

# Guidelines for Human Abies Prevention in Pakistan

by: Dr. Naseem Salahuddin





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# Messages



Rabies remains a significant but most often unrecognized public health issue in many parts of Africa and Asia. Rabies is one of the "Neglected Zoonotic Diseases" affecting mostly poor populations of the less developed world and the first killer zoonosis among them. WHO regularly reviews and updates its recommendations on rabies prevention and control and rabies biologicals. The latest WHO recommendations for animal and human rabies prevention were issued in 2005 (First report of the WHO Expert Consultation on Rabies, TRS 931) and the WHO position paper on rabies vaccines was published in the Weekly Epidemiological Record at the end of 2007. WHO members States are required to consider these recommendations when issuing guidance for rabies prevention.

I am very pleased to introduce the Guidelines for Human Rabies Prevention directed at health care professionals in Pakistan. I would like to commend the work made by Dr Naseem Salahuddin when developing these guidelines. They will go a long way in bringing a better understanding of post-exposure prophylaxis modalities which is essential for an effective management of animal bite victims and vaccine stocks.

Dr François-Xavier Meslin, Director, Department of Neglected Tropical Diseases NTD WHO Headquarters, Geneva Switzerland.



I have reviewed your *Guidelines for Human Rabies* Prevention together with Prof. Hemachudha and found them excellent and very appropriate for your country. I do hope that you can disseminate them and they are used to help reduce the dreadfully high rabies death rate in Pakistan

Henry Wilde, MD, FACP
Professor of Medicine
Chulalongkorn University
WHO Collaborating Center for Rabies Research
Bangkok, Thailand

# Messages

#### Government of Pakistan Ministry of Health



Guidelines for Human Rabies Prevention is a much needed and long overdue booklet for proper management of dog bite which is the cause of the dreaded disease rabies. While the rest of the developed and developing world uses only modern tissue culture vaccine for post exposure prophylaxis, we in Pakistan are constrained to using the obsolete nervous tissue vaccine. We do, however, expect to switch over to tissue culture vaccine in the near future.

I am pleased to endorse the Guidelines to all practitioners who manage dog bites, and encourage them to follow the recommendations as laid down by the World Health Organization.

PROF. DR RASHEED JOOMA Director General Health Government of Pakistan Islamabad



It gives me great pleasure to introduce *Guidelines for Human Rabies Prevention* as a quick reference for health care professionals of Pakistan. I am sure this will be of great help to clinicians in better understanding of post exposure prophylaxis modalities which is essential for an effective management of animal bite victims and vaccine selection.

This guide will serve as an educational tool for prevention and management of rabies cases. It describes First Aid procedures for the dog bite victims and systematic assessment and categorization of wounds which is essential for better management of such cases.

These guidelines describe different types of rabies vaccine available throughout the world and in Pakistan, their schedule and route of administration and advocate its efficacious use depending on the category of wounds. It also deals with post-exposure prophylaxis in special conditions and guide "how to make post-exposure prophylaxis cost effective in resource poor countries" like Pakistan.

In addition to description of post-exposure prophylaxis it also caters for pre-exposure prophylaxis for all persons who are likely to get bitten or exposed to rabid animal secretions.

It also indicates other prophylaxis to be taken for animal bites and animals that transmit rabies and that don't. Further, important tips are listed when to suspect rabies in dog or a cat and how to avoid dog bites and its effects.

I applaud the sole effort of Dr. Naseem Salahuddin in developing such an important guideline, which is very much required for Pakistan.

It is hoped that this booklet will achieve its purpose of promoting prevention and management of animal bites victims.

Dr. Huma Qureshi

Executive Director Pakistan Medical Researchj Council

#### Preface



For centuries rabies has been regarded as the "orphan disease" of underprivileged humanity. In Eastern culture and in the subcontinent particularly, rabies is perceived as a "curse" ordained by destiny, to be treated by mystics and mendicants but inevitably ending in an agonizing, torturous death. Even today modern medicine has not changed mortality from rabies, and neither have public health authorities in many developing countries made serious efforts towards rabies prevention. Fortunately WHO and the dedicated scientists working towards universal prevention of rabies are making tremendous strides towards this objective. The road to elimination is yet distant and needs serious, concerted effort.

Awareness is the best form of defence. Nowhere is this truer than in prevention of rabies. Animal bites may be accidental and unavoidable, but awareness about immediate and correct action may make the difference between living and dying a torturous death. Infectious Disease Society of Pakistan (IDSP) and Rabies in Asia Pakistan Chapter Foundation (RIA Pk) have made every attempt to spread information to the public. The "Guidelines for Human Rabies Prevention" is intended for health care givers who manage animal bites in private and public institutions. Dog bite centers are few and often times far from the scene of dog bite. The delay in reaching a center or fear of multiple painful injections often results in delayed or no care at all. It is our intention that these guidelines should help the treating physician make correct decisions regarding management.

The world has made great strides in making modern safe and effective vaccines. Vaccines derived from nerve tissue such as the sheep brain vaccine have become obsolete and relegated to history. In Pakistan too we must now use modern cell culture rabies vaccine and immuneglobulin strictly as recommended by WHO. Any willing practitioner can apply the Guidelines for immediate management (wound wash and first dose of vaccine) and then refer to a large center for category 3 wound management. Many lives will be saved.

In large centers the same efficacious vaccine can be used by low dose intradermal route. It is important for the physician to be trained in injecting correctly according to schedule, and ensuring strict follow up for subsequent injections. For this, a system must be made in individual institutions. Often times judicious decisions have to be made in unusual circumstances for which consultation may be needed.

