



WHO GUIDE for

Rabies Pre and Post-exposure Prophylaxis in Humans (revised 15 June 2010)



General considerations in rabies Post-Exposure Prophylaxis (PEP)



WHO strongly advocates the use of purified rabies vaccines prepared on cell culture or embryonated eggs for PEP 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 and use of brain-tissue including suckling mouse brain vaccines.

General considerations in rabies PEP

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

Rabies PEP

- is an emergency and as a general rule should not be delayed or deferred;
- does not have contraindications if purified rabies immunoglobulin and vaccine 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 PEP

- wounds should be washed/flushed and disinfected *immediately*. Vaccine and immunoglobulin therapy (when required for the latter) instituted *as soon as possible*,
- If rabies immunoglobulin is not available on first visit its use can be delayed by a maximum of 7 days from date of first vaccine injection,
- initiation of PEP 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 PEP,
- persons who present for evaluation and rabies post-exposure prophylaxis *even months after having been bitten* should be dealt with in the same manner as if the contact occurred recently.



General considerations in PEP

Discontinuing or deferring PEP: an exception in rabies endemic countries or areas!

- ◆ Post-exposure prophylaxis may be discontinued if the animal involved is a dog or cat that remains healthy for an observation period of 10 days after the exposure occurred; or if the animal is humanely killed and proven to be negative for rabies by a reliable diagnostic laboratory using a prescribed test.
- ◆ If the animal inflicting the wound is suspected of being rabid and is not apprehended, post-exposure prophylaxis should be instituted immediately.
- ◆ In areas where canine or wildlife rabies is enzootic, adequate laboratory surveillance is in place, and data from laboratory and field experience indicate that there is no infection in the species involved, local health authorities may not recommend anti-rabies prophylaxis.

Rabies post-exposure Prophylaxis modalities World Health Organization

Wound treatment :

- ◆ should be immediate
- ◆ is essential *even* if the person presents long after exposure
- ◆ consists of:
 - immediate washing and flushing for 15 minutes with soap and water, or water alone,
 - disinfection with ethanol (700ml/l) or iodine (tincture or aqueous solution).

Rabies PEP modalities



Definition of categories of exposure and use of rabies biologicals:

Category III: -single or multiple transdermal bites or scratches, licks on broken skin, contamination of mucous membrane with saliva (i.e. licks) and suspect contacts with bats:

use immunoglobulin plus vaccine

Category II: -minor scratches or abrasions without bleeding or and nibbling of uncovered skin

use vaccine alone

Category I : -touching, feeding of animals or licks on intact skin

no exposure therefore no prophylaxis if history reliable

Rabies PEP modalities



Administration of rabies immunoglobulin (RIG)

wounds infiltration with RIG is of upmost importance in category 3 exposure management

- ◆ 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
 - .remainder if any 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 (HRIG) or 40 IU/ kg of Equine RIG (ERIG)
 - .the total recommended dose should not be exceeded
 - .If RIG is unavailable on first visit and vaccine injection its administration can be delayed by a maximum of 7 days from date of that first injection
 - .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

- There are no scientific grounds for performing a skin sensitivity test prior to administration of ERIG. The treating physician should be prepared to manage anaphylaxis which, however rare, could occur at any stage of the ERIG administration.

Rabies PEP 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

Intramuscular regimens for rabies PEP

Two intramuscular schedules for category 2 and 3 exposures:

- ◆ The 5 dose intramuscular regime: 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;
- ◆ The 2-1-1 regimen may also 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.
- ◆ Vaccines should not be injected into the gluteal region;

Intradermal regimen for rabies PEP

- ◆ As a PEP regimen provided by the intradermal route 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 PEP

- ◆ The decision to implement economical intradermal post-exposure prophylaxis rests with government agencies that define rabies prevention and prophylaxis policies in their own countries.
- ◆ Where the ID route has been endorsed by National Health Authorities and 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.



One intradermal PEP regimen for category 2 and 3 exposures

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

- ◆ **The volume per intradermal site is 0,1 mL for both PVRV (Verorab™) and PCECV (Rabipur™)**
- ◆ **one dose of vaccine, in a volume of 0.1 ml is given intradermally at two different lymphatic drainage sites, usually the left and right upper arm, on days 0, 3, 7 and 28. Vaccine administered intradermally must raise a visible and palpable “bleb” in the skin. In the event that a dose of vaccine is inadvertently given subcutaneously or intramuscularly, a new dose should administered intradermally.**



Intradermal route and rabies vaccine potency requirements

- ◆ The antigenic potency of all the vaccines which can be safely used by the intradermal route 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: new rabies vaccine requirements and adoption of existing regimens

- ◆ To be approved for intradermal use, any new candidate vaccine should be proven potent by the NIH test (at least 2.5 IU per intramuscular dose) and its efficacy and/or immunogenicity and safety should be demonstrated with the volume of 0.1 ml per intradermal site using a recommended PEP regimen.
- ◆ 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 use of rabies vaccines for PEP

In countries where relevant national authorities have approved the intradermal route for rabies PEP and for vaccines recommended for intradermal use manufacturers are requested to add in the vaccine insert a statement saying:

" This vaccine is of sufficient potency to allow its safe use in one of the WHO recommended intradermal post-exposure regimens "

Rabies PEP in immunosuppressed individuals

- ◆ The importance of wound treatment should be further stressed;
- ◆ RIG should be administered deeply into the wound for both category 2 and 3 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 PEP

- When completion of PEP 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 or embryonated egg 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 PEP. This practice should be the exception.



Rabies PEP of previously vaccinated persons

- ◆ Local treatment of wound
- ◆ no RIG should be applied
- ◆ Two PEP schedules (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
 - ↓ or as an alternative a 4-site (one visit only) intradermal PEP consisting of 4 injections of 0.1 mL distributed on each arm and thigh or suprascapular region on days 0.
 - ↓ Decision to use one or the other is left with the health care provider in consultation with the patient.

 - ↓ *However full PEP should be given to persons :*
 - ↓ who received pre-or post-exposure prophylaxis with vaccines of unproven potency or
 - ↓ in patients in whom immunological memory is not longer assured as a result of HIV/AIDS or other immunosuppressive causes

Pre-exposure rabies vaccination



- ◆ Groups of persons at high risk of exposure to live rabies virus (laboratory staff, veterinarians, animal handlers and wildlife officers)
- ◆ Children in highly endemic areas may be considered if vaccine quantities for PEP are adequate

- ◆ 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
 - ↓ Site of injection: deltoid area of the arm for adults; anterolateral area of the thigh acceptable for children

 - ↓ If antimalarial chemoprophylaxis is applied concurrently, intramuscular injections are preferable to intradermal

Booster vaccination and monitoring of previously immunized persons

- ❖ Persons working with live rabies virus in diagnostic laboratories, research laboratories, vaccine production laboratories and others professions (veterinarians, animal handlers, wildlife officers...) at permanent risk of exposure to rabies should have:
 - ❖ one serum sample taken every six months
 - ❖ a booster dose when the titre falls below 0.5 IU/ml

- ❖ Routine booster vaccine doses after primary rabies vaccination are not required for the general public living in areas of risk.