General considerations

- WHO strongly advocates the production and use of modern (inactivated, purified cell culture and duck embryo vaccines containing at least 2.5 IU/dose) in both developed and developing countries.
- WHO supports the trend to limit or abandon completely the production of brain-tissue vaccines where economically and technically feasible.
- If modern vaccines are not available, brain tissue vaccines preferably those prepared on suckling-mouse brain (SMB), may be administered. SMB should have a potency of at least 1.3 IU/dose regardless of the number of doses required for a full PET.

*Immediate wound treatment and combined immunoglobulin and modern vaccine treatment virtually assure prevention of infection.*
Post-exposure treatment

- Categories of exposure and recommended treatments
  - wound treatment plus rabies immunoglobulin plus vaccine for all severe (category III) exposures:
    - single or multiple transdermal bites or scratches
    - contamination of mucous membrane with saliva (i.e. licks)
  - vaccine and disinfection for minor (category II) exposure:
    - nibbling of uncovered skin
    - minor scratches or abrasions without bleeding
    - licks on broken skin
  - no treatment in the absence of (category I) exposure, if history reliable:
    - touching or feeding of animals
    - licks on intact skin
Post-exposure treatment

General considerations

• *pregnancy and infancy* are never contraindications to post-exposure rabies vaccination

• 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

• wound should be treated *immediately* and serum and vaccine therapy instituted *as soon as possible* after any exposure

• initiation of treatment should *never await* the results of laboratory diagnosis
Post-exposure treatment

Deferring treatment

- If the species is unlikely to be infected with rabies, treatment may be deferred pending the outcome of laboratory diagnosis provided that the diagnosis can be made 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, the bitten patient may not need treatment and the dog should be observed for 10 days. If the dog shows any sign of illness during the observation period, the patient should receive urgent full post-exposure treatment.
Post-exposure treatment

Wound treatment

• Immediate
• Essential even if the person presents after a prolonged period (chemical or physical elimination of rabies virus at the site of infection is the most effective mechanism of protection)
• Immediate washing and flushing with soap and water, detergent or water alone is imperative
• Then: ethanol (700mL/l) or iodine (tincture or aqueous solution)
Post-exposure treatment

Administration of rabies immunoglobulin (RIG)

- careful installation in the depth of the wound and infiltration around the wound
- as much as anatomically feasible of the RIG must be infiltrated around the wound even if the lesion has begun to heal
- any remainder should be injected im at a site distant from that of vaccine inoculation e.g. into the anterior thigh (if necessary divided between the two thighs), not in the gluteal region as it may not go into muscle
- postpone suturing if possible; if suturing is necessary ensure that RIG has been applied locally as described above
- apply antimicrobials and tetanus toxoid if necessary
Post-exposure treatment

Administration of rabies immunoglobulin (RIG) cont’d

- dose: 20 IU/kg body weight of human rabies immunoglobulin (HRIG) or 40 IU/kg body weight of equine rabies immunoglobulin (ERIG)
- 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
- ERIG: skin test must be performed prior to administration. However a negative skin test must never reassure the physician that no anaphylactic reaction will occur. Adrenaline/epinephrine should always be ready to treat early anaphylactic reactions.
Post-exposure treatment

Intramuscular schedules for modern vaccines:
(tissue-culture vaccines and duck embryo vaccine)

• Essen regime: one dose of the vaccine should be administered on days 0, 3, 7, 14 and 28. All intramuscular (im) injections must be given into the deltoid region or, in small children, into the anterolateral area of the thigh muscle. Vaccine should never be injected into the gluteal region.

• As an alternative, the 2-1-1 regimen may be used. Two doses are given on day 0. One dose is given in the deltoid region of the right arm and a second dose at the same site in the left arm. In addition one dose is given in the deltoid region on day 7 and one on day 21.
Post-exposure treatment

General considerations on intradermal immunization against rabies:

- These regimens require considerably less vaccine than the im regimens and can produce a comparable degree of protection against rabies. The method is particularly appropriate where vaccine or money is in short supply and in centres dealing with numbers of patients where there is an established cold chain.