I would like to express my profound thanks to Dr F.X. Meslin, Prof. Henry Wilde and Prof. Deborah Briggs for their continuing support and encouragement for writing the Guidelines as well as towards rabies prevention in Pakistan; to Prof. Rashid Jooma, Director General Health Government of Pakistan and Dr. Huma Qureshi, Executive Director Pakistan Medical Research Council, for their kind messages; and to Prof M.K. Sudarshan for sharing Rabies Prevention Guidelines authored by him from Bangalore, India.

I sincerely hope the *Guidelines for Human Rabies Prevention* will be useful for those who wish to save lives from this dreadful disease.

Dr. Naseem Salahuddin Member WHO Expert Advisory Panel on Rabies President, Rabies in Asia Foundation (Pakistan Chapter) January 2009.

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#### 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 own 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 primarily a disease of animals (zoonotic disease) and is transmitted to man by the bite or scratch of an infected animal. 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 as well. Saliva from the infected dog can contaminate the paws, and hence a scratch is capable of transmitting the virus. 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 and the disease is perpetuated. The infected animal demonstrates signs of rabies and dies due to the infection within 5-10 days of showing signs of illness.

After a bite, millions of virus particles enter the tissues through the broken skin or mucous membrane. Within a few days to weeks the virus particles enter nerve endings in the muscle and surrounding tissues and travel along the long peripheral nerves toward the brain. Once they reach the brain tissue, symptoms begin and the disease becomes irreversible and invariably fatal.

Without the benefit of appropriate laboratory tests or a rabies experienced veterinarian it is not possible to accurately diagnose rabies in the rogue animal. Hence one depends upon the animal's observed behavior, i.e. "sick looking", apathetic or aggressive, chewing strange objects, glazed look, or simply "abnormal behavior". Considering the wide range of behavior patterns, it is felt safer to first assess the circumstances, the wound category and apply WHO recommended post exposure prophylaxis. 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 over reaction and excess treatment, but unless one has facilities to impound the animal, observe and rule out rabies, one has little choice if the victim has to be saved from this 100% fatal disease.

# Epidemiology of Rabies

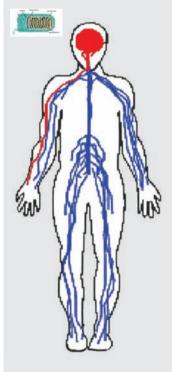
uman mortality from endemic canine rabies is estimated by WHO to be around 55,000 deaths annually. The estimated annual death toll for Asia is over 31,000. Most deaths occur in underdeveloped countries where population is dense and the number of stray and feral dogs is high. India reports the highest incidence in the world with one bite occurring every 2 seconds and one death from rabies every half hour, adding up to over 17 million bites and 20,000 deaths a year. Thailand, Sri Lanka and Phillipines have controlled rabies reasonably well, reporting only a few deaths per year through mass awareness, because of which dog bite victims seek early and proper medical care.

#### There are no reliable data from Pakistan but the number of annual rabies deaths here

is estimated to be between 2000 - 5000. A National Dogbite and Rabies Survey is at present in progress. Rabies remains a major public health problem in many countries in Asia, South and Central America, Africa, and some Pacific Islands, where unvaccinated dogs roam freely. The highest risk countries for travelers include Colombia, Ecuador, El Salvador, Guatemala, India, Mexico, Nepal, Philippines, Sri Lanka, Thailand, and Viet Nam. 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 never reported human rabies. Children under 15 years age are most affected as they usually play in the streets and are unable to run away or defend themselves against an attacking animal.

Only four rabies survivors have been reported in literature, all related to bat bite and presenting with atypical rabies. A few other anecdotal cases have been reported but not substantiated with lab tests.

# Symptoms and Diagnosis



The rabies virus is bullet shaped with a single stranded RNA genome. Bat Lyssavirus is closely related to classical human rabies virus in many parts of the world.

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 into the wound. For instance, a bite on the head, neck, shoulders or arms will produce symptoms earlier than if the bite occurred on the leg or feet.

Classical rabies presents with feverishness, headache, and periods of mental confusion alternating with periods of normal mentation. These symptoms are unique to rabies. Patients with Japanese encephalitis, herpes and other viral encephalitides do not have alternating symptoms. These are signs of viral encephalitis. This is followed by involvement of the muscles of swallowing and breathing, so that the victim has difficulty in swallowing water and actually begins to fear even a glass of water. This is called "hydrophobia". [This symptom is responsible for the myth that drinking water or washing the wound with water is harmful for the victim!) Blowing air on the face also causes spasms, provoking fear of breeze, called "aerophobia". There is intense sweating, tachycardia and acute hypertension as a result of autonomic dysfunction. Over 1 to 7 days the condition worsens, swallowing and breathing become difficult, the number of spasms increase 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 quite dramatic and specific. The initial manifestation of encephalitis may be confused with other viral encephalitides, illicit drug overdose, 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. Approximately one third of patients have the paralytic form, but this occurs more commonly with bat rabies, and only a history of animal bite may lead one to suspect rabies. History taking in a patient presenting with these symptoms is therefore important. The condition is also fatal.

Diagnosis: Rabies is a clinical diagnosis. Rabies virus antigen can be demonstrated by fluorescent antibody technique (FAT) or immunohistochemistry at neck hair follicles, 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.

Neutralizing antibodies (NAB) can be measured in the serum by enzyme linked immunosorbent antibody (EUSA) or rapid fluorescent focus inhibition test (RFFIT). A NAB level of >0.5 is considered a protective level. It is not necessary to measure NAB in most patients, but it may be required in an exceptional patient where antibody titer level is in doubt, such as in an immunecompromised patient or a prior history of vaccination.

