



# **Current WHO GUIDE for**

## **Rabies Pre and Post-exposure Treatment in Humans**



World Health Organization Department of Communicable Diseases Surveillance and Response

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## **General considerations in rabies post-exposure treatment**

**WHO strongly advocates the use of modern (purified products prepared on cell-culture) vaccines for PET that comply with WHO criteria for potency, innocuity and have been assessed satisfactorily in humans in well-designed field trials;**

**WHO supports the trend to abandon completely the production of brain-tissue vaccines;**

**Participants from 14 Asian countries at the WHO/Mérieux Foundation 4th International Symposium on Rabies Control in Asia, Hanoi Vietnam issued a resolution in March 2001 urging Asian countries that still produce nerve tissue vaccine to discontinue its production by 2006.**



# General considerations in rabies post-exposure treatment

Immediate washing/flushing and disinfection of the wound and rapid administration of purified immunoglobulin and modern vaccine according to the modalities described in these guidelines assure prevention of infection in almost all circumstances

## Rabies post-exposure treatment

- is an emergency and as a general rule should not be delayed or deferred;
- does not have contraindications if modern purified rabies biologicals are used;
- must be applied using vaccine regimens and routes of administration that have been proven to be safe and effective.



# General considerations in rabies post-exposure treatment

## Rabies post-exposure treatment is an emergency!

- wounds should be treated *immediately*. Vaccine and serum therapy (when required for the latter) instituted *as soon as possible*,
- initiation of treatment should *not await* the results of laboratory diagnosis or be delayed by dog observation when rabies is suspected,
- *pregnancy and infancy* are never contraindications to rabies post-exposure treatment,
- persons who present for evaluation and treatment *even months after having been bitten* should be dealt with in the same manner as if the contact occurred recently.



# General considerations in rabies post-exposure treatment

## Deferring treatment: an exception in rabies endemic countries or areas!

- ◆ If the species is unlikely to be infected with rabies, wait for laboratory diagnosis if results can be obtained within 48 hours;
- ◆ If the dog at the origin of exposure is more than a year old and has a vaccination certificate indicating that it has received at least 2 doses of a potent vaccine, the first not earlier than 3 months of age and another within 6 to 12 months later, observe the dog 10 days. If the dog shows any sign of illness during the observation period, the patient should receive full rabies post-exposure treatment urgently.



# Rabies post-exposure treatment modalities

## Wound treatment :

- ◆ should be immediate
- ◆ is essential even if the person presents long after exposure
- ◆ consists of:
  - immediate washing and flushing with soap and water, or water alone,
  - disinfecting with ethanol (700ml/l) or iodine (tincture or aqueous solution).



# Rabies post-exposure treatment modalities

Definition of categories of exposure and use of rabies biologicals:

## Category III:

Single or multiple transdermal bites, scratches or contamination of mucous membrane with saliva (i.e. licks)

→ *use immunoglobulin plus vaccine*

## Category II:

Minor scratches or abrasions without bleeding or licks on broken skin and nibbling of uncovered skin

→ *use vaccine alone*

## Category I:

Touching, feeding of animals or licks on intact skin

→ *no exposure therefore no treatment if history reliable*



# Rabies post-exposure treatment modalities

## Administration of rabies immunoglobulin (RIG)

- ◆ **Infiltrate into the depth of the wound and around the wound**
  - .as much as anatomically feasible of the RIG should be infiltrated around the wound
  - .any remainder should be injected at an intramuscular site distant from that of vaccine inoculation e.g. into the anterior thigh
- ◆ **Quantities/volume of RIG: 20IU/ kg for Human RIG or 40 IU/ kg of Equine RIG**
  - .the total recommended dose should not be exceeded
  - .if the calculated dose is insufficient to infiltrate all wounds, sterile saline may be used to dilute it 2 to 3 fold to permit thorough infiltration



# Rabies post-exposure treatment modalities

## Non-specific care

- ◆ Postpone suturing if possible; if suturing is necessary ensure that RIG has been applied locally;
- ◆ Apply antimicrobials and tetanus toxoid if necessary



# Rabies post-exposure treatment intramuscular regimens

## Two intramuscular schedules for modern vaccines:

- ◆ Vaccines should not be injected into the gluteal region;
- ◆ Classical 5 dose intramuscular regime (“Essen” regimen): one dose of the vaccine should be administered on days 0, 3, 7, 14 and 28 in deltoid region or, in small children, into the antero-lateral area of the thigh muscle;
- ◆ As an alternative, the 2-1-1 regimen may be used. Two doses are given on day 0 in the deltoid muscle, right and left arm. In addition one dose in the deltoid muscle on day 7 and one on day 21.



## General considerations on intradermal rabies post-exposure treatment

- ◆ As these regimens require considerably less vaccine than the intramuscular regimens the method is particularly appropriate where vaccine or money is in short supply;



Intradermal injections reduce the volume of vaccine required and vaccine cost by 60% to 80%



# General considerations on intradermal rabies post-exposure treatment

- ◆ The decision to implement economical intradermal post-exposure treatment rests with government agencies that define rabies prevention and treatment policies in their own countries.
- ◆ When the intradermal route is used, precautions include staff training, conditions and duration of vaccine storage after reconstitution, use of appropriate 1 mL syringe and short hypodermic needles.



