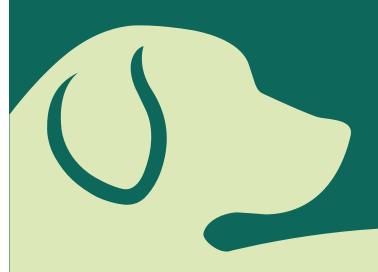


# GUIDELINES for Prevention of Human Rabies















# Provincial Technical Working Advisory Group (PTWAG) for Rabies Prevention







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Publication of

# GUIDELINES FOR PREVENTION OF HUMAN RABIES

was made possible with support from the office of WHO Sindh.



# Message from the Minister of Health Government of Sindh



The Sindh Government recognizes that rabies is one of the most fatal zoonotic diseases in the world. More than 200,000 dog bites in Sindh were reported in 2023, with the numbers rising rapidly. Around 96% of rabies mortality is associated with stray dogs. The Sindh Government is paying close attention to protecting the people from this growing menace by strengthening the prevention and control of dog bites through public awareness and assisting healthcare workers to stay abreast of modern treatment methodologies.

The Provincial Technical Working Advisory Group (PTWAG) is committed to augmenting Rabies Prevention Centers in the Emergency Department of public health facilities throughout Sindh and providing training workshops in the correct methodology of post-exposure prophylaxis (PEP). It emphasizes notifying dog bites and related deaths from rabies and maintaining a registry, which is fundamental for forecasting requirements of essential biologicals. The Sindh Government will implement this all over the province.

I congratulate the PTWAG for their collaborative efforts in developing comprehensive Guidelines for Prevention of Human Rabies. The booklet is easy to read and understand and will guide our health workers in caring for the victims of dog bites and applying the standard WHO PEP. Most importantly, it stresses the importance of washing wounds thoroughly and using precious Rabies Vaccine prudently and economically without compromising safety. Furthermore, considering the strong recommendations of PTWAG, we will include Rabies Immunoglobulin (RIG) in the Essential Drug List to ensure that it is not missed from the armamentarium of PEP in rabies-prone bites.

I hope that this manual will help healthcare personnel at different levels and that adopting the recommendations will be an important step in preventing rabies deaths.

The Provincial Government stands firm in its commitment to bolstering PTWAG's efforts and pledges its unwavering support in the fight against Rabies in Sindh. We are resolute in our mission to eliminate this disease from our province.

DR. AZRA FAZAL PECHUHO MINISTER



ِرللاً سِيلته آرگنائزيشن

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Message from WHO Representative in Pakistan

I am very pleased to see that the Health Department, Government of Sindh has taken the initiative of publishing updated *Guidelines for the Prevention of Human Rabies*. The Guidelines are comprehensive and will serve as an excellent resource for healthcare professionals to follow the modern method of postexposure treatment. Starting with the pathophysiology of rabies. it builds up to its prevention, with risk stratification, staging the severity of the wound, administering quality vaccine and immunoglobulin when needed, and the caveats associated with their use. It emphasizes 2018 WHO recommendation of employing the one-week intradermal regimen, which has been proven to be safe and effective while allowing more persons to be treated with the same ampoule of the vaccine.

The booklet also teaches the benefits of preexposure prophylaxis (PEP) and modified administration in cases of re-exposure of a bite. Frequently asked questions are listed and explained lucidly.

World Health Organization is working closely with the Department of Health, Sindh to curtail infectious diseases and is committed to support further to reduce preventable mortalities and morbidities.

I congratulate the Provincial Technical Working Advisory Group for bringing out an excellent booklet that should be studied and practiced by all who care about preventing human deaths from rabies.

Dr Dapeng Luo WHO Representative/Head of Mission

عالمي ادارهِ صحت . 世界卫生组织 . منظمة الصحة العالمية

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In reply please refer to:

Your reference: PTWAG\_2024

Re: GUIDELINES FOR PREVENTION OF HUMAN RABIES

Geneva, 08 January 2024

To whom it may concern,

Rabies, a neglected tropical disease, continues to cause hardship and harm despite being preventable and having already been successfully eliminated in many contexts. It affects the most vulnerable, burdening people, families, and communities who are already marginalized and disadvantaged.

These guidelines for the prevention of human rabies are essential in bringing the scientific evidence and best practices in a concise, step-by-step, and easy-to-follow guidance for clinicians to put into everyday use. These guidelines may serve as a model for other provinces in Pakistan and endemic countries embarking on improving the delivery of their rabies programs.

In addition, rabies programs require a One Health, a "whole-of-system" approach, that recognizes the relationships between humans, animals, and the environment. Subsequently, with a vision to truly aim for rabies elimination, beyond solely human bite and rabies case management, there is an urgent need to address rabies through increased attention to dog vaccination, population management, and management of environmental drivers.

I would like to congratulate the Provinical Techinical Advisory Group (PTWAG) for Rabies Prevention for their untiring efforts to make progress on the control and elimination of rabies and other neglected diseases to global progress that reduces inequality, improves resilience, and promotes sustainable development to unlock "a better and more sustainable future for all."

Yours sincerely,

B. Sterla

Dr. Bernadette Abela Rabies Lead, Department of Control of Neglected Tropical Diseases

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VETERINARY MEDICINE

Dr. Naseem Salahuddin

Faculty Indus Hospital & Health Network

Karachi, Pakistan

5 January 2024

Dear Dr. Salahuddin,

Thank you for sharing with me your *Guidelines for Human Rabies Prevention*, created by the Provincial Technical Working Advisory Group under the Pakistan Ministry of Health.

Rabies has the highest associated case fatality of any infectious disease and kills tens of thousands of people every year, particularly in Asia and Africa.

Significantly, your document offers modern recommendations on pre- and postexposure prophylaxis against rabies. As such, these guidelines are in vogue with the global program for human rabies elimination caused via dogs by 2030.

In addition, this contribution provides a relevant introduction to the etiology, epidemiology, and pathobiology of this dreaded zoonosis. Combined with mass canine vaccination and human prophylaxis, such background is vital towards disease management in a One Health context.

You and your colleagues are to be congratulated for creating this document to enhance human rabies prevention and animal rabies control in Pakistan and the region.

I wish you the very best in your efforts towards this worthy endeavor.

Sincerely yours,

Charles E. Rupprocht

Charles E. Rupprecht VMD, MS, PhD

Affiliate Professor

World Health Organization Technical Advisor on Rabies

# **Abbreviations**

ARV Anti Rabies Vaccine

CCEEV Cell Culture Vaccine and Embryonated Egg-based Vaccine

DFA Direct Fluorescent Antibody

DHQ District Head Quarter
THQ Tehsil Head Quarter

ERIG Equine Rabies Immunoglobulin
FAO Food and Agriculture Organization

HCP Health Care Professional

HRIG Hum Rabies Immunoglobulin

ID Intradermal

IHHN Indus Hospital & Health Network

IJIDOH International Journal of Infectious Diseases One Health

IM Intramuscular

IPNC Institut Pasteur International Network in Cambodia

NAB Neutralizing Antibody

NITAG National Immunization Advisory Group

PEP Post-exposure Prophylaxis
PMA Pakistan Medical Association

PPHI People's Primary Healthcare Initiative

PPA Pakistan Pediatric Association

PrEP Pre-Exposure Prophylaxis

PTWAG Provincial Technical Working Advisory Group

RABV Rabies Virus

RIG Rabies Immunoglobulin
RPC Rabies Prevention Center

SHCC Sindh Health Care Commission

UNICEF United Nations International Emergency Fund

WHO World Health Organization

WOAH World Organization for Animal Health

# **Contents**

• Preface	08
• Introduction	10
- Epidemiology of Rabies	11
- Pathophysiology of Rabies	12
- Symptoms and Diagnosis	12
- First Aid for the Dog Bite Victim	14
• In the Emergency Room/RPC	16
- Interviewing patient/ history taking	16
- WHO Wound Categories	18
Post Exposure Prophylaxis (PEP)	19
- CCEEVs currently available in Pakistan	19
- Understanding Rabies Vaccines	20
- Intradermal (ID) Regimen	21
- Intramuscular (IM) Regimen	23
- Understanding Rabies Immunoglobulin (RIG)	24
- RIG in Special Situations	27
- PEP in Special Situations	27
<ul> <li>PEP for Previously Immunized Persons</li> </ul>	28
- Booster Schedule or after Re-exposure	28
- Why does PEP sometimes fail?	28
Other Prophylaxis for Animal Bite	29
Pre-exposure Prophylaxis (PrEP)	32
Managing the Patient with Rabies	33
<ul> <li>Animals that can or cannot transmit RABV</li> </ul>	34
- When to Suspect Rabies in a Dog or Cat	35
- Tips on avoiding dog bites	36
Frequently Asked Questions	37
Clinical Dilemmas	
Bibliography	
Addendum	42
- Setting up a Rabies Prevention Center	42
- WHO Documentation Tools	
- One Health	46
- Case Record Form	48
- The Wolf : by Anton Chekov	52

# **Preface**

For centuries rabies has been regarded as a neglected tropical disease of underprivileged humanity. In Eastern culture and the subcontinent particularly, rabies was perceived as a "curse," ordained by destiny, to be treated by mystics and mendicants, but inevitably ending in agonizing, torturous death. Even today modern medicine has not changed mortality from rabies, nor have public health authorities in many developing countries made serious efforts towards rabies prevention. The road to elimination is yet distant and needs a serious, concerted effort on the part of health services at multiple levels. Fortunately, WHO and dedicated scientists working for the universal prevention of rabies are making tremendous efforts towards this objective.