Rabies is one of the most torturous of infectious diseases. Any one who has even once witnessed this horrendous infection will be left with the memory forever.

# First Aid for the Dog Bite Victim

earing protective latex gloves immediately flush the wound/s with clean, flowing tap water and scrub with ordinary soap and water. If the wound is deep, flush with a saline filled syringe. Severe wounds are often contaminated with dust and dirt from the street. By proper cleansing for

10 - 15 minutes, dirt and saliva should be removed and then a local antiseptic like pyodine (but not tincture iodine as this





causes skin and tissue burn), should be applied. Soap causes denaturing of the virus protein and destroys the virus.

Proper and early wound cleansing can reduce chances of developing rabies by 1/3rd.

Wound washing should actually be taught in the community to save time and improve outcome 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.



Very often only one wound is reported. Make sure you do not miss other even "insignificant" wounds. The wound/wounds should be lightly covered with clean gauze till further decision is made.

Advise the victim to be taken to a hospital known for rabies prevention and management. Many times family members are ignorant or careless about further management and use home remedies such as application

of oil, chilly, salt, etc These should be strongly discouraged as not only are they ineffective, they actually help to push the virus deeper into the damaged tissue and introduce bacterial infection.

# In the Emergency Room

Reassurance, Soothing and Counseling: All animal bite victims are fearful and anxious. Handle them gently, reassure him/her, soothe the child and ask him to allow you to examine for bites. With a gentle, caring attitude even a distressed child will let you handle the wound.

Assessment of 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.

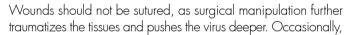
Wound Washing: even if the wound has been washed elsewhere, it should be done again

under proper conditions. If home remedies like oil, chilly, turmeric, etc have been applied, these should be removed with flushing and deep cleansing. The virus may lie hidden in deep wounds; hence thorough, gentle cleansing is emphasized. Every ER should have a proper wound

washing facility separate from the toilet. Improvised arrangement should not be acceptable as wound toilet



is one of the most important aspects of rabies prevention. All ER nurses or assistants should know how to wash wounds thoroughly for at least 10-15 minutes to remove street dirt and animal saliva.



as in the case of 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.







# **Wound Categories**

#### Wound categorization is essential to help guide further management

Category	Depth	Action
I No risk	Touching or feeding of animals, licks on intact skin	Reassurance only No vaccine needed
II Moderate risk	Nibbling of uncovered skin. Minor scratches or abrasions without bleeding	Start Vaccine series Day 0*
III High risk	- Single or multiple transdermal bites or laceration Scratches on broken skin contaminated with saliva Contamination of mucous membrane of eyes, mouth, nose or wounds with saliva or discharges from rabid animals.	Start Vaccine Series Day 0* plus Infiltrate RIG into wound at same time

<sup>\*</sup>If the biting dog is alive and healthy at the end of 10 days, you may discontinue the vaccine series.

In addition to Wound Categorization one must also take into account the behavior of the biting animal. In many instances the animal was either not seen because of cover of darkness, or because it escaped. Thick material of trousers sometimes protects against a deep bite and may 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 and able to 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 vaccine series must at least be started.

A bite from a sick, angry or wild animal is "high risk".

Once you have categorized the wound severity, you can decide on what further action to take regarding PEP.

# Post Exposure Prophylaxis (PEP)

#### Rabies Vaccines

The purpose of using vaccine is to get the humoral arm of the immune system to produce antibodies against the virus actively. A protective antibody level of 0.5 IU/ml or more is achieved in 2 weeks after giving the first 3 doses of the Essen regimen. Thereafter, the 4th and 5th doses boost the immune response further and maintain the protective levels even a year later. Cell vaccines protect against several different rabies virus strains. In Pakistan Nerve Tissue Vaccine (NTV) is produced on sheep brain by Semple method and provided at low cost. NTV is known to be less immunogenic, more reactogenic and very heat labile, and requires 14 injections according to schedule into the abdominal wall. For these reasons NTV has been replaced globally by modern Cell Culture Vaccines (CCV) which are safe and effective, though more costly.

With the advent of new, modern and effective vaccines physicians are often puzzled by names of cell cultures, dosages, routes and methods of administration.

Modern Cell culture vaccines (CCV) are produced on different cell lines. Many different pharmaceuticals produce CCVs but only those reliably produced under strict quality control and maintained at recommended temperature should be used. After all, the difference between good and bad rabies vaccine, correctly administered, will determine survival or death.

Approved vaccine potency is 2.5 IU/dose, which is required to induce immunological response. A minimum neutralizing antibody (NAB) level of > 0.5 is considered a protective level. NAB can be measured by enzyme linked immunosorbent antibody (ELISA) or rapid fluorescent focus inhibition test (RFFIT).

- 1) The earliest of these was **Human Diploid Cell Vaccine (HDCV)** that proved safe and highly immunogenic. However, human diploid cells have a relative poor yield of rabies virus, making the product expensive and scarce. Other equally effective and less expensive CCVs have now taken over the market.
- 2) Purified Vero Cell Vaccine (PVRV) Vero cell line was developed in 1962 from a primary culture of vervet monkey kidney cells. A primary cell bank is now used to produce manufacturer's working cell banks all over the world. Vero cell line is also used in polio vaccine production.
- 3) Purified Chick Embryo Cell Vaccines (PCEC) grown in chicken embryos is a potent, safe and immunogenic vaccine.
- 4) Purified Duck Embryo Vaccine (PDEV) grown in duck embryos is a potent and safe lyophilized vaccine suspension. Unlike Verocell or chick embryo vaccines, this is a suspension rather than a solution.