- A number of precautions should be adhered to when the id route is used, including staff training, conditions and duration of vaccine storage after reconstitution, use of appropriate 1 ml syringe and short hypodermic needles.

- The decision to implement economical id post-exposure treatment rests with government agencies which select policies on rabies prophylaxis in their own countries.
Post-exposure treatment

General considerations on intradermal immunization against rabies:

- Vaccines proven to be efficacious as at today
  - Human diploid cell vaccine (HDCV)
  - Purified vero cell vaccine (PVRV)
  - Purified chick embryo vaccine (PCEC)
  - Purified duck embryo vaccine (PDEV)

- Intradermal regimes demonstrated to be immunogenic
  - 8-site intradermal method (8-0-4-0-1-1) for use with HDC and PCEC
    The 8 sites regimen should be considered when no RIG are available
  - 2-site intradermal method (2-22-0-1-1) for use with PVRV, PCEC, and PDEV
Post-exposure treatment

Intradermal schedules for modern vaccines:

• a) 2-site intradermal method ("2-2-2-0-1-1")

  For use with purified vero cell vaccine (PVRV), purified primary chick embryo cell (PCEC) and purified duck embryo vaccine (PDEV).

  • The volume of the id dose is one fifth of the im dose per site. It varies according to that of the im dose: i.e. if im dose is 0.5 ml, id dose = 0.1 ml/site, if im dose is 1.0 ml, id dose = 0.2* ml/site (*If not technically possible, divide between two sites close together.)

• Regimen:
  • Days 0, 3 and 7: 1 id dose (0.1 ml or 0.2 ml according to vaccine type) of vaccine is given at each of 2 sites, intradermally on upper arm, over each deltoid
  • Days 28 and 90: 1 id dose (0.1 ml or 0.2 ml according to vaccine type) of vaccine is given at one site, on upper arm
Post-exposure treatment

Intradermal schedules for modern vaccines:

- b) 8-site intradermal method ('8-0-4-0-1-1')
  
  For use with human diploid cell vaccine (HDCV) and purified chick embryo cell vaccine (PCEC) where the im dose is 1 ml after reconstitution.

- Regimen:
  
  - Day 0: 0.1 ml of reconstituted vaccine is given at each of 8 sites using the contents of a whole vial. Inject intradermally over deltoid, lateral thigh, suprascapular region and lower quadrant of the abdomen
  - Day 7: 0.1 ml of vaccine is given at each of 4 sites over deltoids and thighs
  - Days 28 and 90: 0.1 ml of vaccine is given at one site, over deltoid
Post-exposure treatment of previously vaccinated persons

Local treatment of wound

- **Vaccination schedule**
  - one dose on days 0 and 3. The dose is either 1 standard im dose (which may be 1 ml or 0.5 ml depending on vaccine type) or one intradermal dose of 0.1 ml for all vaccine types.
  - no RIG must be applied

However full treatment should be given to:

- persons who received pre-or post-exposure treatment with vaccines of unproven potency
- those which have not demonstrated an acceptable rabies neutralizing antibody titer
Pre-exposure immunization

- Groups of persons at high risk of exposure
  - laboratory staff working with rabies vaccines
  - veterinarians
  - animal handlers
  - wildlife officers

- Regime
  - three doses of modern vaccine on days 0, 7 and 28
  - the dose is either: 1 standard *im* dose (0.5 or 1 ml) or 0.1 ml *id*

- Site of injection
  - adults: deltoid area of the arm; children: anterolateral area of the thigh acceptable,
  - never use gluteal area for vaccine application

- Contraindications
  - if antimalarial chemoprophylaxis is applied concurrently, *im* injections are preferable to *id*
Pre-exposure immunization

• Monitoring
  • persons working in
    • diagnostic laboratories
    • research laboratories
    • vaccine production laboratories
  • one blood sample every six months
  • booster when the titre falls below 0.5 IU/ml

• others
  • testing every year
  • booster when the titre falls below 0.5 IU/ml