Awareness is the best form of defence against disease. Nowhere is this truer than in the prevention of rabies. Animal bites may be accidental and unavoidable, but awareness about immediate and correct action will make the difference between living and dying a torturous death. Dog bite centers are few and often far from the scene of an attack. The delay in reaching a center or fear of multiple painful injections often results in delayed or no care. Patients and HCPs are often deluded into the belief that "all is well", until weeks later symptoms of rabies start. By that time it is already too late to reverse the effects of the virus. Many HCPs have not kept pace with the modern methods of PEP; hence, dog bite victims are often left by the wayside and suffer grave consequences. Not having access to PEP, many turn towards traditional and harmful interventions. Sadly, no discipline of human or veterinary medicine or the authorities in public health "owns" rabies; rather, only a few champions fervently believe that no one should die of rabies. Many other diseases compete for priority, limiting the ability to eliminate rabies.

Scientists have made great strides in making modern, safe, and effective vaccines that can be injected into the muscle according to schedule; however, using multiple doses of whole vials of the vaccine in rabies clinics with a large footfall of bite victims is enormously expensive and unsustainable. In such centers, the CCEEV vaccine should be provided for the WHO-approved low-dose 1-week intradermal injection schedule that is safe, effective, and economical.

The HCP must be trained in injecting correctly according to schedule and strictly advising follow-up for subsequent injections. For this, individual institutions must create a system to ensure round-the-clock facilities with trained HCPs and provisions for wound washing, and quality ARV and RIG.

The Guidelines for Human Rabies Prevention are based on current WHO recommendations and are intended for healthcare providers who manage animal bites in private and public institutions. They should help the treating physician understand this deadly disease's complexities and make correct management judgments. Judicious decisions often have to be made in unusual circumstances for which consultation may be needed.

In early 2023, the Sindh Health Minister, Dr. Azra Pechuho, spearheaded a movement to augment and increase the number of Rabies Prevention Centers throughout Sindh. The interim Sindh Minister for Health, Dr. Saad Khalid Niaz, initiated the PTWAG and forwarded the mission, which is taking root. I profoundly thank Dr. Bernadette Abela and Dr. Charles Rupprecht for reviewing the draft and offering valuable suggestions. I am grateful to Dr. Arnaud Tarantola for sharing his slide illustrations.

We thank the Office of WHO Sindh for its continuing support of PTWAG in its mission to promote the PEP *Guidelines*, raise public awareness, strengthen existing centers for PEP, and provide logistic support for future endeavors.

I sincerely hope the *Guidelines for Human Rabies Prevention* will be useful in saving lives from this lethal disease.

Dr. Naseem Salahuddin

Professor Emeritus IHHN Karachi Member WHO Advisory Panel for Rabies naseem.salahuddin@tih.org.pk





# Introduction

"I have seen agony in death only once, in a patient with rabies; he remained acutely aware of every stage in the process of his disintegration over a twenty-four hour period, right up to his final moment." Lewis Thomas, The Lives of a Cell, New York, Bantam Books, 1974.

Rabies is an ancient disease; when faced with a patient presenting as clinically declared rabies, clinicians today are just as helpless in curing the disease as their counterparts were 4000 years ago. Rabies is primarily a disease of animals (zoonotic disease) and is transmitted to man by the bite or scratch of an infected animal after a variable incubation period of 1- 3 months. It presents as an acute, progressive encephalomyelitis and leads to death within 2-5 days in humans.

The rabies virus and related lyssaviruses are bullet-shaped with a single-stranded RNA genome. Many mammals can transmit the rabies virus, but in Pakistan, it is usually spread through infected dogs; however, cats have occasionally been reported to transmit the disease. Bat lyssaviruses are closely related to the classical human rabies virus in many parts of the world. A rabid dog may have bitten other animals, such as another dog, cat, mule, or cattle, which can become rabid as well. Thus, the infection is transmitted from animal to animal, perpetuating the disease. The infected animal demonstrates signs of rabies and dies within 5-10 days of showing signs of illness.

After a bite, millions of virus particles (virions) enter the tissues through broken skin or mucous membranes. Within a few days to weeks, virions enter nerve endings in the muscle and surrounding tissues and travel retrograde along the long neural axions toward the brain where they replicate. From the brain tissue, the virions pass on to the salivary glands. Once symptoms begin, the disease becomes irreversible and invariably fatal. It is one of the most torturous of infectious diseases. Anyone who has even once witnessed this horrendous infection will be haunted with the memory forever.

Without the benefit of appropriate laboratory tests or a veterinarian experienced in rabies, it is not possible to accurately diagnose rabies in a

rabid animal. Hence, one depends upon the animal's observed behavior, i.e. "sick looking," apathetic or aggressive, chewing strange objects, glazed look, randomly biting several persons or animals, or simply "abnormal behavior". Considering the wide range of behavior patterns, it is safer to assess the circumstances and wound category first and apply WHO-recommended post-exposure prophylaxis (PEP). If indeed there is any possibility of this being a rabid animal's bite, this may be the only window of opportunity to prevent the deadly disease. Certainly, there may be a great deal of overreaction and excess treatment, but unless one has facilities to impound the animal and observe and rule out rabies, one has little choice but to treat if the victim has to be saved from this 100% fatal disease.

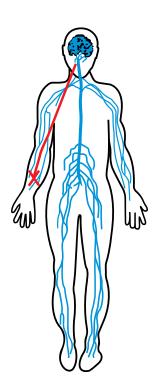
# **Epidemiology of Rabies**

Human mortality from endemic canine rabies is estimated by WHO to be around 65,000 deaths globally annually. It is a major public health problem in many countries in Asia, South and Central America, Africa, and some Pacific Islands, where the population is dense and the number of unvaccinated stray and feral dogs roam freely. The highest-risk countries for travelers include Bolivia, China, Haiti, Nepal, Philippines, Pakistan, India, Sri Lanka, Thailand, and Vietnam. Most human rabies in the Americas and Europe are due to bites by rabid wild animals, including bats. Most rabies cases in the USA and Canada are of bat origin. Australia has reported human rabies from bats.

Children, especially boys under 15 years of age, are most affected as they usually play in the streets and cannot run away or defend themselves against an attacking animal. There are no reliable data from Pakistan but the number of annual rabies deaths here is estimated to be between 2000 – 5000 annually. Only fourteen rabies survivors have been reported in literature, mostly related to bat bites and presenting with atypical rabies. Other anecdotal cases have been reported but not substantiated with lab tests. Not all persons bitten by a rabid dog become infected (30-40%,) but those that do get infected, 100% will develop rabies. Timely and adequate PEP is 100% effective in preventing the progression to rabies.







# **Pathophysiology of Rabies**

- RABV replicates in muscle and subcutaneous tissues at the inoculation site.
- Enters the peripheral nervous system by fording the neuromuscular junction or through direct inoculation into the nerve.
- Retrograde spread to spinal cord and brain @ 15-100 mm/day.
- Clinical symptoms become evident.
- Centrifugal spread to tissues and organs, including salivary glands.
- Incubation period (av. 6-12 weeks).
- Death due to coma, parasympathetic dysfunction, and dysautonomia of circulatory and respiratory functions.

# **Symptoms and Diagnosis**

Symptoms of rabies develop within 2 weeks to 6 months or even longer after a bite. The length of the incubation period depends upon the body site where the bite has occurred, and the number of virus particles entering the wound. For instance, a bite on the head, neck, face, shoulders, or arms will produce symptoms earlier than if the bite occurred on the leg or feet.

Classical or Furious rabies presents with feverishness, headache, restlessness, irritability and mental confusion alternating with periods of normal mentation. These symptoms are unique to rabies. Patients with other viral encephalitides do not have alternating symptoms. This is followed by the involvement of the swallowing and breathing muscles so that the victim has difficulty swallowing water, and begins to fear even a glass of water. This is called "hydrophobia".

(This symptom is responsible for the myth that drinking or washing the wound with water harms the victim!) Blowing air on the face also causes spasms, provoking fear of the breeze, called "aerophobia". There may be intense sweating, tachycardia and acute hypertension from autonomic dysfunction. Over 1 to 7 days, the condition worsens, swallowing and breathing become difficult, the number of spasms increases, and slow, painful death occurs while the doctors and family members watch helplessly. There is no going back once symptoms have started.

This presentation is dramatic and specific. The initial manifestation of encephalitis may be confused with other viral encephalitides, illicit drug overdose, cerebral malaria, and hysterics. The subsequent syndrome is unmistakable and should present no other differential.

Paralytic rabies: one-third of rabies cases may present as slow, ascending paralysis of legs and arms, followed by weakness of cranial nerves and muscles of respiration, similar to the condition of Guillain-Barre Syndrome. Paralytic rabies occurs more commonly with bat bites, and only a history of animal bites may lead one to suspect rabies. History taking in a patient presenting with these symptoms is therefore important. The condition is also fatal.



Encephalitic form: involvement of the brainstem and the cerebrum, particularly the limbic system.



Paralytic rabies: the medulla and the spinal cord are mainly involved by extensive neuronal damage and inflammation. Involvement of the basal ganglia and the thalamus is seen late in the disease.