#### Cell culture Vaccines available in Pakistan

CCV	Brand Name	Pharmaceutical	Volume
Purified Vero Cell Vaccine (PVRV)	Verorab®	Sanofi Pasteur, France	0.5 ml
Purified Vero Cell Vaccine (PVRV)	Abhayrab®	Human Biolog. Institute, India	0.5 ml
Purified Chick Embryo Cell (PCEC)	Rabipur®	Novartis Vaccines Switzerland	1.0 ml
Purified Duck Embryo Vaccine (PDEV)	Lyssavac®	Zydus Cadilla, India	1.0 ml

All are equally safe, potent, effective and easy to administer IM. Only Verorab®, Rabipur® and Lyssavac® are WHO pre-qualified. However, it must be clearly stated that WHO does not endorse any particular product.

Other cell culture vaccines are now manufactured in China, India and South America but are as yet not on the WHO's recognized list.

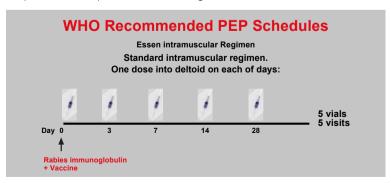
PDEV must be shaken vigorously after reconstituting with the diluent

#### Vaccine Schedule for all Category II and III bites

2 regimens are approved by WHO: Essen and Zagreb Essen Regimen is the gold standard for PEP

Schedule: Day 0, 3, 7, 14, 28 (5 vials, 5 visits)

Day 0 is the day the first dose is given



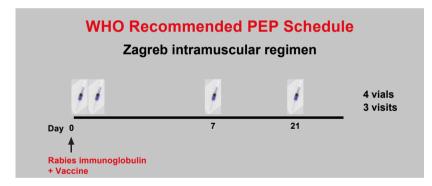


#### Schedule for Essen Regimen

Sun	Mon	Tue	Wed	Thur	Fri	Satu
		1	2	3	4	5
6	7	8	9	10	11	12
13	14	15	16	17	18	19
20	21	22	23	24	25	26
27	28	29	30	31		

#### Zagreb Regimen also called 2-1-1 regimen

One dose of the vaccine is administered each into the left and right deltoid muscle on day 0, followed by a single dose on days 7 and 21 (4 doses, 3 visits). Zagreb regimen is as effective as Essen but the latter remains the "gold standard". It may be used if the patient is traveling and cannot receive vaccine on Days 3 and 14.



#### Schedule for Zagreb regimen

Sun	Mon	Tue	Wed	Thur	Fri	Satu
		1	2 (	3	4	5
6	7	8	9	10	11	12
13	14	15	16	17	18	19
20	21	22	23	24	25	26
27	28	29	30	31		

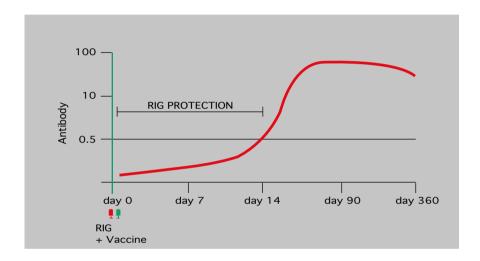
#### Important information for Rabies Vaccines

- There is no contraindication for giving vaccine or RIG. The benefit always outweighs the risk.
- Dose is the same in adults and in children
- Pregnant or lactating women must receive vaccine and RIG if exposed
- Immune compromised patients e.g. those receiving chemotherapeutic agents, steroids, or patients with AIDS, or those who have recently taken chloroquine should receive intramuscular, and not intradermal vaccine
- Since incubation period of rabies is variable, treatment should be started as soon as possible.
- If the biting dog is alive and healthy at the end of 10 days, you may discontinue the vaccine series, or give the last dose and make it a "pre-exposure prophylaxis regimen".
- Animal bite is an urgency, not an emergency. A delay of 12-24 hours for vaccination
  may not make a significant difference if time lapse is unavoidable. However this
  should not be taken as a reason to delay treatment unreasonably. 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, decide about vaccine +/- RIG).
- Most CCV are marketed as 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.
- Try to use the same commercial brand of vaccine throughout the series, unless unavoidable (e.g. non availability). In that case use another WHO recognized tissue culture vaccine and continue the same schedule.
- There are no serious side effects of CCV. 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.
- Choose either Essen (preferably) or Zagreb regimen if the patient is traveling and cannot receive vaccine on Days 3 and 14.
- In Essen regimen always inject vaccine intramuscularly into deltoid, or into the lateral thigh muscle in a child (never, never into the gluteus where fat retards absorption of the vaccine).
- Write out the schedule with dates for further doses for the patient
- The patient must be educated about completing the vaccine series. Incomplete course of 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.

#### Rabies Immune Globulin (RIG)

Since the incubation period of rabies may be several weeks to months, it is important to give immediate protection by giving passive, prepared antibodies that neutralize the virus on site. RIG provides protection for the first 14 days until the vaccine takes effect.

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



Two brands of RIG are available: Equine (ERIG) and Human (HRIG). Either one may be selected.

Equine Rabies Immune Globulin (ERIG) is prepared from heterologous (horse) serum. The dose is higher and it is less costly than HRIG. Currently manufactured ERIG is highly purified and has negligible chances of anaphylaxis. Nevertheless the manufacturers still recommend doing a skin test. There must be adequate measures to counteract drug reaction. Parenteral adrenaline, antihistamine and corticosteroids must be present at hand in case of reaction The dose is 40 IU /kg body weight, maximum 3000 IU.

