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சுகாதார,போசணைமற்றும் சுதேசவைத்தியஅமைச்சு
Ministry of Health, Nutrition& Indigenous Medicine

General Circular Number :- 01-50/2019

All Provincial Secretaries of Health
All Provincial/Regional Directors of Health Services
All Directors of Teaching Hospitals
All Heads of Specialized Campaigns
Medical Superintendents of Provincial Hospitals
District Medical Officers of Base Hospitals
Director, Private Health Sector Development

PROTOCOL FOR ANTI RABIES POST EXPOSURE THERAPY (PET) - 2019

Herewith I am annexing Circular no **01-50/2019** on the protocol for Anti Rabies Post Exposure Therapy (PET) which would help the Medical Officers to update their knowledge on correct patient management. This protocol is based on Rabies Vaccines: WHO position paper No.16, 2018, 93, 20 April 2018 in the WHO Weekly Epidemiological Record and WHO Expert Consultation on Rabies, third report, WHO Technical Report Series 1012, 2018.

This circular replaces the previous circular on revised protocol for anti rabies PET issued by DGHS on 16.03.2016.

It would be essential to circulate this among all the consultants and medical officers. Adhering to these guidelines will ensure correct management of patients and would also prevent wastage of anti rabies serum and vaccines in hospitals.

It would be the responsibility of the Heads of Institutions to ensure the usage of anti rabies serum and vaccines, strictly according to the protocol so the treatment will be uniform island wide.

Please bring the contents of this circular to the notice of all prescribers in your Province/Region and Institutions.

Dr. Anil Jasinghe
Director General of Health Services
Ministry of Health, Nutrition & Indigenous Medicine,
"Suwasiripaya"
385, Rev. Baddegama Wimalawansa Thero Mawatha,
Colombo 10.

Dr Anil Jasinghe
Director General of Health Services

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385. Rev. BaddegamaWimalawansaTheroMawatha. Colombo 10. Sri Lanka.

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Protocol for anti rabies post exposure therapy (PET)

1.0 Initial management of a patient following an animal exposure

1.1 Wounds should be washed immediately with soap and water, at least for 5 minutes.

1.2 Wounds should be cleaned thoroughly at the hospital with 70% alcohol or povidone iodine.

1.3 Anti tetanus immunization should be administered when necessary (DT / aTd for children).

1.4 Antimicrobials should be prescribed if necessary to control bacterial infection.

1.5 Wound dressing could be done to prevent wound infection.

1.6 If suturing is indicated it should be done after infiltration of the wound/s with RIG. Suturing should be delayed for several hours to allow diffusion of the immunoglobulin through the tissues.

1.7 However, as a **life saving measure**, profuse bleeding could be arrested with minimum number of sutures with minimum tension prior to infiltration with RIG.

It is essential to screen the patient and the animal before a decision is made regarding PET

The patient must be clearly advised that the animal (dog/cat) if observable, should be closely monitored for healthiness during the observation period of 14 days from the day of the exposure.

If the animal becomes sick, develops any suspicious behaviour, goes missing or dies, the patient should be advised to **report to the hospital immediately**. In case of death of the animal, patient should be encouraged to send the head of the animal for laboratory confirmation/exclusion of rabies.

2.0 Screening the patient- Categorization of the exposure

2.1 Major exposures:

a) Single or multiple bites with bleeding on head, neck, face, chest, upper arms, palms, tips of fingers & toes and genitalia

b) Single or multiple deep bites with free flowing of blood on any part of the body

c) Single or multiple deep scratches with free flowing of blood on the head, neck and face

d) Contamination of mucous membranes with saliva

e) Bites of wild animals with bleeding

2.2 Minor exposures:

a) Single, superficial bite with oozing of blood or scratches with bleeding on any part of the body

b) Multiple scratches with oozing of blood on any part of the body

c) Nibbling of uncovered skin

d) Contamination of open wounds with saliva

e) Superficial bites and scratches of wild animals without bleeding

2.3 The following are not considered as exposures:

a) Contamination of intact skin with saliva of a proven rabid/suspicious/stray animal
b) Petting, bathing or coming in contact with utensils of a proven rabid/suspicious/stray animal
c) Eating of leftovers which were previously eaten by a proven rabid/suspicious/stray animal
d) Drinking water from a well where an animal has fallen and died
e) Drinking raw milk of a rabid cow or goat
f) Bites from cold blooded animals (reptiles, amphibians) and pecks by birds
g) House rat bites

Anti Rabies PET: after screening the patient, animal concerned and the encounter

When PET is indicated

- Patients in the major category should be given rabies immunoglobulin (ERIG or HRIG) followed by a course of anti rabies vaccine (ARV)
- Patients in the minor category should be given only a course of ARV

3.0 Post exposure therapy for patients presenting without a history of previous anti rabies post/pre exposure therapy

3.1 Management of a patient with a **minor exposure** to dogs and cats:

3.1.1 If the animal is apparently healthy, observable and has had a minimum of one rabies vaccination with documented evidence.
- within 1 year of the incident
- at an age above 3 months
- incident occurring at least 1 month after the last vaccination

PET can be delayed while observing the animal for healthiness / behavioural changes for 14

days from the day of the exposure.