**Diagnosis:** Rabies in the human is mostly a clinical diagnosis, but can be confirmed in the lab with tests, if available. The direct fluorescent antibody (DFA) or immunohistochemistry at the neck hair follicles can demonstrate rabies virus antigen, but these have rarely been of clinical value. In a living patient or animal (antemortem), rabies virus can be detected by PCR in cerebrospinal fluid, saliva, or urine, although the virus may be secreted intermittently. Detection of Negri bodies in the brain has been largely supplanted by PCR.





After vaccination, ARVs actively produce antibodies against the virus and can be measured in the serum by enzyme-linked immunosorbent antibody (ELISA) or rapid fluorescent focus inhibition test (RFFIT). A NAB level of 0.5 IU/ml or more is achieved in 2 weeks after giving the first 3 doses of ARV and is considered an adequate protective level. In clinical studies, all healthy persons tested in accordance with ACIP guidelines after completion of at least a 3-dose regimen of rabies PEP demonstrated an adequate NAB response and continued to maintain adequate levels even many years later. Natural antibodies to rabies virus after a bite do not rise because there is no viremia.

Routine testing of healthy patients completing PEP is not necessary to document seroconversion but may be required in an exceptional patient where antibody titer level in the blood is in doubt, such as in an immunocompromised patient, a prior history of vaccination, or in an animal handler to decide for a booster dose.

# First Aid for the Dog Bite Victim

It cannot be overemphasized that washing the wound immediately and thoroughly is extremely important as a first step in saving the victim's life. Deep cleaning should remove as much virus-containing saliva and street dirt as possible and should be taught in all communities to save time and improve outcomes before the victim reaches a hospital. Even if the wounds have been washed at home, there is no harm in repeating wound cleansing in the hospital or clinic. Proper and early wound cleansing can reduce the chances of developing rabies by 1/3rd.

Flush the wound/s with clean, flowing tap water and scrub with soap and water. If the wound is deep or a puncture wound, flush with a saline-filled syringe. Dirt and saliva should be washed away by proper cleansing for 10 - 15 minutes, and then a local antiseptic like povidone (pyodine) (but not tincture iodine as this causes skin and tissue burn) should be applied. Any brand of liquid or bar soap causes denaturing of the virus protein and destroys the virus. Every ER/RPC should have a proper wound washing facility separate from the toilet. An improvised arrangement should not be acceptable as wound washing is one of the most important aspects of rabies prevention. All ER nurses or assistants should know how to wash wounds thoroughly.

Oftentimes family members are ignorant or careless about further management and use home remedies such as oil, chilly, salt, etc. These should be strongly discouraged in the community, as not only are they ineffective, but they push the virus deeper into the damaged tissue and introduce bacterial infection.







# In the Emergency Room/RPC

# Interviewing patient/ history taking

- 1) Reassure, Soothe and Counsel: All animal bite victims are fearful and anxious. Handle them gently, reassure him/her, soothe the child, and ask them to allow you to examine them for exposure through bites, scratches, or contamination of mucus membranes. With a gentle, caring attitude even a distressed child will let you handle the wound.
- 2) Assess the number, location, and depth of wound/s. There may be one or more wounds. Undress the child to look for more bites and scratches. Children often do not report accurately out of fear. Make sure you do not miss other even "insignificant" wounds.
- 3) If there is any chance of saliva in the eye, rinse thoroughly with water. It is suggested to instill RIG as a safety measure.
- 4) Even if the wound has been washed elsewhere, it should be done again under proper conditions. If home remedies like oil, chilly, turmeric, etc have been applied, these should be removed by flushing with a syringe, and deep cleansing. The virus may lie hidden in deep wounds; hence thorough, gentle cleansing is emphasized.
- 5) The wound/wounds should be lightly covered with clean gauze till further decision is made.
- 6) Obtain the history of the bite and the animal: whether provoked or unprovoked; pet or unowned animal; vaccinated or unvaccinated; homebound or free-roaming; killed or escaped; or whether the animal can be observed for at least 10 days.
- 7) Has the patient ever received PEP or PrEP? If so, ask when and why. Confirm with a written record.
- 8) Immune status of the patient, i.e. advanced HIV disease or on immunosuppressive agents such as chemotherapy or steroids, etc.
- 9) Counsel for return visits according to the schedule.

10) Wounds should not be sutured immediately after RIG, as surgical manipulation further traumatizes the tissues and pushes the virus deeper. Occasionally, as in the case of a severe facial bite, e.g., a torn pinna, nose, or eyelid, RIG should be infiltrated, and loose sutures may be applied. Proper suturing may be done after a delay of 2-3 days.













# **WHO Wound Categories**

Wound categorization is essential to help guide further management. Once you have categorized the wound severity, you can decide what further action to take regarding PEP.

Wound Category	Description	WHO Recommendation	
Category 1	Touching/feeding of animals: Intact skin	No exposure: Reassurance only	
Category 2	Nibbling on uncovered skin: Minor scratches or abrasions without bleeding	Moderate risk: Vaccinate only	
Category 3	Single of multiple transdermal bites or scratches: contamination of mucous membrane with saliva (eyes, mouth)	High risk: Vaccinate plus RIG	

In addition to wound categorization, one must also consider the behavior of the biting animal. In many instances, the animal was either not seen because of the cover of darkness or because it escaped. The thick material of trousers may protect against a deep bite and make it a "low risk" bite. A healthy, regularly vaccinated pet dog or cat poses no or little risk. Possibly the bite was accidental or provoked by interrupting its meal or deliberately teasing or injuring it. A vaccinated pet animal with normal behavior that can be observed at home is probably a safe bet against rabies. A pet that was "probably" vaccinated or not at all could be a "moderate" risk, and a vaccine series must at least be started. A sick, angry, or wild animal bite should be considered "high risk."



# Post Exposure Prophylaxis (PEP)

# **CCEEVs currently available in Pakistan**

Physicians are often puzzled by the names of cell cultures, dosages, routes, and vaccine administration methods. Modern CCEEVs are produced on cell lines such as Vero cells, chick embryos, and duck embryo. WHO pre-qualified CCEEVs are reliably produced under strict quality control and should be used preferably. The established vaccine potency for ARV is 2.5 IU/dose, which is required to induce an immunological response, delivered IM or ID. HCPs should beware of fake or poor quality vaccines marketed by dubious companies.

Vaccine (Cell line)	Brand	Volume	WHO pre- qualified
PCEV (Chick embryo cells)	Vaxirab-N®	1.0ml	Yes
PVRV (Verocell)	Rabivax-S®	1.0ml	Yes
PVRV (Vero cells)	Indirab®	0.5ml	No
PVRV (Vero cells)	Abhayrab <sup>®</sup>	0.5ml	No
PVRV (Vero cells)	Verorab®	0.5ml	Yes
PVRV (Verocell)	Rabio®	0.5 ml	No
PCEV (Chick embryo cells)	ChiroRab®	1.0ml	Yes

Note: Preference should be given to WHO Pre-qualified (Pq) vaccine, as it is ensured for quality, safety, and efficacy. Rabies vaccines that are not Pq must meet international standards of quality and good manufacturing practices and should be reassessed at regular intervals to ensure continuing quality. Untested or poor-quality rabies vaccines can cost patients' lives.



# **Understanding Rabies Vaccines**

- There is no contraindication for giving ARV.
- ARV dose is the same in adults and children.
- CCEEVs can be given IM or ID and are equally immunogenic
- The vaccine must be injected into the deltoid muscle, and not into the gluteus muscle, as absorption is unreliable due to fat in the gluteus.
   The vaccine may be injected into the lateral thigh muscle in very small children.
- Pregnant or lactating women should receive ARV and RIG if exposed.
- Immune-compromised patients, e.g., those receiving chemotherapy, steroids, or patients with advanced AIDS, should receive IM regimen along with RIG.
- Since the incubation period of rabies is variable, treatment should be started as soon as possible.
- An animal bite is an urgency, not an emergency. A delay of 12-24 hours for vaccination may not make a significant difference if a time-lapse is unavoidable. However, this should not be taken as a reason to delay treatment unreasonably. A thorough wound toilet should have been done immediately.
- Even if the patient arrives days to weeks later, treat as if the patient has only just arrived (i.e., categorize wound severity and decide about vaccine +/- RIG). If 10 days have passed and the dog is reliably alive and healthy, PEP is not required.
- Most CCEEVs are marketed as a freeze-dried powder (lyophilized) which is relatively heat stable. However, after reconstituting with the diluent the vaccine should be used immediately or kept refrigerated and used within 6-8 hours.
- Preferably use the same CCEEV throughout the series unless unavoidable (e.g., non-availability). In that case, use another WHO approved tissue culture.
- vaccine and continue the same schedule (WHO Expert Consultation Report on Rabies, 3rd Report, 2018).
- There are no serious side effects of CCEEV. Mild local pain, redness and fever may be negligible side effects.
- Concern is often raised about egg allergy from chick or duck embryo vaccines. These vaccines are so highly purified that the risk of anaphylaxis is remote. PVRV can be used if there is anxiety on the part of the patient or physician.

- Write out the schedule with dates for further doses.
- The patient must be educated about completing the vaccine series. An incomplete course of the vaccine may be a cause of PEP failure.
- Despite your advice, some patients may default on timing. If there has been a delay of 2-3 days, do not restart, simply continue the series.
- If you are referring a patient to another PEP center, be sure to write clearly your findings and the treatment given.