# General considerations on intradermal vaccination against rabies

Three vaccines have proven to be efficacious

- ◆ Human diploid cell vaccine (HDCV) Rabivac™
- ◆ Purified vero cell vaccine (PVRV) Verorab™, Imovax™ , Rabies vero™, TRC Verorab™
- ◆ Purified chick embryo cell vaccine (PCECV) Rabipur™



# General considerations on intradermal vaccination against rabies

## Recommended intradermal regimens and vaccines for use by the intradermal route

- ❖ 8-site intradermal method (8-0-4-0-1-1) for use with HDC (Rabivac™) and PCECV (Rabipur™)
  - ❖ *The 8 sites regimen should be particularly considered in emergency situations when no RIG is available;*
- ❖ 2-site intradermal method (2-2-2-0-1-1) for use with PVRV (Verorab™, Imovax™, Rabies vero™, TRC Verorab™) and PCECV (Rabipur™).



# Intradermal PET regimens for modern rabies vaccines

8-site intradermal method ('8-0-4-0-1-1')

for use with

- ◆ human diploid cell vaccine (HDCV) (Rabivac™) and
  - ◆ purified chick embryo cell vaccine (PCECV) (Rabipur™)
- both vaccines at 0,1 mL per intradermal site



# Intradermal PET regimens for modern rabies vaccines

2-site intradermal method ('2-2-2-0-1-1')

The volume per intradermal site is:

- ◆ 0,1 mL for PVRV (Verorab™, Imovax™ , Rabies vero™, TRC Verorab™ )
- ◆ 0,2 mL for PCECV (Rabipur™) or *as an option*
- ◆ 0,1 mL for PCECV (Rabipur™) may be considered for use by national health authorities. This does not apply to any other vaccine brand.



# Intradermal route and rabies vaccine potency requirements

- ◆ The antigenic potency of all the WHO approved vaccines has proven similar and is well above the minimum value of 2.5 IU/ampoule;
- ◆ WHO minimum potency requirement for human rabies vaccines for intradermal use should not be increased beyond 2,5 IU (per single intramuscular dose) by national authorities unless the need for a change is substantiated by clinical or field studies ;



# **Intradermal route and rabies vaccine potency requirements**

- ◆ **To be approved for id use, any new candidate vaccine should be proven potent by the NIH test and its immunogenicity and safety should be demonstrated with the volume intended for humans;**
- ◆ **Any country willing to adopt an id regimen of proven efficacy with the recommended vaccines need not repeat immunogenicity studies in their own population.**



## Vaccine vial insert for intradermal application of rabies vaccines

For vaccines recommended by WHO to be used intradermally, the vaccine insert should contain a statement saying:

*“This vaccine is of sufficient potency to allow its safe use in one of the WHO recommended intradermal post-exposure regimens in countries where relevant national authorities have approved the intradermal route for rabies PET”.*



# Rabies PET in immunosuppressed individuals

- ◆ The importance of wound treatment should be further stressed;
- ◆ RIG should be administered deeply into the wound for all exposures;
- ◆ Vaccine should always be administered and no modification of the recommended number of doses is advisable;
- ◆ An infectious disease specialist with expert knowledge of rabies prevention should be consulted.



## **Interchangeability of modern rabies vaccine types and routes for PET**

- Interchangeability of modern rabies vaccine is not recommended;
- When completion of PET with the same modern rabies vaccine is not possible, the switch can be done provided that it is one of the WHO recommended cell culture vaccine;
- No study has been done yet on vaccine immunogenicity and change of the route of vaccine administration (e.g. from intramuscular to intradermal) during PET. This practice should be the exception.



# Rabies post-exposure treatment of previously vaccinated persons

- ◆ Local treatment of wound
- ◆ Vaccination schedule (with vaccines fulfilling WHO requirements)
  - one dose on days 0 and 3. The dose is either 1 standard intra muscular dose (which may be 1 ml or 0.5 ml depending on vaccine type ) or one intradermal dose of 0.1 ml per site
  - no RIG should be applied
  - *However full treatment should be given to persons :*
  - who received pre-or post-exposure treatment with vaccines of unproven potency or
  - who have not demonstrated an acceptable rabies neutralizing antibody titer.



# Pre-exposure rabies vaccination

- ◆ Groups of persons at high risk of exposure to live rabies virus (laboratory staff, veterinarians, animal handlers and wildlife officers)
- ◆ Toddlers and children in highly endemic areas may be considered
- ◆ Regimen (with vaccines fulfilling WHO requirements)
  - three doses of vaccine on days 0, 7 and 28
  - A dose is either 1 standard *intramuscular* dose (0.5 or 1 mL) or 0.1mL *intradermally* (if antimalarial chemoprophylaxis is applied concurrently, *intramuscular* injections are preferable to *intradermal*)
  - Alternative regimens are being tested for preventive vaccination of toddlers and children in highly endemic areas
- ◆ Site of injection (never use gluteal area for vaccine application)
  - adults: deltoid area of the arm;
  - children: anterolateral area of the thigh acceptable



# Pre-exposure rabies vaccination

## Monitoring

- ◆ Persons working with live rabies virus in
  - ❖ diagnostic laboratories
  - ❖ research laboratories
  - ❖ vaccine production laboratories
  - ➔ one serum sample every six months
  - ➔ booster when the titre falls below 0.5 IU/ml
- ◆ Others professions (veterinarians, animal handlers, wildlife officers...) at permanent risk of exposure to rabies
  - ◆ testing every year
  - ➔ booster when the titre falls below 0.5 IU/ml