3.1.2 PET for superficial scratches with bleeding, caused by healthy observable domestic animals **(irrespective of vaccination status of the animal)** also could be delayed while observing the animal for 14 days.

If the animal becomes sick, develops any suspicious behaviour, goes missing or dies, the patient should be advised to report to the hospital immediately to commence PET.

3.1.3 If the animal is having suspicious behavior or sick but observable **(irrespective of the vaccination status)** initiate PET while observing the animal. Discontinue PET if the animal is healthy after 14 days.

3.1.4 If the animal is having rabies (confirmed by laboratory diagnosis) or unobservable (stray animal, animal dead, killed, missing; **irrespective of the vaccination status**) initiate PET and continue the full course .

PET for minor exposures: only anti rabies vaccine is indicated even if the animal is proven to be rabid.

3.2 Management of a patient with a **major exposure** to dogs and cats:

3.2.1 If the animal is apparently healthy, observable with a reliable history and has documented proof of
- a minimum of 2 rabies vaccinations given not more than 2 years apart
- with the last vaccination given within 1 year of the incident

PET could be delayed while observing the animal for 14 days.

3.2.2 If the animal is **apparently healthy, domestic and observable with a reliable history**

In situations where the animal is improperly vaccinated or not vaccinated
- If the wounds are not in the head and neck
- If the wound/s does not need surgical manipulations or suturing
- If the bite was due to a provoked situation
- If the patient/ parent of a child is responsible and reliable
- If the patient is immune-competent

Patient could be managed with **modified ID 4 site schedule (4-2-2-0-2) in place of RIG,** while observing the animal for 14 days for healthiness.

Clear instructions should be given to the patient to <u>report back to hospital immediately</u>, if the animal becomes sick, develops any suspicious behavior, goes missing or dies during this observation period.

If the patient report back within 7 days of initiation of modified ARV 4 site schedule, **<u>infiltration of wound/s with RIG should be done and initiate a fresh course of 2 site ID ARV.</u>**
If a dose of ARV had been given within 24 hours prior to the infiltration of RIG, that dose of ARV could be considered as the D0 of the fresh schedule.

If the patient reports back after the day 7 dose (3rd dose) of ARV, **<u>continue and complete the modified 4 site ID ARV schedule</u>**, RIG is not recommended. In such situations, additional doses of ARV could be considered after seeking expert opinion.

3.2.3 If the animal is sick (**irrespective of the vaccination status**), having rabies (confirmed by laboratory diagnosis) or unobservable (animal dead, killed, missing or stray animal) **<u>initiate PET immediately with rabies immunoglobulin (RIG) and follow with a full course of anti rabies vaccine (ARV)</u>**.

4.0 Rabies Immunoglobulin (RIG)

- Administration of RIG should be considered as an **emergency**. Rabies immunoglobulin should be given immediately / as early as possible after the incident.

- If the patient reports late, RIG could be given up to 3 months after exposure, if the patient has not taken the anti rabies vaccine.

4.1 Types of RIG available in Sri Lanka at present:

Equine rabies immunoglobulin (ERIG)
Human rabies immunoglobulin (HRIG)

4.2 Dosage of RIG

Maximum dose of Equine rabies immunoglobulin (ERIG) 40 IU/ Kg body weight
Maximum dose of Human rabies immunoglobulin (HRIG) 20 IU/Kg body weight
There is no minimum dose

4.3 Administration of equine rabies immunoglobulin (ERIG)

- The present WHO guideline does not recommend skin testing (ST) before administration of Equine Rabies Immunoglobulin (ERIG), as such tests poorly predict severe adverse events and their results should not be the basis for non-administration of ERIG when indicated

- However the treating medical officers should be prepared to manage anaphylaxis, which although rare, could occur during the administration of ERIG which is heterologous serum

- The entire immunoglobulin dose or as much as anatomically feasible should be infiltrated carefully into or as close as possible to all wounds

- WHO no longer recommends injecting the remainder of the calculated RIG dose IM at a distance from the wound/s, as evidence suggest that there is no or little additional protection against rabies as compared with infiltration of the wound/s alone

- In situations with multiple bites, where the volume of RIG is insufficient for infiltration in and around all wounds (especially in children), RIG could be diluted with sterile N. Saline up to twice or a maximum of 3 times.