# **Intradermal (ID) Regimen**

The cost of a 4-dose IM course for PEP is high and unaffordable in a public hospital. To decrease vaccine volume and make quality cell culture products affordable, WHO has developed ID schedules that, if properly administered, have the same efficacy and safety as the IM regimen. The rationale behind the ID regimen is that the antigen is delivered directly to the antigen-presenting cells (APC) in the dermal layer of the skin at different sites, thus triggering an enhanced immune response rapidly and to high levels. The preferred sites of ID administration, ie over the deltoids, suprascapular or lateral thigh is because of proximity to lymph glands. In the IM route, the antigen has to be first absorbed into the circulation before it reaches the APC, which stimulates antibody production.

The vaccine's potency must be at least 2.5 IU per dose, whether given IM or ID. ID regimen is cost-effective if at least 2 patients are present within eight hours in a single day. One ampule of vaccine can be shared with 2.5 patients using the 0.5 ml, or 5 patients using the 1.0 ml vial.

Any leftover reconstituted vaccine should be refrigerated at  $+2^{\circ}\text{C}$  -  $+8^{\circ}\text{C}$  and used within 6-8 hours. Instead of discarding the remaining volume, give PrEP to an HCP if possible. Specific care to avoid contamination of the vial should be taken when removing the successive ID doses since rabies vaccines do not contain preservative or bacteriostatic components.





**Method:** Draw out 0.5 ml or 1 ml of the diluent fluid according to the brand of vaccine and mix it with the dried powder. Shake well till dissolved. Using insulin syringes, draw out 0.2 ml of the vaccine (2-2.5 syringes) if using 0.5ml vial, or (4-5 syringes) if using 1.0ml vial). One syringe per victim can be used on each deltoid.



Insert the tip of the needle, bevel upwards, and almost parallel to the skin surface of the upper arm, and slowly inject the vaccine into the uppermost layer of skin. A raised papule should begin to appear immediately, causing an orange peel appearance. If the vaccine is injected deep into the skin, and a papule is not seen, repeat in a different site nearby. ER/RPC personnel should be given adequate practice and training before starting the ID regimen. The procedure is similar to giving ID BCG.

Give 0.1 ml on each deltoid on days 0, 3, and 7 (called 2-2-2 IPC-ID regimen), and it requires only 3 outpatient visits. Give the patient a vaccine record and a return appointment. Infiltration into the wound with RIG should be done on the same day. If RIG is not immediately available, then it may be deferred to no later than 7 days. Day 0 is the day the first dose of vaccine is given.

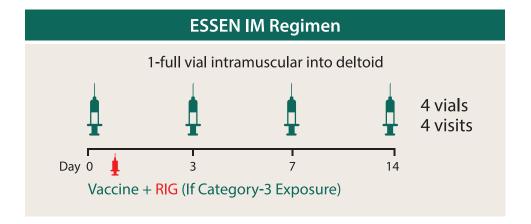
IPC ID Regimen						
2-Site low dose Intradermal 1-week (2-2-2) 0.1ml per deltoid						
<b>1 1</b>		<b>1</b>	1-2 vials 3 visits			
Day 0	3	7				
Vaccine + l	RIG (If Catego	ry-3 Exposure	2)			

SUN	MON	TUE	WED	THU	FRI	SAT
		1	2	3	4	5
6	7	8	9	10	11	12
13	14	15	16	17	18	19
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27	28	29	30	31		

# Intramuscular (IM) Regimen

The WHO recommends the Essen IM regimen in hospitals/clinics with low caseloads in private setups.

Schedule: Days 0, 3, 7, 14 (4 whole vials, 4 visits). Give the patient a vaccine record and a return appointment. Infiltration into the wound with RIG in Category 3 should be done on the same day as the vaccine. If RIG is not immediately available, then it may be deferred to no later than 7 days. Day 0 is the day the first dose of vaccine is given. It is preferable to use the same CCEEV and route in the same patient. However, it often happens that the first injection is given IM in a private setting, and then the patient shows up at a government institution where only the ID regimen is used. It is better to continue the series ID.





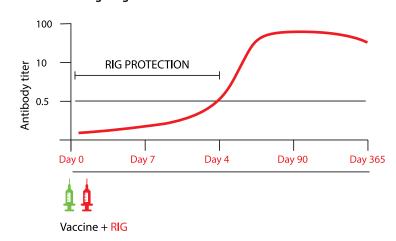


SUN	MON	TUE	WED	THU	FRI	SAT
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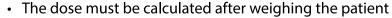
# **Understanding Rabies Immunoglobulin (RIG)**

Since rabies incubation period may be several weeks to months, it is important to provide immediate protection by giving passive, prepared antibodies that neutralize the virus on site. RIG protects for the first 14 days until the vaccine takes effect. RIG is imported and not always in stock, but it must be considered a life-saving biological in severe wounds. Many rabies deaths have occurred because of the absence of RIG. The hospital or clinic management must make every attempt to provide RIG in the RPC or ER.

### **Rationale for giving RIG**



• RIG must be given in all Category III wounds once, simultaneously as the vaccine on Day 0. If, for any reason, RIG was not given on Day 0 along with ARV, it may be given up to Day 7, but not later since it is likely to interfere with vaccine-induced antibody production.



- · RIG must be infiltrated into every single wound
- Two types of RIG are available: Equine (ERIG) and Human (HRIG).
- RIG is in liquid formulation

**Equine Rabies Immune Globulin (ERIG)** is prepared from heterologous (horse) serum. A skin test for ERIG is not required as the newer production is free of side effects (WHO Expert Consultation Report on Rabies, 3rd Report, 2018). The dose is 40 IU/kg body weight, maximum 3000 IU.

One 5 ml vial of ERIG contains 1000 IU potency.

Weight in Kg	IU	ml	Number of vials of ERIG
25	1000	5	1
50	2000	10	2
75	3000	15	3

**Human Rabies Immune Globulin (HRIG)** is prepared from human serum and has a longer half-life. The efficacies of HRIG and ERIG is comparable but HRIG is many times more costly than ERIG. A self-paying patient must be offered the choice. The dose of HRIG is 20 IU/kg body weight, maximum 1500 IU.

One 2 ml vial of HRIG contains 300 IU

Weight in Kg	IU	ml	Number of vials of HRIG
15	300	2	1
30	600	4	2
45	900	6	3
60	1200	8	4





- Weigh the patient and calculate the exact quantity of RIG required. Do not guess or estimate the dose. Excess RIG may suppress antibody production from the vaccine.
- If there is a small, single wound, draw the entire calculated amount in a syringe with a needle of appropriate gauge.
- If there are several wounds, draw up the RIG, plus an estimated amount of normal saline to dilute the RIG.
- Do not use an insulin syringe to infiltrate a large wound as a small needle will not penetrate the wounds.
- Wearing latex gloves infiltrate into the depth and around all sides of the wound in all directions, to neutralize virus particles at the site.
- Note: It was previously taught to infiltrate the wound with half the amount of RIG and inject the rest into the muscle. This is no longer valid. RIG should be infiltrated as much as anatomically possible into and around the wound to neutralize the virus and the remaining should be saved with sterility for the next patient.
- RIG production is expensive and labor-intensive. It is frequently in short supply in many countries. Hence, despite the WHO's strong advice to use RIG in Cat 3 wounds, it is not always used.
- An alternative to RIG is an Anti-Rabies Human Monoclonal Antibody (Mab) containing a cocktail of at least two antibodies against RABV.
   Commercial production of MAb will be easier and less costly and may ultimately replace RIG.



1. Weigh the patient



2. Draw up the exact calculated amount of RIG



3. & 4. Using an appropriate size needle, infiltrate the required amount as much as is anatomically possible into and around the wound.



# **Important Tips**

- RIG can be given up to 7 days after the first vaccine when endogenous vaccine-triggered antibodies appear. Giving RIG later may become counterproductive by suppressing antibody production.
- If you are not confident about infiltrating a face, eyelid, or finger wound, consult an experienced person or a plastic surgeon.
- Do not suture the wound unless unavoidable. Cover with dry, clean gauze.
- As previously practiced, do not inject RIG into muscles; it is now known that injecting RIG into distant muscles does not benefit rabies prevention (WHO Expert Consultation Report on Rabies, 3rd Report, 2018).
- Thorough wound wash is again emphasised.

# **RIG in Special Situations**

- If a limited amount of RIG is available, RIG allocation should be prioritized for severely exposed patients:
- The behavior of the biting animal is suggestive of, or confirmed rabies.
- Several persons were also bitten by the same dog.
- Multiple deep bites.
- Bites to highly innervated parts of the body, such as the head, face, neck hands and genitalia.
- Exposure to mucus membranes.
- In unusual or difficult situations, the HCP should use their best clinical judgment, or consult with a more experienced person.

# **PEP in Special Situations**

- Saliva sprayed into the eye or mouth is very high risk and must be dealt with immediately. There is no strong recommendation from WHO for this circumstance, but it would be advisable to rinse the eyes and mouth immediately and thoroughly with water. RIG may be instilled into the eye or swished in the mouth.
- If the dog or cat is reliably vaccinated with animal ARV within the last year, showing normal behavior, and the bite is accidental or provoked, there is no need for PEP, but observing the animal for 10 days should be advised.





