

Pre-exposure and Post-exposure Prophylaxis for Rabies



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Prevention

Rabies is almost 100% preventable

**Post-exposure Prophylaxis
(PEP)**



**Immediately following a potentially
rabid exposure**

**Pre-exposure Prophylaxis
(PrEP)**



Individuals at high risk

Post-exposure prophylaxis (PEP)

WOUND MANAGEMENT

ACTIVE IMMUNIZATION (ARV)

PASSIVE IMMUNIZATION (RIG)

Exposure Category

Category	Type of contact	Type of exposure	Recommended PEP
I	Touching or feeding of animals Licks on intact skin	None	None , if reliable case history available
II	Nibbling of uncovered skin Minor scratches/abrasions without bleeding	Minor	Administer vaccine immediately
III	Single or multiple transdermal bites, scratches or licks on broken skin Contamination of mucus membranes with saliva (licks) Exposure due to direct contact with bats	Severe	Administer rabies immune globulin and vaccine immediately

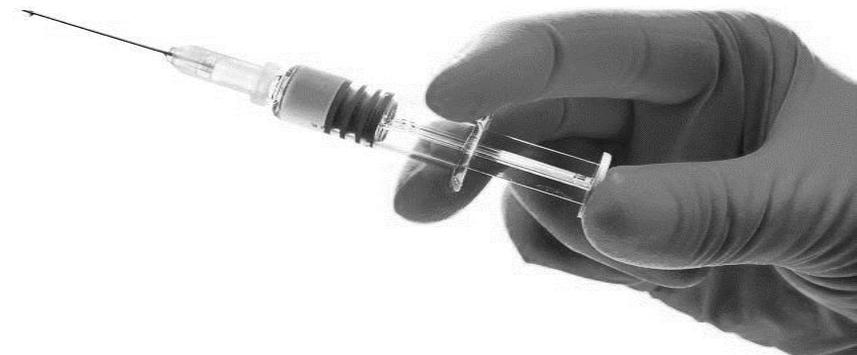
Wound Management

- **Immediate wound care following an exposure**
- **Often a neglected step; reduces the risk (50–70%)**
 - Immediate washing and flushing with water alone or by using soap and water (running water; 10-15 minutes)
 - Disinfection of the wound using povidone iodine
 - AVOID covering the wound with dressings or bandages
 - Suturing of the wound is usually avoided/postponed; if it is necessary ensure that RIG has already been applied locally
 - Antimicrobials and tetanus toxoid can be administered if needed



Rabies Vaccines

- **WHO recommends only embryonated egg/cell culture-based vaccines**
- **Vaccines available in India**
 - **Purified chick embryo cell vaccine (PCECV)**
 - **Purified vero cell vaccine (PVRV)**



Route of Administration

- **Intramuscular (IM)**
- **Intradermal (ID)**
- Administering minute doses (0.1mL) of vaccine into the layers of skin
- Rational and Scientific; Highly Immunogenic, Safe and Efficacious
- Reduction in volume and costs (60-80%)
- Approved by WHO since 1992; Used in many countries



ID vaccination-Limitations/Challenges

- Vaccine wastage-Opened vials to be used within 6 h
- Confusion regarding vaccine type/dose
- Administration in children
- Off Label Use in many countries

Intradermal rabies vaccination is cost-effective!!!

Dog bite is responsible for more than 95% of human rabies cases.

Intramuscular (I/M) rabies vaccination is costly

Intradermal (I/D) rabies vaccination is:

- ✓ A proven cost-effective, safe and reliable technique
- APPROVED Approved and recommended by WHO

Cost	Dose (ml)	Vials	Visits
100	0.5 or 1	4 vials	3-4
20	0.1x2	1 vial	3

Use I/D schedule to improve availability, accessibility and affordability of rabies vaccine!