One 5 ml vial of ERIG (Favirab® Sanofi Aventis) contains 1000 IU potency

Weight in Kg	IU	ml	# 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, It has a longer half life and is free of side effects. The efficacy of both is comparable but it is many times more costly than ERIG. A self paying patient must be offered the choice. The dose is 20 IU/kg body weight, maximum 1500 IU.

One 2 ml vial of HRIG contains 300 IU (Sanofi Aventis).

Weight in Kg	IU	ml	# 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 dose of RIG may suppress antibody production from vaccine.



If there is a small, single wound, draw the entire calculated amount in a syringe with 26 G needle.



If there are several wounds, then draw up the RIG, plus an estimated amount of normal saline to dilute out the RIG If you are using ERIG, always do a skin test. Do not use if there is a strong reaction. In that case use HRIG.

Wearing latex gloves infiltrate into the depth and around all sides of the wound in all directions, to neutralize virus particles. If there is any remaining RIG, inject deep into a muscle away from the vaccine site- (thigh muscle if the vaccine is being given id, or deltoid if vaccine is IM).



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. As far as possible most of the RIG should be infiltrated into the wound and only the remaining left over should be injected into the deltoid muscle away from the vaccine site, or into the lateral thigh muscle.

The production of RIG is expensive and labor intensive. It is frequently in short supply in many countries. Hence, despite strong advice by WHO to use RIG in Cat 3 wounds, it is not always used as it should be in many developing countries. It is imperative therefore to develop an alternative. There has been much research on Anti rabies Human Monoclonal Antibody (MAb). Commercial production of MAb will be easier and less costly. It may ultimately replace RIG.

#### Important Tips

- RIG can be given up to 7 days after the first vaccine when endogenous vaccine triggered antibodies appear. Giving RIG later may actually become counterproductive by suppressing antibody production.
- If you are not confident about infiltrating into a face or finger wound, consult an experienced person or a plastic surgeon.
- Do not suture the wound. Cover with dry, clean gauze. If someone else has not infiltrated RIG but already sutured it a few days back, you should still infiltrate the bite wound with RIG, but not if vaccine was given 8 days back.
- Inject vaccine and remaining RIG, if any, deep into a muscle away from the vaccine site (thigh muscle if the vaccine is being given id, or deltoid if vaccine is IM).
- Very often patients present to the ER a week after the dog bite. Even though the
  effectiveness of PEP decreases with time, it is important to still administer vaccine and
  RIG in Category III. wounds.

Failure to use RIG in a Category III bite is one of the causes of failure of post exposure prophylaxis despite good vaccine injection.

# How to make PEP cost effective in resource poor countries: intradermal (id) regimen

Any experienced ER physician will realize that the cost of a complete treatment course for PEP is very expensive. Short cuts into treatment will only endanger the patient's life. In an effort to decrease vaccine volume and make quality cell culture products affordable WHO has developed intradermal (id) schedules which, if properly administered, have the same efficacy as the intramuscular regimen.

The rationale behind id regimen is that the antigen is delivered directly to the antigen processing cells (APC) in the dermal layer of the skin at different sites, thus triggering the antibody response rapidly and to high levels; in IM route the antigen has to be first absorbed into the circulation before it reaches the APC which stimulate antibody production.

- Id regimen must be used only with high potency PVRV (Verorab® Sanofi Pasteur), and PCEC (Rabipur® Novartis Vaccines) that are WHO pre-qualified. The potency of the vaccine must be at least 2.5 IU per dose. Any vaccine of lower potency or inferior quality may not give the same level of protection intradermally and may fail to give protection.
- Id regimen is cost effective only if there are at least 2.5 patients if using PVRV, or 5 patients if using PCEC. One can use 2 vials of PVRV if using for 5 patients at the same time or within 6-8 hours.
- Opened vials must be used immediately or within eight hours and kept refrigerated between 2-8°C. 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.
- Id. regimen can be used in all cases of PEP and PreP, except in immune compromised persons or those receiving chloroquine, in which case IM route is recommended.
- Do not interchange IM and id routes. 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 id regimen is used. It is better to continue the series id.



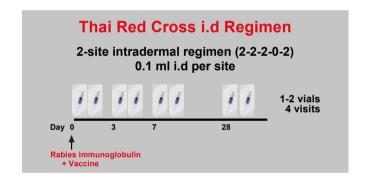
**Method:** Draw out 1 ml of the diluent fluid if using the PCEC, and mix with the dried powder, or 0.5 ml if using PVRV. Shake well till dissolved. Using insulin syringes, draw out 0.1 ml of the vaccine (5 if using 1 vial of PVRV, 10 if using 1 vial of PCEC).

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 orange peel appearance. If the vaccine is injected deep into the skin, and a papule is not seen, repeat in a different site nearby. Adequate practice and training should be given to ER personnel



before starting id regimen The procedure is similar to giving BCG intradermally.

- There are at least two WHO approved regimens for id administration: Oxford (8-site) and the Thai Red Cross (2-site). The latter is preferable and the schedule is described here.
- Give two 0.1 ml on days 0, 3, 7, 28 (called 2-2-2-0-2 regimen. 0 means none on day 14). The instruction for days is given according to Essen schedule. This regimen is called the Thai Red Cross intradermal (TRC- id) regimen and requires 4 outpatient visits. In order to treat 5 patients, you use 1 vial of PCEC (1 ml) or 2 vials of PVRV (0.5 ml each). Give the patient a vaccine record and return appointment.