- Every attempt should be made to obtain RIG in Cat III wound; however, in a desperate situation where RIG is not available, wound toilet should be done as thoroughly as possible and an additional IM dose of ARV may be given between days 14 – 28 (but this is not the substitute for RIG).
- Alternatively, the 4-4-4 regimen may be adopted, i.e., ID into each deltoid and suprascapular areas on D 0, 3, 7.

# **PEP For Previously Immunized Persons**

If a patient has received complete PEP or PreP (IM or ID) with a quality vaccine even 10 years back and is now bitten by a proven or probably rabid animal, give only booster dose. Wound toilet is essential, but RIG is not to be given because a booster shot will increase the antibodies rapidly to an adequate level (anamnestic response).

## **Booster Schedule or after Re-exposure**

Within 3 months	After 3 months (ID regimen)	After 3 months (IM regimen)
No PEP	0.1 ml on one deltoid only	Full vial
(wound care only)	Day 0, 3 (+ wound care)	Day 0, 3 (+ wound care)

# Why does PEP sometimes fail?

Despite having performed all the motions of PEP, some victims may still die of rabies. If that happens, the case must be analyzed to avoid errors in future. Some possibilities are:

- Delayed management.
- Interrupted schedule.
- Inadequate wound management:
  - Failure to wound wash thoroughly.
  - Failure to use soap and antiseptic.
  - Multiple wounds were not identified and managed.
  - The wound was sutured before RIG infiltration, further spreading the virus.



- The eye or mucosa was contaminated with dog saliva.
- An exceptionally large rabies viral load was introduced.
- The bite was directly into a nerve.

### Problems with Vaccine:

- ARV was of poor quality.
- Cold chain was not maintained.
- ID injection was not administered correctly.
- The vaccine was injected into the gluteus, where absorption is poor.

### • Problems with RIG:

- RIG was of poor quality.
- Cold chain after reconstitution was not maintained.
- RIG was either not used at all, or not all bite wounds were infiltrated
- Inadequate calculation of RIG volume, or not diluted to sufficient volume to cover all wounds.
- A small insulin needle was used to infiltrate RIG into a large wound.
- RIG was given more than 7 days after receiving ARV.
- Unrecognized and unreported deviations from WHO protocol.

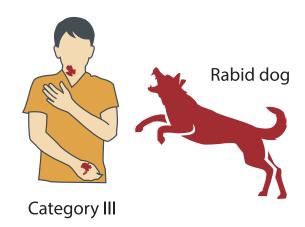
# Other Prophylaxis for Animal Bite

- Prescribe antibiotic amoxicillin/clavulanate for 3-5 days in case of category III wound for prevention of bacterial infection.
- Prescribe antibiotic doxycycline in case of a cat scratch. In children azithromycin may be given.
- Tetanus prophylaxis to tetanus-prone wounds.
- Post-exposure prophylaxis counseling includes:
  - Follow up for subsequent doses for the complete course.
  - Keep the wound clean.
  - Keep the RPC card safe for future reference.

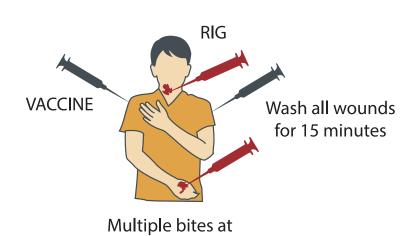




# Post-exposure Prophylaxis (PEP)

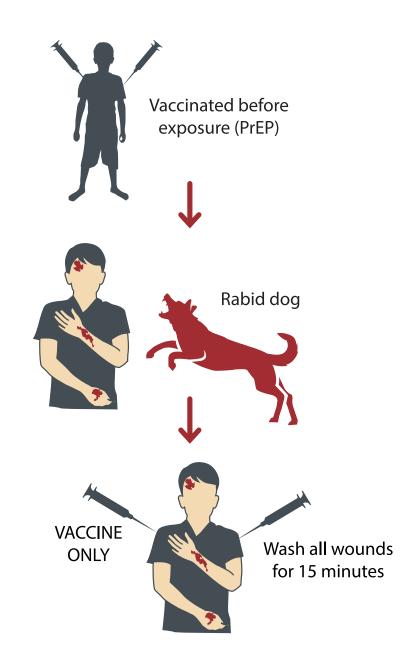






sensitive locations

# Pre-exposure Prophylaxis (PrEP)







# **Pre-exposure Prophylaxis (PrEP)**

PrEP should be considered for all persons who are likely to get bitten or exposed to rabid animal secretions. PrEP has a major advantage: in case of a rabid bite wash the wound and give rabies vaccine boosters on Days 0 and 3 IM or ID. Neither full series nor RIG is required because memory cells from existing antibodies would be boosted from 2 additional injections (anamnestic response), providing adequate immunity even 5-10 years after PrEP.

PrEP is especially recommended for the following:

- Veterinarians and animal handlers such as zoo keepers.
- Dog catchers.
- Janitorial/sanitary workers.
- Children living in endemic areas.
- · Pet owners.
- Law enforcement agencies (Police or military personnel).
- Travelers to rabies-endemic countries.
- Those handling infected material from autopsies of animals.
- Lab personnel handling live rabies virus.
- Healthcare providers in contact with rabies suspected cases.

A booster is advisable for vulnerable populations every 2-3 years, unless serology demonstrates an adequate rabies virus antibody level of at least 0.5 IU/ml.

### **PrEP Schedule**

ID	IM
0.1 ml	1 full vial
on each deltoid on days 0, 7	into deltoid on days 0, 7

If there are no more patients in the clinic, rather than let the vaccine be wasted, it is better to PreP an HCP.

Considering the high risk for rabid dog bites in an endemic area, and the high cost and scarcity of RIG, PrEP would be the ideal way to replace PEP. Practically speaking, PrEP on a large scale would require a great deal of logistical organization.



The disease is invariably fatal. The news must be communicated to the family in a quiet room and explained with empathy the futility of intensive care. The few recorded rabies survivors have been under exceptional circumstances and may not be taken as examples of the outcome. In rural areas particularly, people accept the finality of death from rabies, and they either do not take the patient to a hospital or take them to alternative care or to a shrine. Most, however, keep the victim home till death overcomes them.

However, if a rabies patient is encountered in a hospital emergency room, the administration and medical officers generally react with discomfort because of misplaced apprehension that rabies may be contagious to hospital personnel. The fact is, rabies has never been known to spread nosocomially. The virus is not carried in blood and only intermittently in saliva, CNS fluid, urine, and within some tissues. Sensible precautions against contamination with the patient's oral secretions must be observed.

The patient needs comfort care in a quiet, draft-free room. Large doses of sedatives such as diazepam infusion, morphine or barbiturates may be given to prevent spasms; an intravenous line for fluid and medications may be kept open and oxygen given through nasal prongs. There should be no attempt to intubate or ventilate the patient since not only is this futile, it may cause a splattering of secretions and risk spreading the virus. The patient should be allowed to die with dignity.

Death usually occurs within 5-10 days after the onset of first symptoms. Early disposal of the body for burial is recommended while avoiding contamination with oral secretions.

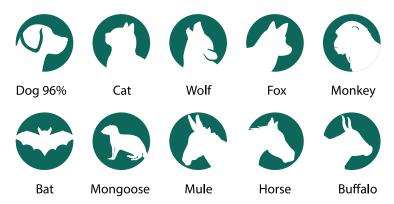




# Animals that can transmit the Rabies Virus

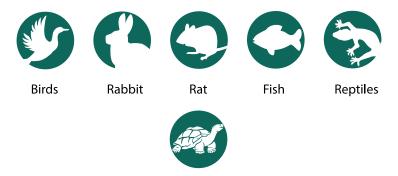
Dog 96%, bat, wolf, monkey, fox, mule, cat, mongoose, horse, buffalo. Rabies due to bat bites has been reported in North and South America, Europe, S. Africa, A and Asia1 (but not in Pakistan)<sup>1</sup>.

[Ref. 1(Poleshchuk EM, Tagakova DN, Sidorov GN, Orlova TS, Gordeiko NS, Kaisarov AZ. [lethal cases of lyssavirus encephalitis in humans after contact with bats in the Russian Far East in 2019-2021] Vopr Virusol. 2023 Mar 11;68(1):45-58. Russian. doi: 10.36233/0507- 4088-156. PMID: 36961235].



# Animals that cannot transmit the Rabies Virus

Birds, reptile, amphibians (turtles, other sea animals), fish, rabbit, rats, mice and other rodents.



Turtles, amphibians and other sea animals



# When to Suspect Rabies in a Dog or Cat

- Observing the behavior of the animal is important.
- A normally excitable and happy dog becomes dull and ill-looking, or a normally well-behaved dog becomes aggressive.
- Cats get rabies from the bite of a stray, rabid dog. Any change in a cat's behavior must be viewed with suspicion.
- Unusual drowsiness or depression and withdrawal from company
- Refusal to eat.
- Chewing aggressively on wood, paper, or other inanimate objects
- Choking sensation "bone in throat".
- Biting people and other animals without provocation.
- Excessive drooling of saliva.
- Running aimlessly and bumping into objects.
- Death from illness.
- A pregnant or postpartum bitch is usually overprotective and may bite if the puppies are threatened.
- Most persons who come to ERs for dog bites are bitten by stray, escaped dogs, sometimes in poor light, and the victim has been unable to assess the animal's behavior. In such cases, it should be assumed that the dog was rabid. Full PEP should be given according to category.