- Administration of ERIG could be done in a centre where emergency care facilities are available. i.e. PCU, ETU, A&E, ICU etc.
  (PCU-Primary care unit, ETU- Emergency treatment unit, A&E- Accident and Emergency, ICU- Intensive care unit)

- Drug of choice for management of anaphylaxis is 1:1000 adrenaline, 0.5ml in adults and 0.01ml/kg with a maximum of 0.3ml in children given intramuscularly (IM) into the mid anterol lateral thigh immediately. This dose can be repeated after 5 to 15 minutes later or even earlier if necessary. Mild sensitivity reactions could be managed with antihistamine therapy. Oral or parenteral steroids should be best avoided.

- ARV should be administered preferably on the same day after RIG, but at a different site.

4.4 Administration of human rabies immunoglobulin (HRIG)

HRIG is a very costly biological with limited availability. Hence this product should be used strictly for the following indications, if / when available.

1. History of severe allergic reaction/anaphylaxis to red meat or cow's milk
2. Patients who developed severe allergic reaction/anaphylaxis while infiltrating wounds with ERIG, before completing the wound infiltration
3. Patients who report back later with a missed wound/s, after infiltration of wound/s with ERIG

5.0 Anti Rabies Vaccines (ARV)

Following anti rabies vaccines are registered in Sri Lanka.

a) Purified Vero cell rabies vaccine (PVRV)
b) Purified chick embryo cell culture vaccine (PCEC)

5.1 Intradermal (ID) schedules of ARV

- WHO recommends the use of ID schedules as there is a global shortage of ARV and for developing countries, where cost of vaccines is a major limiting factor.
- The **recommended ID dose is 0.1ml per site for both PCEC and PVRV.**
- For all age groups, ID injection sites are the deltoid region, anterolateral thigh or suprascapular regions.

- It is recommended to use fixed needle 1ml disposable syringes for intradermal administration of ARV to minimize vaccine wastage.

5.1.1 The 2 site ID schedule (2-2-2-0-2 schedule)

The standard schedule used in government hospitals: One dose each (0.1ml) is given at 2 sites, on both arms (over deltoids) on D0, D3, D7 and D30.

5.1.2 The modified 4 site ID schedule (4-2-2-0-2 schedule)

One dose each (0.1ml) is given at 4 sites on day D0 (deltoids and lateral thighs) one dose each (0.1ml) given at 2 sites on D3, D7 and D30.

This schedule could be recommended for patients with minor exposures with late presentation, borderline exposures and major exposures from **healthy observable domestic animals** as stated in 3.2.2.

5.1.3 Precautions that should be taken when using ID- ARV schedules.

- All injections should be administered only by trained staff under supervision of a medical officer.
- Once the vaccine is reconstituted, the contents should be used as soon as possible (preferably within 6 hours, stored at 2 - 8^0C).
- Separate disposable syringes and needles should be used for each patient.
- If a dose of ARV has gone subcutaneously (where the bleb is not observed), an extra dose of ID ARV is recommended.

5.2 Intramuscular (IM) schedules of ARV

5.2.1 For major exposures: 5 dose regimen with RIG

IM-ARV one dose* each on D0, D3, D7, D14, & D30

This schedule is recommended for patients who are immunocompromised and for international travelers.

5.2.2 For minor exposures: 4 dose (2-1-1) regimen

2 doses * of IM-ARV one in each deltoid on D0, followed by 1 dose* each on D7 & D21.

*1 dose - PCEC 1ml (1 vial) / PVRV 0.5ml (1vial)

- IM injections should be given into the deltoid muscle or into the anterolateral aspect of the thigh in small children.
- Administration of ARV **on the buttocks is not recommended** as absorption is poor

5.3 ARV Postexposure therapy for immunocompromised patients

- This category includes: patients on chemotherapy, cytotoxic drugs, on long term steroids, on long term anti-malarials, positive for HIV/AIDS, organ transplant recipients and stem cell transplant patients on immunosuppressive therapy etc.
- **Intradermal schedules of ARV is not recommended for immunocompromised patients.**
- Often these patients may require RIG, and should be administered the IM-ARV schedule.
- In high risk situations, after obtaining expert advice from MRI, rabies antibody assessment could be offered for these patients.

6.0 Anti rabies pre-exposure therapy

- This form of therapy is indicated for persons who are at a higher risk of exposure to rabies virus i.e. laboratory staff handling live rabies virus, veterinarians and support staff, rabies control staff (vaccinators), wild life officers, employees in animal quarantine premises and zoological establishments etc.
- Presently in Sri Lanka the recommended schedules are ID 0.1ml single dose or IM-ARV-1 dose each on D0, D7 & D28.
- A booster dose is given 1 year after the primary course. Additional booster doses are given once every 5 years.
- Administration of RIG is not indicated in persons on pre-exposure therapy following an exposure.
- They should only be given additional doses of ID 2 sites or IM- ARV 1 dose each on D0 and D3 as boosters even in a case of a major exposure to a confirmed rabid animal.