Sun	Mon	Tue	Wed	Thur	Fri	Satu
		1	2	3	4	5
6	7	8	9	10	11	12
13	14	15	16	17	18	19
20	21	22	23	24	25	26
27	28	29	30	31		

RIG must still be given on day 0 in all cases of Category 3 bite even with TRC id schedule

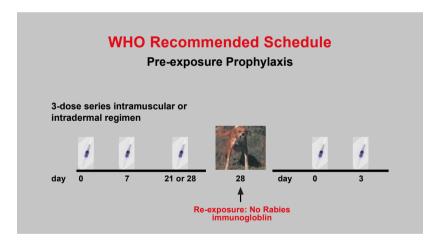
# Pre exposure Prophylaxis (PreP)

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 only wound wash and rabies vaccine boosters on Day 0 and 3 need be given IM or id. Neither full series nor RIG is required, because memory cells from existing antibodies would get a boost from 2 additional injections (anamnestic response) and provide 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
- Street cleaners/jamadars
- Children living in endemic areas
- Pet owners
- Travelers to rabies endemic countries.
- Those handling infected material from autopsies of animals

Schedule for PreP: Days 0, 7, 21 (or 28) either 1 vial IM, or 0.1 ml id. If several persons are to be vaccinated, it would be economical to use id route. Three 0.5 ml vials would be sufficient to vaccinate 5 persons. Only quality vaccine should be used for PreP just as it should be for PEP.



While giving PEP if the biting dog is known to be alive and healthy on day 10, the person will have already received 3 vaccine doses (0,3,7 IM or id). Rather than let the vaccine lapse and get wasted, it is better to give a 4th injection on day 21 (or 28) and be considered as PreP.

Considering high risk for rabid dog bites in an endemic area, and the high cost and scarcity of RIG, PreP would be the ideal way out. However, PreP on a large scale would require a great deal of logistical organization.

### Post Exposure Prophylaxis in special situations

- 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 2 booster doses on days 0 and 3 IM or low dose 0.1 ml id. Wound toilet is essential but RIG is not to be given.
- 2. Persons who have previously received nerve tissue vaccine should receive PEP as a fresh case.
- 3. Immune compromised patients eg on steroids, with HIV/AIDS or on chloroquine should not receive id regimen.
- 4. Children and pregnant women should be managed in the routine manner.
- 5. Every attempt should be made to obtain RIG in Cat III wound; however in the desperate situation where RIG is not available wound toilet should be done as thoroughly as possible. Give 2 doses of a CCV in each deltoid IM on day 0, then continue with Essen regimen (and hope for the best!). There is no evidence to show that this really works, especially when the wounds are multiple and severe.

# Other prophylaxis for animal bite

Although tetanus has never been known to be transmitted through animal bite, the rationale for giving tetanus prophylaxis is that the wound may have got soil from the victim's fall or struggle with the dog. Hence it is reasonable to start tetanus toxoid series at the same time according to schedule on Day 0, 6 weeks, and 6 months for complete immunization. If the patient is already immunized then either no prophylaxis or a booster may be given. If the person is unimmunized and the wound is large, dirty and tetanus prone, then Tetanus immune globulin (TIG) 250 IU IM may be given as a single one time dose plus the tetanus vaccine series started.

Animal saliva contains many other bacteria as well that are potentially dangerous. To prevent bacterial infection it is recommended to give an oral antibiotic such as Amoxicillin/Clavulanate 325 mg tds for 5 days.

# How to manage a patient with rabies

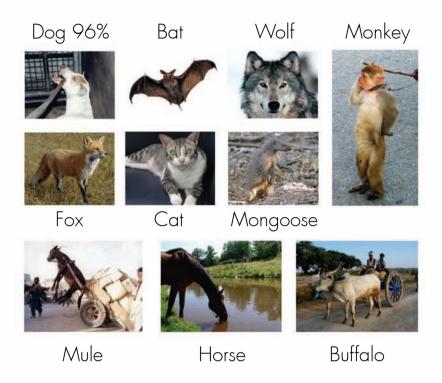
The disease is invariably fatal. The few recorded rabies survivals have been under exceptional circumstances and may not be taken as examples of the final outcome. In rural areas particularly, people accept the finality of death from rabies and they either do not take the patient to a hospital, or take them to alternative care to a pir or murshid. Most, however, keep the victim home till death overcomes.

If, however, 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. Obviously one must observe sensible precautions against contamination with the patient's oral or tracheal secretions. Gloves and a mask should be used.

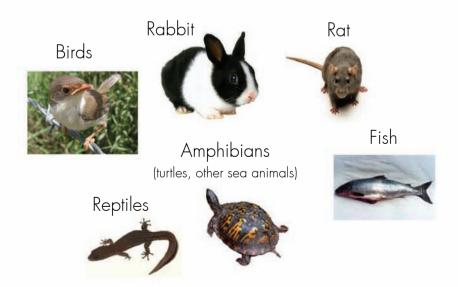
What the patient needs most is comfort care in a quiet, draft free room. Large doses of sedatives such as morphine or barbiturates may be given to prevent spasms; an intravenous line for fluid and medications may be kept open and oxygen given through nasal prongs. There should be no attempt to intubate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

Death usually occurs within 5-10 days after onset of first symptoms. The family should be counseled that the disease is fatal. Sympathy and comfort should be given in an effective manner and the patient should be allowed to die in dignity. Early disposition of the body for burial is recommended.

## Animals that can transmit Rabies



## Animals that do not transmit Rabies



# When to suspect Rabies in a dog or cat

#### Observing 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 post partum bitch is usually over protective 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 not been able to assess the animal's behavior. In these cases it should be assumed that the dog was rabid. Full PEP should be given according to category.