Rabid dogs and cats get worse day by day. If there is any improvement, it probably is not rabies. Pet dogs must be vaccinated with a potent modern vaccine, kept updated, and a record maintained. Unless this is so, one should not blindly trust a verbal statement from the owner. Both patient and doctor should jointly decide on receiving PEP versus only observing the biting animal.

A rabid animal never survives beyond 5-10 days of onset of infection, during which period it may have bitten other persons or animals during its bout of aggressive behavior. Hence it is important to observe the dog for 10 days after the bite. If it dies, it may be taken as indirect "proof" of rabies. If the dog lives on, it is not rabid.





These are only suggestions. Animals can be ill from other viral infections, distemper, etc. A competent veterinarian should be consulted in case of signs of illness.

If there is uncertainty about the animal's behavior, it is safer to start the vaccine series and continue on days 0, 3, and 7.

Often people report that a biting dog has survived a rabies victim. There is possibly a mistake in the identity of the dog. A rabies "carrier state" has never been proven.

### **Tips on Avoiding Dog Bites**

## Likely places where people get bitten:

- Pedestrians or cyclists
- A stray dog can be lying under your car, and bite if disturbed
- Feral dogs roam around in isolated graveyards, sea shore, empty plots, construction sites, parking lots, near meat shops or by the roadside.

# How to avoid gettig bitten:

- Avoid eye contact with a dog.
- Pretend to ignore it.
- Move cautiously, do not run away. This will only alert or provoke the dog.
- Do not pet an unfamiliar dog.
- Do not throw a stone, disturb or provoke if the dog is sitting idly.
- Carry a stick with you when out on a walk or an errand in a dog-infested area.
- Teach your child to not provoke an animal, especially if it is feeding, resting or playing.
- Pet owners should get their dog or cat immunized.
- Pet owners should get themselves vaccinated (see PreP).
- Neuter your dog. It will be less likely to be aggressive.
- Train your dog to obey orders.
- Never leave a child or infant alone with a dog.



# In case a dog is about to attack:

- Keep presence of mind.
- Put something between it and you, like a bag, purse, stick.
- Protect your face and head with your handbag or parcel.
- Shout for help.







# **Frequently Asked Questions**

There may not always be a single best answer to all questions about dog bites and PEP. There can be many "gray zones", and despite the best advice and guidelines, many unusual situations and queries may arise. Here are some questions and circumstances that may arise outside of the ordinary.

# Q.1 Is there any specific treatment for a rabies patient?

Once the symptoms of rabies develop, there is no treatment. Counsel the family in a quiet room and talk to them firmly and with compassion. If admitted, the patient should be completely sedated with tranquilizers and/or anesthetics.

# Q.2 Does a rat bite require post-exposure prophylaxis (PEP)?

There is no risk of rabies transmission from a rat. PEP is not needed.

### O.3 Is it safe to consume the meat of a rabid animal?

Cooked meat does not transmit rabies; however, it is not advisable to consume the meat of a diseased animal.

# Q.4 Is it necessary to perform a serological test on the patient following rabies vaccine series?

No, unless there is doubt about a patient's vaccine uptake or immune compromise. Quality rabies vaccines are proven to give robust antibody levels in the average person.



# Q.5 How does ID rabies vaccination work when the dose is so small? Does it fully protect against rabies virus exposure?

Provided the ARV used has a minimum potency of 2.5 IU/ml or higher, IM or ID route efficacy is the same.

# Q.6 If IM or ID route has been initiated and is not available for the next dose, is it OK to interchange the brand or vaccination route? It is preferable to use the same brand and route, however, if it is not possible, another brand or route can be used safely

# Q.7 Is simply observing the biting dog or cat for 10 days without starting treatment justified?

It is advisable to start rabies PEP in a rabies-endemic country unless the biting animal is reliably vaccinated against rabies and shows normal behavior.

# Q.8 Can rabies be transmitted from consuming the milk of a rabid cow?

The rabies virus is not passed into the animal's milk. Hence there is no danger of rabies. PEP is not needed.

# Q.9 How do I know I am protected after PEP?

Neutralizing antibodies (NAB) can be measured in the lab if resources and facilities permit. A level > 0.5 IU/ml is considered adequate as evidence of an immune response to vaccination.

# Q. 10 If an unvaccinated pet dog bites delivers a category 3 wound, should we give RIG along with the vaccine?

If it is a homebound pet that does not go out on the street, then it is unlikely to have rabies. If the behavior is generally good, and this was a defensive or protective attack, then there is no need for PEP. But if the dog has been roaming outside or its behavior is unusual, then give full PEP. Keep the dog under observation for 10 days.

# Q. 11 Can a patient with rabies transmit infection to others?

Rabies has never been known to transmit from person to person, except in rare tissue or organ transplant cases. However, precautions should be taken against exposure to the patient's saliva or secretions. In case of exposure, Category II or III PEP may be given according to the situation.



Animal bites or wounds contaminated with saliva or dirt may lead to tetanus (lockjaw), caused by Clostridium tetani bacterial spores. Tetanus, causing over 34,000 deaths worldwide in 2019, is prevalent in Asia and Africa.

Earlier signs of tetanus may be mistaken for rabies or vice versa. Tetanus usually starts with stiffness of the jaw , spreading to limbs and back as intermittent spasms/relaxation occurring at irregular intervals. The mind remans clear in tetanus. Rabies begins with fever, headache, intermittent confusion, then progresses over days to difficulty in swallowing, breathing, hydrophobia, and aerophobia. It is important to distinguish the two, as tetanus is treatable and many patients recover if managed optimally and intensively.

Prevention involves administering the tetanus vaccine. If the last tetanus dose is uncertain, a shot should be given within 72 hours after injury, especially if the previous shot was not administered within 5-10 years.

Not infrequently, the person taking care of a rabies patient presents with similar symptoms of throat pain and "tightness". This could be a "conversion reaction" that has occurred after watching a rabies patient. Taking a clear history should be followed with reassurance.

A wound from human or animal bite can develop infection from bacteria normally present in saliva. The wound should be washed immediately with soap and water, and antibiotic prescribed. Preferred antibiotic is Amoxicillin-Clavulanate.

In case of cat scratch Doxycycline or Azithromycin is recommended.





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# Addendum

### **Setting up a Rabies Prevention Center: (RPC)**

Dog bite victims should receive PEP in a place where treatment is free, is equipped with essentials, and, most importantly, within a reasonable distance from the place of the trauma. RPCs should be equipped with the following:

- 1. Dedicated wash area with liquid soap in a dispenser (image #1).
- 2. Refrigerator
- 3. Supply of ARV
- 4. Supply of RIG
- 5. Weighing scale
- 6. 3, 5, 10 ml syringes
- 7. # 21, 23 size needles
- 8. Insulin syringes for ID
- 9. Swabs, antiseptic, gloves, dressings, sharps disposal container

The center should preferably function from 8:00 a.m. to 8:00 p.m., at least at DHQ and THQ levels. Other health facilities (below THQ) should develop strong referral mechanisms to the designated RPCs after hours.

In case of non-availability of RIG, the wound(s) should be thoroughly washed, the first dose of ARV should be given, if possible, and the patient should be strictly counseled to return in the morning for subsequent management at designated RPCs. The referral note should give an accurate account of treatment received.

As many HCPs are unfamiliar with and hesitant to apply PEP correctly, IHHN, in collaboration with the Health Department, Government of Sindh, has designed an extensive PEP workshop and hands-on for HCPs at designated RPCs to learn and apply their knowledge and teach others.



Rabies Prevention & Training Center



Cold storage and all required disposables must be handy



Dedicated wound washing space



PEP lecture



Training in session



Wound wash



Intradermal injection, raising a bubble



RIG infiltration into catagory III wound





# **WHO Documentation Tools**

Documentation of dog/animal bite cases is the cornerstone of rabies **Exposed** individual prevention in public health. It enables a swift and effective response to potential rabies virus exposure, supports surveillance efforts, and contributes to developing evidence-based strategies for protecting individuals and communities from the risk of rabies. Patient Following is a comprehensive data form to document dog / animal **Enrollment** information bite victims: **Healthy Patient** III Patient Rabies **Exposure wound Exposure risk PEP** decision Management **Outcome** assessment assessment assessment RIG administration (if PEP schedule Any symptoms Date of exposure Type of animal • Risk assessment. Consistent with rabies? indicated): anatomical completed? • Anatomical location. • Animal tested for rabies? • History of vaccination. location, amount, product Performed diagnostics? · Number of bite wounds. Animal showed signs • Immune status. name/lot. Death of patient for rabies? Selected vaccination according to • WHO wound category Animal currently alive and schedule (ID/IM, regimen). case definition? (I-III). available for assessment? • Rabies vaccination Vaccine administration: Specimen submitted • Prior wound treatment. Animal vaccinated? anatomial location, recommendation for testing? product name/lot. Animal provoked? • RIG recommendation. • If positive for rabies: Adverse reactions? Animalexposed to rabies? Rabies virus variant? Next scheduled visit. Animal has bitten other people/animals?

**Documentation of dog/animal bite patients** 





### **One Health:**

In response to the escalating dog-bite incidents in Karachi, the Indus Hospital Research Center (IHRC) undertook a pilot project of One Health, advocated by the Tripartite WHO, FAO and the WOAH that calls for "collaborative efforts of multiple disciplines working locally, nationally, and globally, to attain optimal health for people, animals and the environment". Elimination of the virus reservoir in the dog can be attained by mass vaccination of dogs, and animal population control by surgical sterilization of male and female dogs.