Rabies Vaccination: Dose/Site

Dose

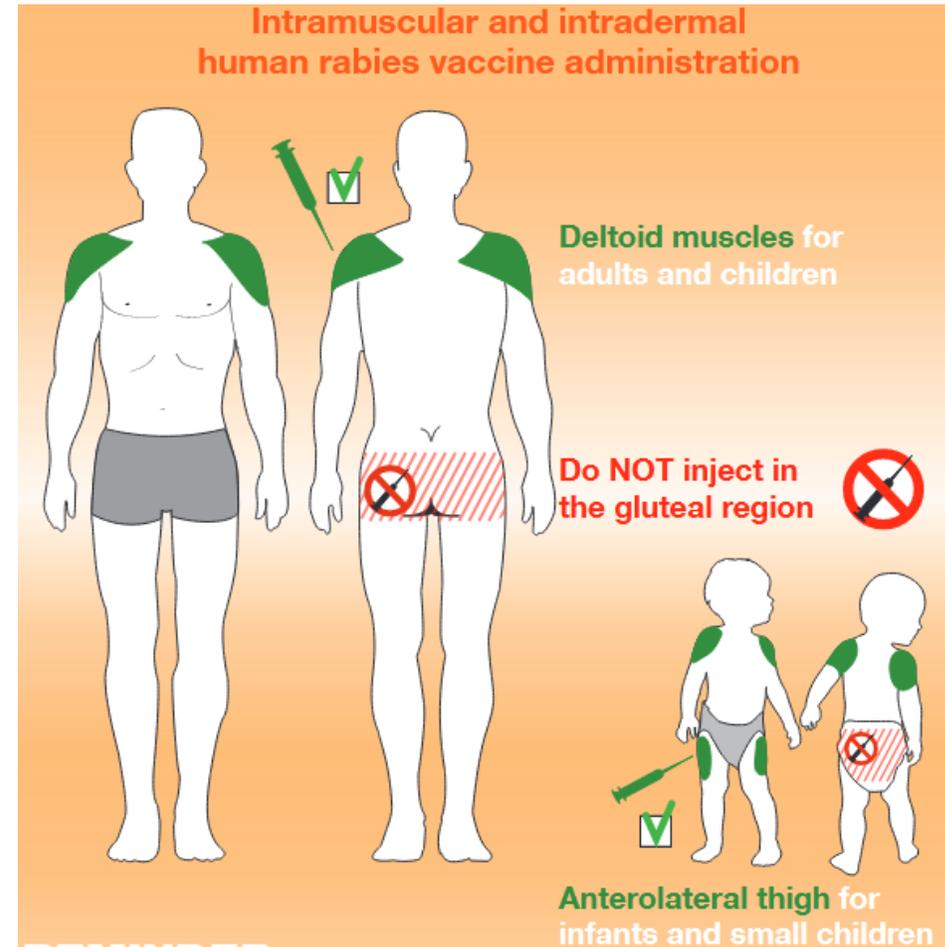
One IM dose-entire vial (0.5 or 1 mL)

One ID dose-0.1 mL

Vaccination Site

IM: Deltoid,
Anterolateral thigh (Children <2 yrs)

ID: Deltoid,
Anterolateral thigh, Suprascapular



Rabies PEP Regimens

	Route	Regimen	Days				
			0	3	7	14	28
Previous WHO Guidelines (2010)	IM	Essen					
Current WHO Guidelines (2018)	IM	Shortened Essen					

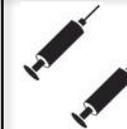
Primary Regimens (Intramuscular)

Rabies PEP Regimens

	Route	Regimen	Days				
			0	3	7	14	21
Previous WHO Guidelines (2010)	IM	Zagreb					
Current WHO Guidelines (2018)	IM	Zagreb					

Primary Regimens (Intramuscular)

Rabies PEP Regimens

	Route	Regimen	Days				
			0	3	7	14	28
Previous WHO Guidelines (2010)	ID	Updated Thai Red Cross					
Current WHO Guidelines (2018)	ID	Institut Pasteur du Cambodge (IPC)					

Primary Regimens (Intradermal)

Rabies PEP Regimens

	Route	Regimen	Days				
			0	3	7	14	28
1	ID	Updated Thai Red Cross	2	2	2	0	2
2	ID	1-month, simplified 4-site	4	0	2	0	1
3	ID	1-week, 4-site	4	4	4	0	0

Alternative Regimens (WHO 2018)

Rabies PEP Regimens

In previously Immunized PrEP/PEP (WHO 2018)

	Route	Regimen	Days				
			0	3	7	14	28
1	IM	1-site	1	1			
2	ID	1-site	1	1			
3	ID	Single-visit 4-site	4				

- Passive Immunization not required

Rabies Vaccination: Facts

- **Day 0** is the day when the **first dose of vaccine** is administered.
- Vaccine dose and regimen is the **same** for any age group
- **No contraindications** for rabies PEP
- Rabies vaccines should **never** be administered in the **gluteal** region.