Dogs and cats get worse day by day. If there is any improvement, it probably is not rabies.

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 vet should be consulted in case of signs of illness. We do not yet have tests available for lab diagnosis.

Since there is uncertainty about the animal's behavior, it is safer to start the vaccine series and continue on days 0, 3, 7. If the dog remains alive and healthy, one may stop the vaccine series now. However, since 2 or 3 injections have already been given it is better to give an additional injection on day 21 and convert it to "pre exposure prophylaxis" rather than waste the series.

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

In addition to the above prescribed PEP, the treating doctor must understand that a dog bite is physically as well as psychologically a very traumatic experience for the victim and the family. There is pain, anguish, fear, uncertainty. The victim must be soothed, comforted and reassured, the wound washed with care, and vaccine and RIG given with confidence and reassurance.





# 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, empty plots, and construction sites, parking lots, near meat shops or by the roadside

#### How not to get 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 to chase
- Do not pet an unfamiliar dog. It could have rabies
- 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
- Shout for help



#### Unusual situations

There may not always be a single best answer to all questions about dog bite 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 hypothetical questions and circumstances that may arise outside of the ordinary.

- Earlier signs of tetanus may be mistaken for rabies or vice versa. Tetanus usually starts
  with jaw stiffness, spreading to limbs and back in the form of intermittent spasms/relaxation
  occurring at irregular intervals. Rabies begins with fever, headache, intermittent confusion,
  then progresses over days to difficulty in swallowing, breathing, hydrophobia,
  aerophobia. It is important to distinguish the two, as tetanus is treatable and many
  patients recover if managed optimally and intensively.
- It has often happened that 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.
- Rabies has never been known to transmit from person to person. However, universal
  precautions should be taken against exposure to the patient's saliva or secretions. If
  there has been exposure, Category II or III PEP may be given according to the situation.
- A patient presents to the Emergency Room with hydrophobia and history of dog bite. There is much apprehension among hospital staff and administration over management in the ER or hospitalization.
- Such a patient should be given maximum attention, care and comfort, even if it means hospitalization. Even though there is no chance of survival, the family must be told clearly, and comfort care given to the best of one's ability. Often times the family realizes the futility of admitting and wishes to take the patient home to die. If they prefer to be admitted, keep him/her in a quiet, separate room. Administer large doses of chlorpromazine, analgesics, antipyretics, anticonvulsants to keep him sedated and free of painful throat spasms. Death is slow and painful over 3-5 days.
- Natural antibodies to rabies virus do not rise because there is no viremia. The virus travels up nerve tissue to the brain and then to target organs. By that time brain stem neuronal cells are destroyed and the patient dies from respiratory arrest.
- Not all cases of rabies present with encephalitis and hydrophobia. One third present with rapidly ascending paralysis (resembling Guillain Barre Syndrome). All patients presenting with these symptoms should be questioned about dog bite in recent past, i.e. few weeks to few months back. Prognosis is poor.
- Cases of human rabies deaths have been reported after transplantation of cornea, liver
  and kidney from patients who died of rabies. Before harvesting an organ, death from
  rabies should be ruled out.
- Consumption of raw milk or meat from a rabid cow has never been known to cause rabies. In case of concern or anxiety, give vaccine series.

 Pet dogs must be vaccinated with good 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 make a decision for receiving PEP versus observation only of the biting animal.



- It is preferable to use the same brand and route of vaccine for the entire series of Essen regimen or TRC ID. However, if a situation of non availability arises, it may be interchanged.
- Cell culture vaccines are usually lyophilized (powder form) and relatively heat stable
  until re-constituted. After re-constitution, the vaccine should be refrigerated and used
  within 8 hours. RIG should always be stored in the refrigerator at 2-8°.
- Any person who has received PEP (5 doses), or PreP (3 doses) in the past even up to 10 years back, need not receive full PEP if bitten again. Only 2 doses on day 0 and 3 are sufficient to boost the antibody response rapidly. Even RIG is not required. However, both patient and treating physician should be certain of the past history of correct vaccination with quality vaccine.
- A patient comes weeks or months after a dog bite and wants to know if he is still in danger of rabies. There is no clear answer since incubation period varies from few days to few months. It is better to assess the circumstances and category, make a decision as if the bite just happened and treat as per category II or III.
- A patient may have received only vaccine series and not RIG in Category III wound. A week or more later he now asks for RIG. It is not recommended to give RIG days after giving vaccine as it may interfere with natural antibody response. However, if the doctor feels that the wound was rabies prone and use of RIG was essential, it may be infiltrated now into the wound even if it is healed, or alternatively IM into the muscle away from the vaccine. An extra dose of vaccine may be given up to day 90.
- It is believed that puppies cannot transmit rabies. Rabies can be transmitted by a dog of any sex, breed or age.
- Many persons ask if the vaccine series plus RIG produced adequate antibodies.
   Neutralizing antibodies can be measured in the lab if resources and facilities permit.
   The serum level should be > 0.5 IU / ml to be considered protective.
- Municipalities periodically kill stray dogs to reduce dog population. This has never shown to provide long term results in any country. Many countries have shown the best way to reduce dog population is to catch stray dogs, vaccinate, neuter and release. Over time their numbers will naturally reduce. This of course needs tremendous cooperation between the local government and veterinary services.

# Why does PEP fail?

- 1. RIG not used at all, injected only IM and not into wounds, or not all bite wounds injected.
- 2. Vaccine or RIG of poor quality.
- 3. Vaccine injected into gluteus, where absorption is poor.
- An exceptionally large rabies viral load was introduced and the wound not properly washed.
- 5. Virus was injected directly into a nerve.
- 6. Wound was sutured prior to RIG infiltration, further spreading the virus.
- 7. Inadequate calculation of RIG volume, not diluted to sufficient volume to cover all bite wounds.
- 8. Unrecognized and unreported deviations from WHO protocol.
- 9. RIG was given more than 8 days after vaccine.