The project took place in 2019-2022 in a fishing village in Karachi and was published in the One Health International Journal of Infectious Disease: (IJIDOH).

Naseem Salahuddin, M. Aftab Gohar, Naila Baig-Ansari, et al. How a private organization in Pakistan initiated One Health Project to eliminate rabies al https://doi.org/10.1016/j.ijidoh.2023.100011.



Master trainer from South Africa in Ibrahim Hyderi, Karachi



Catching a stray dog



Vaccinating with animal rabies vaccine



Vaccinating another stray dog



Rabies Free Pakistan on wheels



Improvised operation theatre



Neutering a male dog in process



Veterinarians in action



It's all team work





# **Case Record Form**

Date of Visit	Name	CNIC	Age	Date of Exposure	Geographical Area	Wound Washed Yes / No	Anatomical Wound/s Site	Dog/ Other

Observable/ Escaped/Killed	Provoked/ Unprovoked	Wound Category I/II/III	Prior Vaccination Yes / No	RIG Yes / No	ARV ID/IM	Day 0	Day 3	Day 7	Date of Start of Rabies Symptoms	Comments







# Name of the Health Facility

# Rabies Prevention 23773713

MR. No.	
Name	يان كراتو8-10-من
S/D/W of	
Age	ì
Address	ىمى جهاں گتا كائے كى بيارى <u> </u>
Tel. No.	,

COLLECTION			

そぶり

1- گتا کا یئز کے نورا اُجدر زنم کوصاین اور پاڈ بئک دھوئیں۔

2- گھر پیوٹونگوں کا استعال ہرگزندکریں

3- مریش کونوراا یے بہتال میں کے جا<sup>7</sup> بچاوکا علاج اچھی طرح سے ہوتا ہو۔

4- اس كار ڈ كو بميث سنجال كررگيں -

	kg	
Category	Body Weight	

SIGNATURE

Rabies Immune Globulin:as much as possible into wound/sERUG 40 I.U. /Kg Volume:mI)(Max Dose: 3000 IU)

	DAIE	DOSE GIVEN	SIGINALURE
1 W	1 Week Intradermal	nal	Day 0.3.7
	DATE	DOSE	SIGNATURE
0			
3			

		Day 0.3.7.14	SIGNATURE				
		mal	DOSE				
		2 Weeks Intradermal	DATE				
'n	7	2 W		0	3	7	14

Tetanus Toxoid 0.5ml IM

SIGNATURE	خاظتی شیکه
DOSE	ولې کے پھوں پرئیس اُ
DATE	گا نے چاہیں۔

زخم والي عبكه	ا الرون ا بازو ا عاج	جانور کی فت		مریش کوتوت مدافعت کی کمزوری ہے	ئ <sup>.</sup> بىن
	ا سالم جام معمولی ا شیرین ز	جانور کا حیثیت	ا الله الله الله الله الله الله الله ال	ا ا ا ا ا ا ا ا ا ا ا ا ا ا ا ا ا ا ا	
بخم كانوعيت	ا سالم جلد پراها ب لگانا 1 cat: 1 معمولی زخم اجتیزخون شب 2 cat: 2 ا شکیسی زخم جس میل خون بها بود ( cat: 3	اگرجانور پالتو ہے (خانتی تیکے لگے ہیں)	2y.?	کیا مریض کو پیلے ریمیز سے بچاؤک کیکے گئے ہیں	اگربان ال کاه سیم ال کاه سیزاند

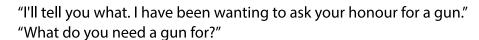




n their way back from hunting one evening, squire Nilov, a strong, robust man known all over the province for his unusual physical strength, and the investigator Kuprianov dropped into old Maxim's mill. It was only two versts to Nilov's state, but the hunters were so tired they did not want to go any further and decided to make a long halt at the mill.

This decision was all the more sensible because Maxim had tea and sugar. And the hunters a good supply of vodka, brandy and various home made comestibles. After a glass and a bite to eat, the hunters began to drink tea and chat.

"What's new, old fellow?" Nilov asked Maxim. "What's new?" the old man grinned.



"Well, I don't exactly need one. I was only going to ask for appearance's sakeo My eyesight's no good for shootin' in any case. A mad wolf has turned up from somewhere.

This is the second day I've seen it runnin' around here Yesterday evening it killed a foal and two dogs by the village, and today I went out at daybreak and there it was sittin' under the willow tree, the devil, beatin' its face with its paw. "Phoo!" I shouts at it, but gives me a look like it were the devil himself. I went and threw a stone at it, then it gnashed its teeth, and its eyes shone like candles, and off it went into the aspen grove. It fair scared me to death."





"Well, I never" the investigator muttered. "We 're sitting here. With a mad wolf running about."

"So what? We got guns with us."

"But you wouldn't»t try to shoot a wolf with small shot."

"Why shoot it anyway? You could kill it with the butt."

And Nilov proceeded to explain that there was nothing easier than killing a wolf with the butt of your gun, and recalled an occasion when with a single blow from an ordinary walking stick, he had killed on the spot a mad dog which attacked him.

"It's all very well for you to talk!" sighed the investigator, gazing enviously at his broad shoulders, "You got the strength of ten, lucky fellow. You could kill a dog with your little finger, to say nothing of a walking stick, find a place to hit and the rest of it, the dog will have bitten him five times over. It's a most unpleasant business There's no disease more painful and terrible than rabies. When I first saw a madman, I walked around in a daze for five days and began to hate all dogs and dog- owners. Firstly, the suddenness, the unexpectedness of this illness is terrible. A perfectly healthy person is walking along quietly, when suddenly up comes a mad dog and bites him! The person is immediately overwhelmed by the terrible thought that he is sure to die, and that nothing can save him. After this you can imagine the tormenting, oppressive waiting for the illness, which never leaves the bitten man for a single moment. And after the waiting comes the illness itself. The worst thing of all is that it is incurable. Once you got it, you can write yourself off. As far as I am aware, there isn't the ghost of a chance of being cured by medicine."

"They can cure it in our village, sir!" said Maxim, "Miron can cure anyone you like."

"Nonsense," Nilov sighed. "As far as Miron's concerned that's just a lot of empty talk. Last summer Styopka was bitten by a dog and no Mirons could help him. They gave him all sorts of rubbish to drink, but he went mad just the same. No, old fellow, there's nothing that can help. If it were to happen to me, if I were bitten by a mad dog, I'd put a bullet straight through my head."

The terrible stories about rabies had their effect. The hunters gradually fell silent and went on drinking in silence. Each could not help reflecting on the fatal dependence of human life and happiness on accidents and trifles, things not worth a tinker's cuss, as the saying goes. Everyone began to feel sad and miserable.

After the tea Nikov stretched and got up. He felt like going outside. After walking around a bit by the corn bins, he unlatched the small door and went out. The twilight had long since faded and it was now really dark. You could sense the still, deep slumber of the river. There was not a scrap of shade on the moonlit weir: in the middle of the neck a broken bottle shone like a star. Two small wheels, half hidden in the shade of the spreading willow tree, stared out angrily and miserably.

Nilov took a deep breath and looked at the river. Nothing was moving. The water and banks were asleep, and even the fish were not splashing but suddenly Nilov thought he saw a shadow like a black ball slip past the opposite bank, above the willow bushes. He strained his eyes. The shadow disappeared, only to reappear quickly zigzagging down to the river. "The wolf" Nilov remembered.

But by the time it occurred to him that he should run back, to the mill, the dark ball was running along the weir, not straight towards Nilov, but zigzagging. "If I start running it'll go for me from behind," Nilov thought, feeling his scalp creep. "Oh, my goodness, I haven't even got a stick! Well, I'll just stand here and choke it with my bare hands!" So Nilov began to watch the wolf's movements and the expression of its figure carefully. The wolf was running along the edge of the weir and was almost level with him.

"It 's going past!" thought Nilov, not taking his eyes off it. But at that moment the wolf almost reluctantly and without looking at him, uttered a mournful rasping cry, turned its head towards him and stopped. It seems to be deliberating whether to attack or ignore him.

"I'll hit it on the head with my fist," Nilov thought. "Knock it out."
Nilov was so confused that he did not know who started the fight, him or





the wolf. He only knew that some very terrible, critical moment had come, when he had to concentrate all his strength in his right hand and grab the wolf by the scruff of the neck. Then something quite extraordinary happened, which is hard to believe, and which seemed like a dream to Nilov himself. The wolf howled pitifully and struggled so hard that the fold of cold, wet skin in Nilov's hand slipped through his fingers. Trying to free itself from his grasp, the wolf reared up on its hind legs. Nilov grabbed its right paw in his left hand and pressed hard, right by the armpit, then quickly let go of the wolf's neck and gripped its left armpit with his right hand, lifting the wolf into the air. All this happened in a flash. To stop the wolf from biting his arms and turning its head, Nilov plunged both his thumbs like spurs into its neck near the collarbone. The wolf dug its paws into his shoulders and, using this as a support, began to struggle like fury. It could not bite Nilov's arms up to the elbow. The thumbs pressing so painfully on its neck stopped its head from reaching his face and shoulders.