Rabies Immune Globulin (RIG)

Type of Product	Description	Maximum Dose	Remarks
Equine rabies immunoglobulin (ERIG)	Derived from blood of immunized horses; polyclonal	40 IU/kg body weight	Heterologous serum, risk of anaphylaxis (low)
Human rabies immunoglobulin (HRIG)	Derived from blood of immunized humans; polyclonal	20 IU/kg body weight	Risk of transmission of blood borne pathogens

Rabies Monoclonal Antibodies (Rmabs)

- Homogenous population of antibodies produced by a single clone of plasma B cells

Type of Product	Description	Maximum Dose
Rabishield (2016) (Serum Institute of India)	Single Mab (binding to antigenic site III of rabies G protein)	3.33 IU/kg body weight
TwinRab (2019) (Zydus Vaxxicare)	Cocktail of 2 Mabs (binding to antigenic sites III / I and site II of rabies G protein)	40 IU/kg body weight

Rabies Monoclonal Antibodies (Rmabs)

- Available data suggests Rmabs safe and comparable to RIG
- Will help fill critical health gaps
 - more rapid production capability
 - greater consistency
 - less prone to availability/purity/safety issues
 - concentrated product-small volume required
- No blood-borne pathogen transmission risk
- No skin sensitivity test required

- New products; limited post-usage data available
- WHO encourages use of RmAbs for rabies PEP-recommends maintenance of a registry to monitor the clinical use and outcomes

Passive Immunization

- Necessary in **all category III exposures** (and Cat II exposures in immunocompromised individuals) in addition to vaccines
- RIG administered only ONCE, preferably within 24 h of exposure
- Can be given within 7 days of first vaccine dose
 - The maximum dose of RIG calculated according to body weight
 - The maximal volume of RIG that is anatomically feasible is infiltrated locally into and around all wounds.
 - For large or multiple wounds, dilute with sterile physiological saline to ensure coverage of all wounds.
 - The remainder of the calculated dose can be injected IM, at a site distant from the wound and vaccination site. However, it affords little or no additional benefit.



Passive Immunization

To confer the maximum public health benefit, WHO (2018) recommends:

- The remainder of the calculated dose of RIG does not need to be injected IM
- Can be fractionated in smaller, individual syringes to be used for other patients

Intramuscular RIG recommended

(as close as possible to the presumed exposure site):

- **Where there is a high likelihood of additional small wounds**
- **Exposure was to bats**
- **Mucosal exposure with no wound**
- **Suspected exposure to aerosols/Other non-bite exposures**

Pre-exposure prophylaxis (PrEP)

- Pre-exposure prevention is indicated for those who are at a continual and high-risk of rabies exposure
 - Veterinarians
 - Animal handlers
 - Animal control officers
 - Rabies researchers
 - Travelers to rabies-endemic areas
 - Children in rabies endemic areas

Travelers: Individual risk assessment for PrEP

Country, duration of stay, outdoor activities, location (rural/urban), access to PEP etc

Rabies PrEP Regimens

	Route	Regimen	Days		
			0	7	21/28
Previous WHO Guidelines (2010)	IM	Single site 3-dose regimen			
Current WHO Guidelines (2018)	IM	Single site 2-dose regimen			

Primary Regimens (Intramuscular)

Rabies PrEP Regimens

	Route	Regimen	Days		
			0	7	21/28
Previous WHO Guidelines (2010)	ID	3-visits Single-site			
Current WHO Guidelines (2018)	ID	2- visits 2-sites			

Primary Regimens (Intradermal)

Rabies PrEP Regimens

Alternative* Primary Regimens (WHO 2018)

Route	Regimen	Days		
		0	7	21/28
		0	7	21/28
IM	Single visit 1-site			
ID	Single visit 2-site			

