

# 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
<b>I</b>	Touching or feeding of animals Licks on intact skin	<b>None</b>	<b>None</b> , if reliable case history available
<b>II</b>	Nibbling of uncovered skin Minor scratches/abrasions without bleeding	<b>Minor</b>	<b>Administer vaccine immediately</b>
<b>III</b>	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	<b>Severe</b>	<b>Administer rabies immune globulin and vaccine immediately</b>

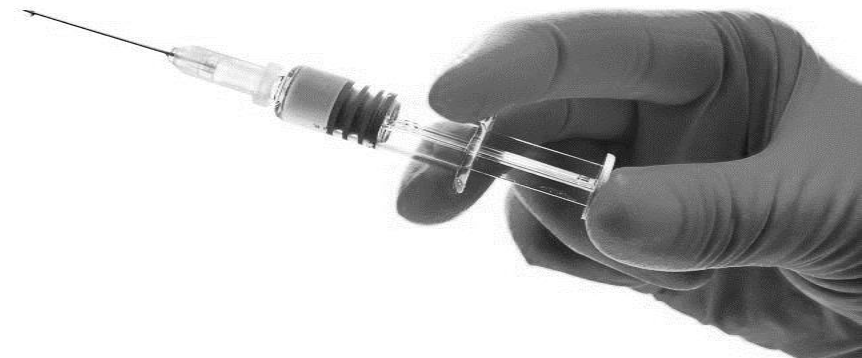
# Wound Management

- **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



# Rabies Vaccination: Dose/Site

## Dose

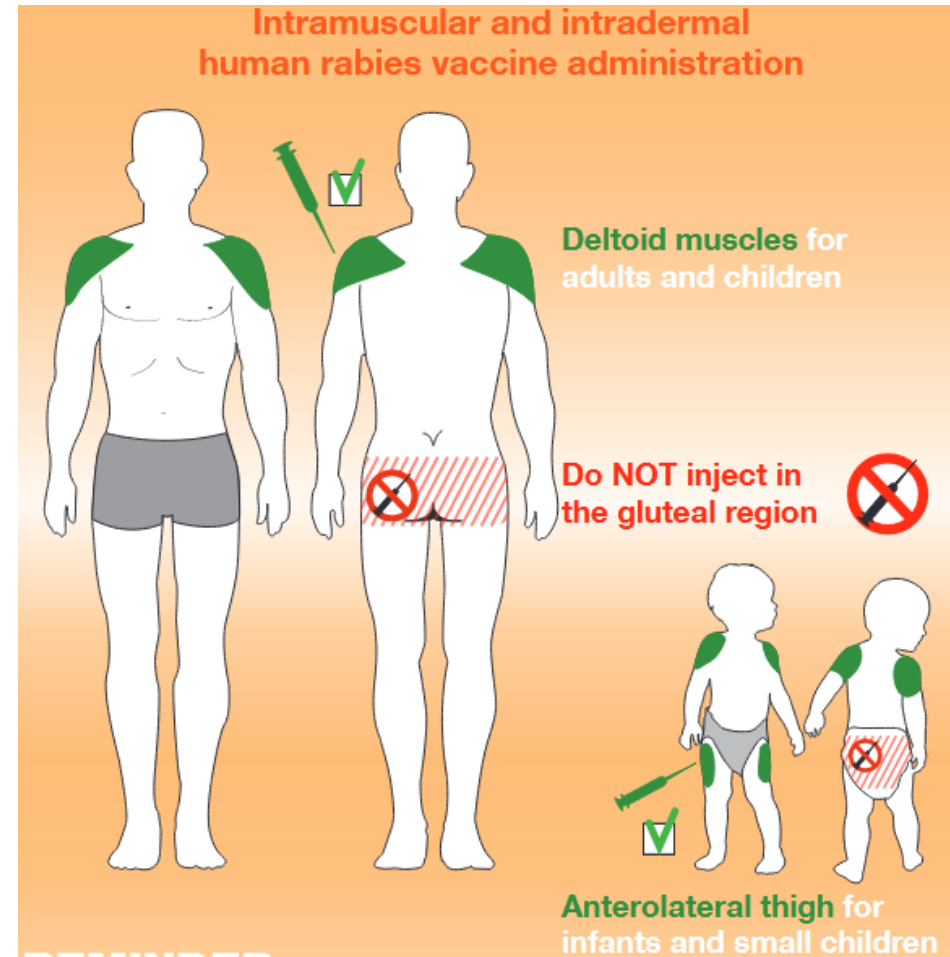
One IM dose-entire  
vial (0.5 or 1 mL)

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
<b>Previous WHO Guidelines (2010)</b>	IM	Zagreb					
<b>Current WHO Guidelines (2018)</b>	<b>IM</b>	<b>Zagreb</b>					

**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
<b>Equine rabies immunoglobulin (ERIG)</b>	Derived from blood of immunized horses; polyclonal	<b>40 IU/kg</b> body weight	Heterologous serum, risk of anaphylaxis (low)
<b>Human rabies immunoglobulin (HRIG)</b>	Derived from blood of immunized humans; polyclonal	<b>20 IU/kg</b> 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
<b>Rabishield (2016)</b> (Serum Institute of India)	<b>Single Mab</b> (binding to antigenic site III of rabies G protein)	3.33 IU/kg body weight
<b>TwinRab (2019)</b> (Zydus Vaxxicare)	<b>Cocktail of 2 Mabs</b> (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
<b>Previous WHO Guidelines (2010)</b>	IM	Single site 3-dose regimen			
<b>Current WHO Guidelines (2018)</b>	<b>IM</b>	<b>Single site 2-dose regimen</b>			

**Primary Regimens (Intramuscular)**



# Rabies PrEP Regimens

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

**Primary Regimens (Intradermal)**

# Rabies PrEP Regimens

## Alternative\* Primary Regimens (WHO 2018)

Route	Regimen	Days		
		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