"Ugh!" Nilov thought, drawing his head away as far as possible. "His spittle has landed on my lip. I'm done for; even if I manage to get rid of it by some miracle." "Help!" he cried. "Maxim, help!"

The two of them, Nilov and the wolf, their heads on the same level, stared into each other's eyes. The wolf kept gnashing it teeth, uttering rasping cries and spraying him with spittle. Its hind legs, seeking support, tried to dig into Nilov's knees. Its eyes reflected the moon, but held no trace of anything resembling anger; they were crying and human-like.

"Help!" Nilov cried again. "Maxim!"

From Miron, whom he did not believe, he drove to Ovchinnikov at the hospital. After receiving some belladonna pills and being advised to go to bed, he changed the horses and, ignoring the terrible pain in his arm, rode off to town, to see the town doctors.

Late one evening, about four days later, he rushed in to see Ovchinnikov and collapsed on the couch. "Doctor!" he began, panting and wiping the sweat off his pale, haggard face with his sleeve. "Gregory Ivanych! Do what you like with me, but I cannot go on like this any longer! Either

heal me, or poison me, but don't leave me like this! For the love of God! I've gone out of my mind!" But they did not hear him in the mill.

He felt instinctively that to shout louder would sap his strength, so he shouted quietly. "I'll walk backward " he decided. "Walk as far as the door and then shout." He began to walk backwards, but had only gone about two yards when he felt his right arm growing weak and stiff. Shortly after that he heard his own, heart-rending cry and felt a sharp pain on his right shoulder and a warm wetness spreading suddenly over his whole arm and chest. Then he heard Maxim's voice and saw the horrified expression on the face of the investigator who had run out. He did not let go of his enemy until they forced his thumbs open and showed him that the wolf was dead.

Dazed by strong sensations and already feeling the blood on his hips and in his right foot, he returned to the mill feeling very faint. The light and the sight of the samovar and bottles brought him around, reminding him of what he had just endured and of the danger that was just beginning for him. Pale, with dilated pupils and a wet head, he sat down on the sacks and dropped his hands in exhaustion. The investigator and Maxim took off his clothes and began dressing his wound. It turned out to be quite a big one. The wolf had lacerated the skin all over his shoulder and even reached the muscles. "Why didn't you throw it in the river?" asked the pale-faced investigator who was staunching the blood. "Why didn't you throw it into the river, eh?"

"I didn" think of it! I just didn think of it!" The investigator wanted to console and reassure him, but after the lurid colors which he had laid on so generously when describing rabies earlier, any attempt at consolation would have sounded unconvincing, so he deemed it better to keep quiet. Bandaging the wound as best he could, he sent Maxim the state horse, but Nilov would not wait for the carriage and set off home on foot. Next morning at six o'clock, pale and dishevelled, his face pinched from pain and sleepless night, he arrived at the mill. "Take me to Miron, old fellow!" he said to Maxim. "Quickly! Get into the carriage and we'll be off!" Maxim, also pale after a sleepless night, looked awkward, glanced around several times and said in a whisper:





"No need to go to Miron, Sir Excuse me, but I can treat it too." "Very well, only hurry, please!"

Nilov stamped his feet impatiently. The old man turned him to face the east, whispered something and gave him a mug of some foul warm liquid that tasted like wormwood. "But Styopka died" Nilov muttered. "They said they are folk remedies, but in that case why did Styopka die? You better take me to Miron!" "You must go to bed," said Ovechinnikov. "Oh damn you and your going to bed! I am asking you straight in plain and simple Russian what should I do? You're a doctor and you should help me! I am suffering! All the time I think I'm going mad. I can't sleep, can't eat, and can't do a single thing! There's a revolver in my pocket. I keep getting it out to put a bullet through my brain! Grigory Ivanych, help me please, for the love of God! What must I do? Perhaps I should go and see the professors, eh?" "It won't make any difference. Go if you like. "Listen, say I was to announce a competition and offer fifty thousand rubles to the person who cured me? What do you think of that, eh? But by the time it was printed. I'd have gone mad ten times over. I'd gladly give up everything I possess! Cure me, and I'll give you fifty thousand! Say you will treat me, for the love of God! I cannot understand this infuriating indifference! Don't you see, I even envy flies now. I am so miserable! And my family is miserable too! Nilov»s shoulders shook and he began to cry.

"Now listen." Ovechinnikov comforted him. "In part I find it hard to understand your excited state. Why are you crying? And why exaggerate the danger so? The chances are far greater that you will not fall ill, than the reverse. Firstly, only thirty out of every hundred people bitten do fall ill. And it is most important that the wolf bit you through your clothing, that is, the poison stayed on your clothes. If any did get into the wound, it must have been washed away by the blood, because you bled heavily. About rabies, my mind is completely at rest. What worries me, if anything, is just the wound, you are behaving so carelessly that you could easily get erysipelas or something of the sort."

"Do you really think so? Are you serious or just trying to comfort me?"
"Upon my word, I am quite serious. Take this and read it!"
Ovechinnikov took a book of the shelf and began to read the chapter on rabies to Nikov, leaving out the frightening bits.

"So there's no need at all for you to worry," he said when he had finished reading. "Especially if on top of all that we add the fact that we don't know whether the wolf was mad or healthy." "Hmm, yes." Nikov agreed, smiling. "Now I see, of course. So it s all a load of rubbish."

"Quite." "Well, many thanks, my dear fellow," Nikov laughed, rubbing his hand joyfully.

"I won't worry anymore, thanks to you, clever old chap I'm pleased, even happy, and honestly I am. Yes, really. Even happy."

Nikov embraced Ovechinnikov and kissed him three times. Then he suddenly had a fit of that boyish ardor to which kind-hearted, physically strong people are so prone. He grabbed a horseshoe off the table and tried to bend it, but weak from joy and the pain in his shoulder he could not: so he contented himself with putting his left arm around the doctor just below his waist, lifting him up and carrying him on his shoulder out of the consulting room into the dining room. He was happy and cheerful when he left Ovechinnikov; even the little tears shining on his big black beard seemed to be rejoicing with him. Walking down the steps, he gave a deep bass laugh and shook the balusters on the porch so hard that one of them fell out. The whole porch shook under Ovechinnikov's feet.

"What a giant!" Ovechinnikov thought, gazing admiringly at his huge back. "What a fine fellow!"

Getting into his carriage, Nikov again began to recount from the very beginning and in great detail, how he had fought with the wolf on the weir. "It was quite a game!" he finished, laughing gaily. "I'll have something to remember in my old age. Giddup there. Trishka!"





# FAISAL AND THE DOG

Faisal and his little friends were playing in the narrow dusty lane outside his house. The boys didn't notice a dog lying under a push cart not far off. Suddenly the dog stood up and growled at the boys. One of them threw a stone and started running away. The dog chased Faisal. Faisal fell on the ground and the dog dug its sharp teeth into his leg, his arm and his neck. Neighbours heard Faisal screaming and chased away the dog which ran to bite more children. Then the neighbours picked up Faisal.

"Don't wash the wound", shouted one person. "Apply red chilies", called another from his window. "Apply oil", said another. A nurse who lived nearby said calmly. "Do not panic. The first thing to do is to wash the dog's wounds thoroughly with soap and water for ten minutes. This will wash away the dog's saliva and remove the deadly rabies virus in the wound. Then clean with an antiseptic." This was done immediately from the neighbourhood tap.



Faisal's father was called and he quickly took Faisal to a hospital where Dr. Sumaira asked a lot of questions and said. "This dog could be having rabies which is a very dangerous disease and can kill your son in a few days to few months."

Then the doctor checked Faisal's weight and calculated the exact amount of Rabies Immune Globulin (RIG). She examined all the wounds and injected the RIG into each of the wounds. Then she injected Anti-Rabies Vaccine (ARV) into the arm and instructed Faisal's father to complete the vaccine series on the 3rd and 7th days.

Faisal would be saved from getting the deadly rabies.

# **Stay Safe**

- 2. If a dog bites, wash the wound immediately with soap and flowing water for 10 minutes then clean with antiseptic.
- 3. Take the person to a hospital as soon as possible for proper treatment.
- 1. Do not play with or disturb stray dogs. 4. The doctor will decide to give RIG and vaccine in case of a serious bite specially on the face, neck or hand.
  - 5. Complete the entire vaccine series.
  - 6. Get your pet dog or cat vaccinated against rabies. This will protect your pet and you and your family.

# RABIES POST-EXPOSURE PROPHYLAXIS (PEP) DELIVERY



Rabies PEP is a gateway to reach the global goal of "zero human rabies deaths", together with mass dog vaccination and community engagement.



Wound treatment.



Risk evaluation and assessment of the need for rabies biologicals.



Administration of RIG/RmAbs\* and rabies vaccine (if needed).



Patient counseling.

The 1-week intrademal vaccination regimen improves availability, accessibility and affordability of rabies vaccine and is recommended by WHO.

Zero by 30: the global strategic plan to end human deaths from dog-mediated rabies by 2030.

\*RIG = rabies immunoglobulin, RmAbs = rabies monoclonal antibodies



گلی کے کتوں کو نہ چھیٹریں
 گلی محلے کوصاف ستھرار کھیں
 زخم کوصابن اور پانی سے اچھی طرح دھویں
 گھریلو ٹو ککے ہرگز استعال نہ کریں





Technical Video for Rabies PEP