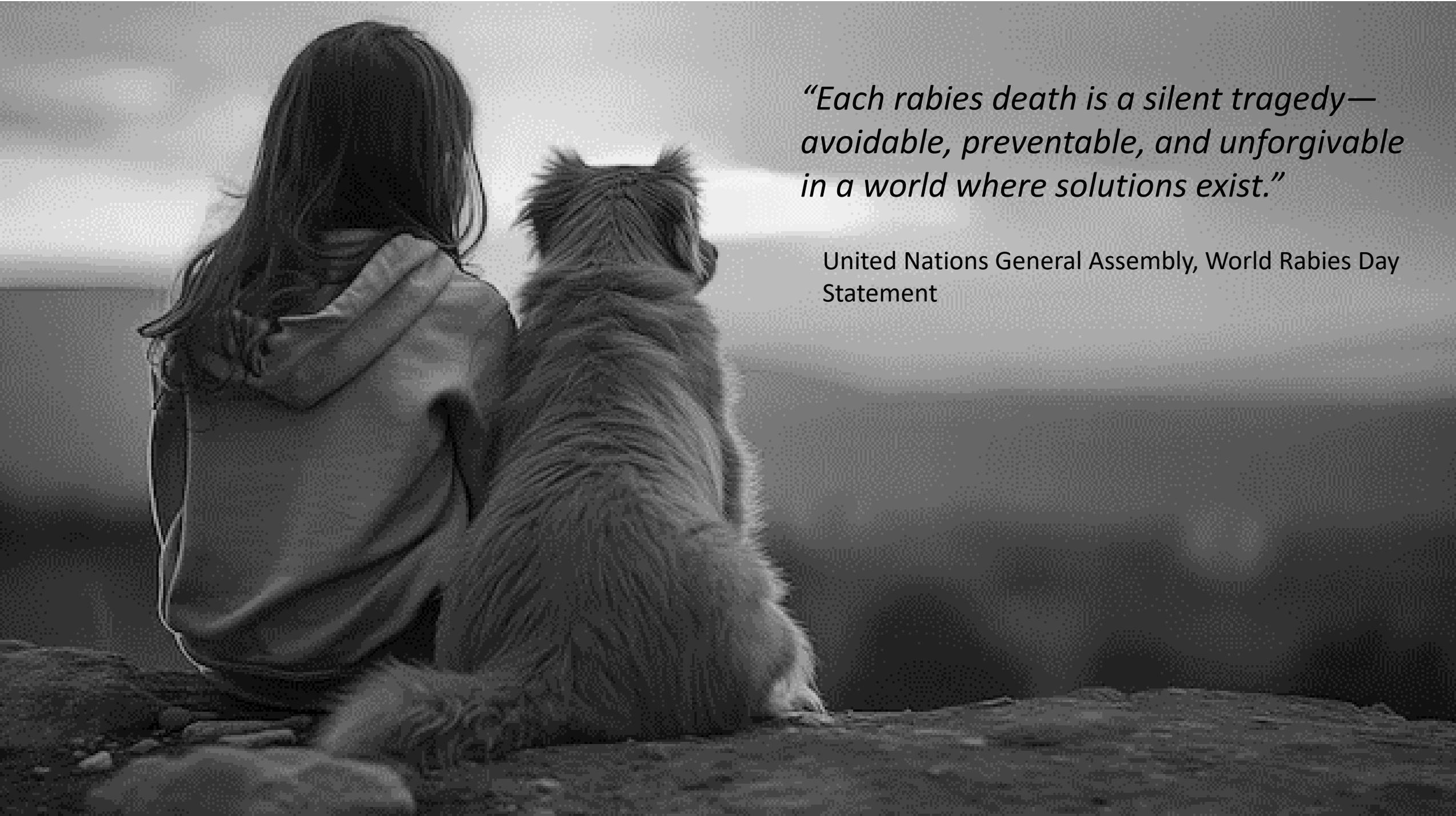
*Incomplete PrEP-In emergency only

Duration of Immunity

- Virus neutralizing antibodies-VNA
- Adequate post-vaccination seroconversion-0.5 IU/mL
- Most healthy individuals achieve this level by day 7-14 of PEP/PrEP
- Sero-monitoring not needed after routine PEP/PrEP
- For professionals at continual and high risk: periodic monitoring of VNA (1-2 yrs); booster (single dose) if titres <0.5 IU/mL
- **Vaccine booster doses are not necessary for people living in or travelling to high-risk areas -who have received a primary series of PrEP or PEP**

PEP Failures?

- **True PEP failures extremely rare**
- **Deviations in PEP protocols**
 - Incorrect advice/regimen
 - Wound care Inadequate/Not done
 - Suturing of wounds without RIG
 - Delay in initiating PEP
 - Inadequate dosage of vaccine
 - Incorrect site of vaccine administration
 - Inappropriate administration of RIG (only IM)
 - Omission of RIG even in category III exposures
- **Counterfeit vaccines/ Cold-chain lapses**



“Each rabies death is a silent tragedy—avoidable, preventable, and unforgivable in a world where solutions exist.”

United Nations General Assembly, World Rabies Day Statement