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# THE WOLF

(From the collection of translated short Russian stories of Anton Chekov 1885-1887)



On 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 verst 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.

"I'll tell you what. I been wantin' to ask your honour for a gun."

"What do you need a gun for?"

"Well I don't exactly need one. I was only going to ask for appearance's sake... 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 evenin' 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 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, found 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 mad man, I walked around in a daze for five days and began to hate all dogs and dogowners. 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, 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 felt 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, 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....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 gripping 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 collar bone. 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...'85lts hind legs, seeking for 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 humanlike.

"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 wit his sleeve. "Gregory Ivanych! Do what you like with me, but I can't 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 backwards..." 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...'85 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 which was just beginning for him. Pale, with dilated pupils and 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't think of it! I just didn't 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... 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 and.... 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 is 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. With regard to 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 any more, thanks to you, clever old chap...'851'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 ardour to which kind-hearted , physically strong people are so prone. He grabbed a horseshoe of 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 round 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!"



# CASE-RECORD FOR HUMAN EXPOSURE TO RABIES POST EXPOSURE PROPHYLAXIS (PEP)

Case No.		Ref	erred by	
Name	Sex		Date of bit	e
Age	_	Loc	ality of biting episod	le
Home address		_ Site		dy
		_ Na		
		Sing	gle 🗆	Cat. 1
		Mul	tiple 🗆	Cat. 2 $\square$
Other persons (if any)		1		
bitten by the same animal		2		
First time animal bite? Yes/No				
Present PEP				
Treatment		Pa	tient's weight (k	(g)
Local wound treatment: W	ashed for at least 1	0 mts	Yes/No	
Ą	oplied Home remedy	у	Yes/No	
Immunoglobulins: RIG: f	for Cat 3 bite			
Human 🗆	Equine $\square$			
Manufacturer and Batch # _				
Results of sensitivity test:	:	Size or o	quantity administered	J
Date administered				

Vaccine:	1 1			
,,				
IM into deltoid		Dose administered		
Intradermal		_		
Dates administered		_		
Were there undesire	able effects following trea	 tment? If yes, specify treatm	nent, nature c	of side-
effects and outcome				
	ed person after 6 m	onths: (if known)		
Alive				
Died of rabies		Date of death		
Died of other causes				
	ons bitten by the same ani	mal, if known:		
Biting animal:	ons bitten by the same ani	mal, if known:		
Status of other person  Biting animal:  Animal species	ons bitten by the same ani			
Status of other personal:  Biting animal:  Animal species	ons bitten by the same ani			
Status of other personal: Biting animal: Animal species Breed	ons bitten by the same ani	Age		
Status of other personal: Biting animal: Animal species Breed	ons bitten by the same and	Age		
Status of other personal:  Biting animal:  Animal species  Breed  Stray  Was the animal vaccons	ons bitten by the same and	Age		
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Status of other personal:  Biting animal:  Animal species  Breed  Stray  Was the animal vaccing animal vaccing animal vaccing animal vaccing animal vaccing animal vaccing and animal vaccing animal vac	ons bitten by the same and ons bitten by the same and one Owned cinated against rabies?	Age	Escap	ed 🗆
Status of other personals:  Biting animal:  Animal species  Breed  Stray  Was the animal vaccing stray  Outcome:  Under observation  Outcome after days:  Signs of rabies	Owned cinated against rabies?	Age	Escap	ed 🗆
Status of other personal:  Biting animal:  Animal species  Breed  Stray  Was the animal vaccin  Under observation  Outcome:  Under observation  Outcome after days:  Signs of rabies  Healthy	ons bitten by the same ani ons bitten by the same ani ons bitten by the same ani	Age	Escap positive	ed 🗆
Status of other personals:  Biting animal:  Animal species  Breed  Stray  Was the animal vaccing stray  Outcome:  Under observation  Outcome after days:  Signs of rabies	ons bitten by the same and	Age	Escap	negative

n

- Rule of thumb for PEP: Wash wound, assess wound category, Cat 2 vaccinate only, Cat 3 RIG plus vaccine.
- If properly managed according to WHO guidelines, rabies is completely preventable.
- Counseling the patient and family about the life saving value of PEP will build their trust and confidence and secure compliance.
- Follow WHO recommendations for PEP to the letter. Any deviation may lead to unfortunate results.
- id regimen is safe, effective, easy and economical.
- id regimen should be used in centres seeing 5 or more new of follow ups per day.
- A rabid animal always dies within 5-10 days.
- Awareness is the best defence. Educate your patient and the community.
- Rabies can be transmitted by a dog of any sex, breed or age.
- Failure to use RIG in a Category III bite is one of the causes of failure of PEP despite good vaccine injection.
- Use exact amount of calculated RIG.
- Very often only one wound is reported. Make sure you do not miss other even "insignificant" wounds.
- Do not use RIG 8 days after vaccine has been given.
- Proper and early wound cleansing can reduce chances of developing rabies by 1/3rd.
- Vaccines prepared from nerve tissue such as sheep brain should be abandoned.
- Infiltrate as much RIG as possible into the wound. If any left over, inject into the thigh muscle.
- Rat bite does not require rabies prophylaxis.
- Incomplete course of vaccine may be a cause of PEP failure.
- If there has been a delay of 2-3 days, do not restart, simply continue the series.



