, A, Lang, J, Lienard, M, *et al,* 1998: Antibody persistence following preexposure regimens of cell-culture rabies vaccines: 10-year follow-up and proposal for a new booster policy. J. Infect. Dis. 177:1290.

Suwansrinon, K, Jaijareonsup, W, Wilde, H, *et al,* 2007: Sex- and age-related differences in rabies immunoglobulin hypersensitivity. Trans. R. Soc. Trop. Med. Hyg. 101:206-9.

Taha, NA, Abd El Hameed, HS, El Sayed, D MS, Abdel-Mordy, MA, 2023: Effect of Health Educational Program for Rural Population on Prevention of Rabies. J, Nurs. Sci. Benha Univ. 4, 1:650-60

Varner, MW, McGuinness, GA, Galask, RP, 1982: Rabies vaccination in pregnancy. Am. J. Obstet. Gynecol. 143:717.

Vora, NM, Clippard, JR, Stobierski, MG, *et al,* 2015: Animal bite and rabies postexposure prophylaxis reporting--United States, 2013. J. Publ. Hlth. Manag. Pract. 21:E24.

Wang, XJ, Lang, J, Tao, XR, *et al,* 2000: Immunogenicity and safety of purified Vero-cell rabies vaccine in severely rabies-exposed patients in China. Southeast Asian J. Trop. Med. Publ. Hlth. 31:287.

Warrell, MJ, Nicholson, KG, Warrell, DA, *et al,* 1985: Economical multiple-site intradermal immunisation with human diploid-cell-strain vaccine is effective for post-exposure rabies prophylaxis. Lancet 1:1059.

WHO, 2010: Publication. Rabies vaccines: WHO position paper-recommendations. Vaccine 28:71-40.

WHO, 2013: Expert Consultation on Rabies, second report: Technical Report Series, No. 982. http:// apps.who.int/iris/bitstream/10665/85346/1/9789240690943_eng.pdf.

WHO, 2017: Weekly epidemiologic record: Meeting of strategic advisory group of expertson immunization, conclusions and recommendations, conclusions and recommendations https://reliefweb.int/sites/reliefweb.int/files/resources/

WHO, 2018: Rabies http://www.who.int/ith/vaccines/rabies/en/ (Accessed on January 03).

Wilde, H, Khawplod, P, Hemachudha, T, Sitprija, V, 2002: Postexposure treatment of rabies infection: can it be done without immunoglobulin? Clin. Infect. Dis. 34:477.

Wilde, H, Tipkong, P, Khawplod, P, 1999: Economic issues in postexposure rabies treat-

ment. J. Travel Med. 6:238.

Table 1: Rabies pre-exposure prophylaxis schedule - United States, 2008 (Route I.M.)

Vaccination	Regimen
Primary	Human diploid cell vaccine (HDCV) or purified chick embryo cell vaccine (PCECV); 1 mL (deltoid area), one each on days 0*, 7,& 21 or 28
Booster¶	HDCV or PCECV; 1 mL (deltoid area), day 0 only

* Day 0 is the day the first dose of vaccine is administered.

Table 2: Rabies postexposure prophylaxis

Vaccination category	Biological	Schedule
Not vaccinated	RIG	Total dose 20units/kg body weight. As much of full dose as feasible must be infiltrated around wound(s) and any remaining given IM.
	Vaccine	*Human diploid cell vaccine (HDCV) or purified chick embryo cell vaccine (PCECV) 1ml, IM (deltoid area), 1 each on days 0, 3, 7 & 14
Previously vaccinated	RIG	Not indicated
	Vaccine	HDCV or PCECV 1 mL, IM (deltoid area), 1 each on days 0 and 3

RIG: rabies immune globulin, * For persons with immunosuppression, rabies postexposure prophylaxis must be administered using all five doses of vaccine on days 0, 3, 7, 14, and 28.

Table 3: Currently available Human rabies biologics - United States, 2008

Rabies vaccine	Name	Manufacturer	Dose	Route	Given
Diploid cell vaccine	Imovax® Rabies*	Sanofi Pasteur Phone: 800-822-2463 Website: http://www.vaccineplace.com/products/	1ml	I.M.	Pre- or post-exposure
Purified chick embryo cell vaccine	RabAvert®	Novartis Vaccines and Diagnostics Phone: 800-244-7668 Website: http://www.rabavert.com	1ml	I.M.	Pre- or post-exposure
Rabies immune globulin	Imogam® Rabies-HT	Sanofi Pasteur Phone: 800-822-2463 Website: http://www.vaccineplace.com/products/	20 IU/kg	Local	Post-exposure only
	HyperRab® S/D	Talecris Biotherapeutics Bayer Biological Products Phone: 800-243-4153 Website: http://www.talecris-pi.info	20 IU/kg	Local	Post-exposure only

* Imovax rabies I.D., administered intradermally, is no longer available in the United States.

Table 4: Rabies pre-exposure prophylaxis guide - United States, 2008

Risk category	Nature of risk	Typical populations	Pre-exposure recommendations
Continuous	Virus present continuously, often in high concentrations. Specific exposures likely to go unrecognized. Bite, non-bite, or aerosol exposure	Rabies research laboratory workers; rabies biologics production workers.	Primary course. Serologic testing every six months; booster vaccination if antibody titer is below acceptable level.*
Frequent	Exposure usually episodic, with source recognized, but exposure also might be unrecognized. Bite, non-bite, or aerosol exposure	Rabies diagnostic laboratory workers, cavers, veterinarians and staff, and animal-control and wildlife workers in areas where rabies is enzootic. All persons who frequently handle bats.	Primary course. Serologic testing every two years; booster vaccination if antibody titer is below acceptable level
Infrequent (greater than population at large)	Exposure nearly always episodic with source recognized. Bite or non-bite exposure.	Veterinarians and animal-control staff working with terrestrial animals in areas where rabies is uncommon to rare. Veterinary students. Travelers visiting areas where rabies is enzootic and immediate access to appropriate medical care including biologics is limited.	Primary course No serologic or booster vaccination
Rare (population at large)	Exposure always episodic with source recognized. Bite or non-bite exposure.	US population at large, including persons in areas where rabies is epizootic.	No vaccination necessary. .* Primary course. testing

* Minimum acceptable antibody level is complete virus neutralization at a 1:5 serum dilution by the rapid fluorescent focus inhibition test. A booster dose should be administered if the titer falls below this level.

Manning SE, Rupprecht CE, Fishbein D, et al. Human rabies prevention-United States, 2008: recommendations of the Advisory Committee on Immunization Practices. MMWR Recomm Rep 2008; 57:1.

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