7.0 Management of patients following previous rabies PET

7.1 Patients presenting with exposures from healthy, observable domestic animals (irrespective of the vaccination status)

Following a full or a partial course of ARV (3 doses of ID /IM ARV) irrespective of the time duration for both major and minor exposures, PET could be delayed while observing the animal for 14 days.

If the animal becomes sick, develops any suspicious behaviour, goes missing or dies during the observation period, the patient should be advised to report to the hospital immediately to commence PET (Refer 7.2.1 & 7.2.2).

7.2 Patients presenting with exposures from proven rabid, suspicious, sick, dead or unobservable animals

7.2.1 With a documented evidence of a full course of ARV-

a) with an exposure occurring within 3 months, neither RIG nor ARV is needed. Only wound treatment is required.

b) with an exposure occurring after 3 months of the previous course of PET, irrespective of the time duration,

- RIG is not indicated
- ID ARV 2 doses each or IM ARV one dose each, should be given on D0 and D3 as boosters. As an alternative to this, the patient may be offered a single visit 4 site intradermal doses (0.1ml ID) over deltoids and supra-scapular/anterolateral thigh areas.

7.2.2 With a documented evidence of a partial course of ARV (3 doses) -

a) RIG is not indicated irrespective of the time duration from the previous course of ARV.

b) If the patient presents with an exposure occurring within one month from the initiation of the course, it could be completed with the D30 ARV dose.

c) If the patient presents within 10years - ID ARV 2 doses each or IM ARV one dose each should be given on D0 and D3 as boosters.

d.) If the patient presents after 10years – ID / IM ARV full course is recommended.

8.0 Important points to be noted

- Ideally RIG should be administered before starting on ARV.
- Pregnancy/breast feeding is not a contraindication for RIG (ERIG/HRIG) and ARV therapy when indicated.
- All patients who receive rabies PET should be given a document/card, clearly stating the **date, month & the year** of vaccination, **the type of vaccine** used and RIG given or not.
- In situations where the animal is not vaccinated, encourage the owner to vaccinate the animal concerned after the observation period.
- Laboratory confirmation of rabies should always be encouraged.
- Human to human transmission of rabies has not been reported (except through corneal or organ grafts)

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- In a case of suspected human death due to rabies, it is mandatory to order a postmortem and fresh brain (without preservatives) sent to MRI for laboratory confirmation.

- For any person who has had direct or indirect contact with a rabies patient, PET is not recommended except in special situations. Please refer to General Circular No: DGHS/Circular/2016-127(MRI-Gu-HR) Guidelines to be followed in a case of human rabies/death and disposal of the body.

- Any allergic reactions following RIG/ARV should be documented on the patient's immunization card for future reference.

Please note that all health care staff managing anti rabies PET patients should strictly adhere to the guide lines given in this protocol. For any clarification, contact Consultant Virologist, Dept of Rabies and Vaccines, MRI. Telephone numbers: 011-2698660, 011-2693532-4.

It is essential that all institutions using RIG and ARV should send a monthly return (Annexure 1) in 03 copies and sent to the following before 5th of the following month.

1. Consultant Virologist, Dept. of Rabies and Vaccine QC, MRI
2. Director, Public Health Veterinary Services, 6th Floor, 555/5, Elvitigala Mw, Colombo 05
3. Regional Epidemiologist

Any adverse reactions following rabies PET should be informed in writing to Director/MSD, Chairman/NMRA and Virologist/Dept. of Rabies and Vaccine QC, MRI.

Annexure I

Monthly vaccine return for Anti Rabies Post Exposure Therapy

Name of the institution .....

Year.....Month.....

1	**Patient Immunization**					
	Type of immunization	No of vials used				
1.1	**Anti Rabies Serum**					
	ERIG					
	HRIG					
1.2	**Anti Rabies Vaccine**					
1.2.1	**Intradermal**	1st dose	2nd dose	3rd dose	4th dose	5th dose
	2 site schedule (2-202-0-2)					
	4 site schedule (4-2-2-0-2)					
1.2.2	**Intramuscular**					
	5 dose schedule (1-1-1-1-1)					
	Minor exposure schedule (2:1:1)					

2	**Movement of ARV and RIG**	**ARV**	Rabies Immunoglobulin (RIG)		
			ERIG	**HRIG**	
				300 IU	750 IU
2.1	Number of vials available at the beginning of the month				
2.2	Number of vials received during the month				
2.3	Number of vials consumed during the month				
2.4	Number of vials available at the end of the month				

3	Number of patients where PET was not initiated according to treatment guideline	

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Signature of nursing officer in charge
Name.....
Designation.....
Date .....

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Signature of the Medical Officer in charge
Name.....
Designation.....
Date.....